MODULATORS OF DIACYGLYCEROL ACYLTRANSFERASE 2 (DGAT2)

Sequence Listing

The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled BIOL0178WOSEQ_ST25.txt created June 8, 2016, which is 1 mb in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

Field

The present embodiments provide methods, compounds, and compositions for treating, preventing, or ameliorating a disease associated with nonalcoholic fatty liver disease, including non-alcoholic steatohepatitis (NASH) and hepatic steatosis, by administering a diacylglycerol acyltransferase 2 (DGAT2) specific inhibitor to an individual.

Background

Nonalcoholic fatty liver diseases (NAFLDs) including NASH (nonalcoholic steatohepatitis) are considered to be hepatic manifestations of the metabolic syndrome (Marchesini G, et al. Hepatology 2003; 37: 917-923) and are characterized by the accumulation of triglycerides in the liver of patients without a history of excessive alcohol consumption. The majority of patients with NAFLD are obese or morbidly obese and have accompanying insulin resistance (Byrne CD and Targher G. J Hepatol 2015 Apr; 62(1S): S47-S64). The incidence of NAFLD/NASH has been rapidly increasing worldwide consistent with the increased prevalence of obesity, and is currently the most common chronic liver disease. Recently, the incidence of NAFLD and NASH was reported to be 46% and 12%, respectively, in a largely middle-aged population (Williams CD, et al. Gastroenterology 2011; 140: 124-131).

NAFLD is classified into simple steatosis, in which only hepatic steatosis is observed, and NASH, in which intralobular inflammation and ballooning degeneration of hepatocytes is observed along with hepatic steatosis. The proportion of patients with NAFLD who have NASH is still not clear but might range from 20-40%. NASH is a progressive disease and may lead to liver cirrhosis and hepatocellular carcinoma (Farrell GC and Larter CZ. Hepatology 2006; 43: S99-S112; Cohen JC, et al. Science 2011; 332: 1519-1523). Twenty percent of NASH patients are reported to develop cirrhosis, and 30-40% of patients with NASH cirrhosis experience liver-related death (McCullough AJ. J Clin Gastroenterol 2006; 40 Suppl 1: S17-S29). Recently, NASH has become the third most common indication for liver transplantation in the United States (Charlton MR, et al. Gastroenterology 2011; 141: 1249-1253).

Currently, the principal treatment for NAFLD/NASH is lifestyle modification by diet and exercise. However, pharmacological therapy is indispensable because obese patients with NAFLD often have difficulty maintaining improved lifestyles.

Lipodystrophy syndromes are a group of rare metabolic diseases characterized by selective loss of adipose tissue that leads to ectopic fat deposition in liver and muscle and the development of insulin resistance, diabetes, dyslipidemia and fatty liver disease (Shulman GI. N Engl J Med 2014; 371: 1131-1141; Garg A. J Clin Endocrinol Metab 2011; 96: 3313-3325; Chan JL and Oral EA. Endocr Pract 2010; 16: 310-323; Garg A. N Engl J Med 2004; 350: 1220-1234). These syndromes constitute a significant medical unmet need as these patients are refractory to current therapies, mainly used to treat diabetes and elevated TG levels, in an attempt to reduce the risk of serious associated complications (coronary artery disease, diabetic nephropathy, cirrhosis and pancreatitis).

Partial Lipodystrophy has a higher prevalence (estimated ~2-3 in one (1) million) than generalized lipodystrophy, but the extent of the prevalence is unknown because these patients are greatly under-diagnosed (Chan JL and Oral EA. Endocr Pract 2010; 16: 310-323; Garg A. J Clin Endocrinol Metab 2011; 96: 3313-3325). Partial lipodystrophy is further divided into acquired partial lipdystrophy (APL) or Familial partial lipodystrophy (FPL). The diagnosis of PL is mainly clinical and needs to be considered in patients presenting with the triad of insulin resistance (with or without overt diabetes), significant dyslipidemia in the form of hypertriglyceridemia, and fatty liver (Huang-Doran I, et al. J Endocrinol 2010; 207: 245-255). Patients often present with diabetes and severe insulin resistance requiring high doses of insulin.

Current treatment includes lifestyle modification such as reducing caloric intake and increasing energy expenditure via exercise. Conventional therapies used to treat severe insulin resistance (metformin, thiazolidinediones, GLP-1s, insulin), and/or high TGs (dietary fat restriction, fibrates, fish oils) are not very efficacious in these patients (Chan JL and Oral EA. Endocr Pract 2010; 16: 310-323; Garg A. J Clin Endocrinol Metab 2011). Partial Lipodystrophy is an ultra-orphan indication for which there is a significant unmet medical need. Diabetes, NASH, and/or hypertriglyceridemia associated with this condition can lead to serious complications (Handelsman Y, et al. Endocr Pract 2013; 19: 107-116).

Diacylglycerol *O*-acyltransferase (DGAT) catalyzes the final step in triglyceride (TG) synthesis by facilitating the linkage of *sn*-1,2-diacylglycerol (DAG) with an acyl-CoA. There are two isoforms of DGATs (DGAT1 and DGAT2), and studies indicate that both DGAT1 and DGAT2 play important roles in TG synthesis. DGAT1 is most highly expressed in small intestine and white adipose tissue (WAT), whereas DGAT2 is primarily expressed in liver and WAT (Cases S, et al. Proc Natl Acad Sci USA 1998; 95, 13018-13023; Cases S, et al. J Biol Chem 2001; 276, 38870–38876). Although both DGAT1 and DGAT2 catalyze the same reactions in TG synthesis with DAG or monoacylglycerol (MAG) and acyl-CoA as substrates, they are functionally distinguished not only by their tissue expression, but by their differences in catalytic properties (Cao J, et al. J Lipid Res 2007; 48: 583–591; Cheng D, et al. J Biol Chem 2008; 283:

29802–29811), subcellular localization (Stone SJ, et al. J Biol Chem 2004; 279: 11767-11776), and physiological regulation (Meegalla RL, et al. Biochem Biophys Res Commun 2002, 298, 317–323). For example, suppression of DGAT2, but not of DGAT1, by antisense oligonucleotide treatment improved hepatic steatosis and blood lipid levels independent of adiposity in rodent models of obesity and the data indicated that these effects were related to decreased hepatic lipid synthesis (Yu XX, et al. Hepatology 2005; 42: 362–371).

These studies demonstrate that DGAT2 inhibition may improve NAFLD/NASH, as well as the metabolic profile of patients with lipodystrophy syndromes by reducing triglycerides, improving insulin sensitivity, and decreasing hepatic steatosis.

Summary

The present embodiments provided herein are directed to potent and/or tolerable compounds and compositions useful for treating, preventing, ameliorating, or slowing progression of NAFLD, such as NASH, as well as lipodystrophy syndromes, such as partial lipodystrophy.

Several embodiments provided herein are directed to several antisense compounds that are more potent and efficacious than antisense oligonucleotides from an earlier published application, WO 2005/019418. Several embodiments provided herein are directed to compounds and compositions that are potent and tolerable.

Detailed Description

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

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

It is understood that the sequence set forth in each SEQ ID NO in the examples contained herein is

independent of any modification to a sugar moiety, an internucleoside linkage, or a nucleobase. As such, antisense compounds defined by a SEQ ID NO may comprise, independently, one or more modifications to a sugar moiety, an internucleoside linkage, or a nucleobase. Antisense compounds described by ISIS number (ISIS #) indicate a combination of nucleobase sequence, chemical modification, and motif.

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

"2'-deoxynucleoside" means a nucleoside comprising 2'-H(H) furanosyl sugar moiety, as found in naturally occurring deoxyribonucleic acids (DNA). In certain embodiments, a 2'-deoxynucleoside may comprise a modified nucleobase or may comprise an RNA nucleobase (*e.g.*, uracil).

"2'-O-methoxyethyl" (also 2'-MOE and 2'-O$(CH_2)_2$-OCH_3) refers to an O-methoxy-ethyl modification at the 2' position of a sugar ring, e.g. a furanose ring. A 2'-O-methoxyethyl modified sugar is a modified sugar.

"2'-MOE nucleoside" (also 2'-O-methoxyethyl nucleoside) means a nucleoside comprising a 2'-MOE modified sugar moiety.

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

"3' target site" refers to the nucleotide of a target nucleic acid which is complementary to the 3'-most nucleotide of a particular antisense compound.

"5' target site" refers to the nucleotide of a target nucleic acid which is complementary to the 5'-most nucleotide of a particular antisense compound.

"5-methylcytosine" means a cytosine modified with a methyl group attached to the 5 position. A 5-methylcytosine is a modified nucleobase.

"About" means within ±10% of a value. For example, if it is stated, "the compounds affected at least about 70% inhibition of DGAT2", it is implied that DGAT2 levels are inhibited within a range of 60% and 80%.

"Administration" or "administering" refers to routes of introducing a compound or composition provided herein to an individual to perform its intended function. An example of a route of administration that can be used includes, but is not limited to parenteral administration, such as subcutaneous, intravenous, or intramuscular injection or infusion.

"Administered concomitantly" or " co-administration" means administration of two or more compounds in any manner in which the pharmacological effects of both are manifest in the patient.

Concomitant administration does not require that both agents be administered in a single pharmaceutical composition, in the same dosage form, by the same route of administration, or at the same time. The effects of both agents need not manifest themselves at the same time. The effects need only be overlapping for a period of time and need not be coextensive. Concomitant administration or co-administration encompasses administration in parallel or sequentially.

"Amelioration" refers to a lessening of at least one indicator, sign, or symptom of an associated disease, disorder, or condition. In certain embodiments, amelioration includes a delay or slowing in the progression of one or more indicators of a condition or disease. The severity of indicators may be determined by subjective or objective measures, which are known to those skilled in the art.

"Animal" refers to a human or non-human animal, including, but not limited to, mice, rats, rabbits, dogs, cats, pigs, and non-human primates, including, but not limited to, monkeys and chimpanzees.

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

"Antisense compound" means a compound comprising an antisense oligonucleotide and optionally one or more additional features, such as a conjugate group or terminal group. Examples of antisense compounds include single-stranded and double-stranded compounds. Examples are antisense oligonucleotides, ribozymes, siRNAs, shRNAs, ssRNAs, and occupancy-based compounds.

"Antisense inhibition" means reduction of target nucleic acid levels in the presence of an antisense compound complementary to a target nucleic acid compared to target nucleic acid levels in the absence of the antisense compound.

"Antisense mechanisms" are all those mechanisms involving hybridization of a compound with target nucleic acid, wherein the outcome or effect of the hybridization is either target degradation or target occupancy with concomitant stalling of the cellular machinery involving, for example, transcription or splicing.

"Antisense oligonucleotide" means an oligonucleotide having a nucleobase sequence that is complementary to a target nucleic acid or a region or segment thereof. In certain embodiments, an antisense oligonucleotide is specifically hybridizable to a target nucleic acid or a region or segment thereof.

"Bicyclic nucleoside" or "BNA" means a nucleoside comprising a bicyclic sugar moiety. As used herein, "bicyclic sugar" or "bicyclic sugar moiety" means a modified sugar moiety comprising two rings, wherein the second ring is formed via a bridge connecting two of the atoms in the first ring thereby forming a

bicyclic structure. In certain embodiments, the first ring of the bicyclic sugar moiety is a furanosyl moiety. In certain embodiments, the bicyclic sugar moiety does not comprise a furanosyl moiety.

"Branching group" means a group of atoms having at least 3 positions that are capable of forming covalent linkages to at least 3 groups. In certain embodiments, a branching group provides a plurality of reactive sites for connecting tethered ligands to an oligonucleotide via a conjugate linker and/or a cleavable moiety.

"Cell-targeting moiety" means a conjugate group or portion of a conjugate group that is capable of binding to a particular cell type or particular cell types.

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

"cEt" or "constrained ethyl" means a bicyclic sugar moiety comprising a bridge connecting the 4'-carbon and the 2'-carbon, wherein the bridge has the formula: 4'-$CH(CH_3)$-O-2'.

"Chemical modification" means a chemical difference in a compound when compared to a naturally occurring counterpart. Chemical modifications of oligonucleotides include nucleoside modifications (including sugar moiety modifications and nucleobase modifications) and internucleoside linkage modifications. In reference to an oligonucleotide, chemical modification does not include differences only in nucleobase sequence.

"Chemically distinct region" refers to a region of an antisense compound that is in some way chemically different than another region of the same antisense compound. For example, a region having 2'-O-methoxyethyl nucleotides is chemically distinct from a region having nucleotides without 2'-O-methoxyethyl modifications.

"Chimeric antisense compounds" means antisense compounds that have at least 2 chemically distinct regions, each position having a plurality of subunits.

"Cleavable bond" means any chemical bond capable of being split. In certain embodiments, a cleavable bond is selected from among: an amide, a polyamide, an ester, an ether, one or both esters of a phosphodiester, a phosphate ester, a carbamate, a di-sulfide, or a peptide.

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

"Complementary" in reference to an oligonucleotide means the nucleobase sequence of such oligonucleotide or one or more regions thereof matches the nucleobase sequence of another oligonucleotide or nucleic acid or one or more regions thereof when the two nucleobase sequences are aligned in opposing directions. Nucleobase matches or complementary nucleobases, as described herein, are limited to adenine

(A) and thymine (T), adenine (A) and uracil (U), cytosine (C) and guanine (G), and 5-methyl cytosine (mC) and guanine (G) unless otherwise specified. Complementary oligonucleotides and/or nucleic acids need not have nucleobase complementarity at each nucleoside and may include one or more nucleobase mismatches. By contrast, "fully complementary" or "100% complementary" in reference to oligonucleotides means that such oligonucleotides have nucleobase matches at each nucleoside without any nucleobase mismatches.

"Conjugate group" means a group of atoms that is directly or indirectly attached to a parent compound, *e.g.*, an oligonucleotide.

"Conjugate linker" means a group of atoms that connects a conjugate group to a parent compound, *e.g.*, an oligonucleotide.

"Constrained ethyl nucleoside" (also cEt nucleoside) means a nucleoside comprising a bicyclic sugar moiety comprising a 4'-CH(CH_3)-O-2' bridge.

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

"Designing" or "Designed to" refer to the process of designing an oligomeric compound that specifically hybridizes with a selected nucleic acid molecule.

"DGAT2" means any nucleic acid or protein of DGAT2. "DGAT2 nucleic acid" means any nucleic acid encoding DGAT2. For example, in certain embodiments, a DGAT2 nucleic acid includes a DNA sequence encoding DGAT2, an RNA sequence transcribed from DNA encoding DGAT2 (including genomic DNA comprising introns and exons), including a non-protein encoding (*i.e.* non-coding) RNA sequence, and an mRNA sequence encoding DGAT2. "DGAT2 mRNA" means an mRNA encoding a DGAT2 protein.

"DGAT2 specific inhibitor" refers to any agent capable of specifically inhibiting DGAT2 RNA and/or DGAT2 protein expression or activity at the molecular level. For example, DGAT2 specific inhibitors include nucleic acids (including antisense compounds), peptides, antibodies, small molecules, and other agents capable of inhibiting the expression of DGAT2 RNA and/or DGAT2 protein.

"Dose" means a specified quantity of a pharmaceutical agent provided in a single administration, or in a specified time period. In certain embodiments, a dose may be administered in two or more boluses, tablets, or injections. For example, in certain embodiments, where subcutaneous administration is desired, the desired dose may require a volume not easily accommodated by a single injection. In such embodiments, two or more injections may be used to achieve the desired dose. In certain embodiments, a dose may be administered in two or more injections to minimize injection site reaction in an individual. In other

embodiments, the pharmaceutical agent is administered by infusion over an extended period of time or continuously. Doses may be stated as the amount of pharmaceutical agent per hour, day, week or month.

"Dosing regimen" is a combination of doses designed to achieve one or more desired effects.

"Double-stranded antisense compound" means an antisense compound comprising two oligomeric compounds that are complementary to each other and form a duplex, and wherein one of the two said oligomeric compounds comprises an antisense oligonucleotide.

"Effective amount" means the amount of compound sufficient to effectuate a desired physiological outcome in an individual in need of the agent. The effective amount may vary among individuals depending on the health and physical condition of the individual to be treated, the taxonomic group of the individuals to be treated, the formulation of the composition, assessment of the individual's medical condition, and other relevant factors.

"Efficacy" means the ability to produce a desired effect.

"Expression" includes all the functions by which a gene's coded information is converted into structures present and operating in a cell. Such structures include, but are not limited to the products of transcription and translation.

"Fully modified" in reference to an oligonucleotide means a modified oligonucleotide in which each nucleoside is modified. "Uniformly modified" in reference to an oligonucleotide means a fully modified oligonucleotide in which at least one modification of each nucleoside is the same. For example, the nucleosides of a uniformly modified oligonucleotide can each have a 2'-MOE modification but different nucleobase modifications, and the internucleoside linkages may be different.

"Gapmer" means a chimeric antisense compound in which an internal region having a plurality of nucleosides that is positioned between external regions having one or more nucleosides, wherein the nucleosides comprising the internal region are chemically distinct from the nucleoside or nucleosides comprising the external regions. The internal region may be referred to as the "gap" and the external regions may be referred to as the "wings." In certain embodiments, the structure of a gapmer may support RNase H cleavage.

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

embodiments, complementary nucleic acid molecules include, but are not limited to, an antisense oligonucleotide and a nucleic acid target.

"Identifying an animal having, or at risk for having, a disease, disorder and/or condition" means identifying an animal having been diagnosed with the disease, disorder and/or condition or identifying an animal predisposed to develop the disease, disorder and/or condition. Such identification may be accomplished by any method including evaluating an individual's medical history and standard clinical tests or assessments.

"Immediately adjacent" means there are no intervening elements between the immediately adjacent elements of the same kind (e.g. no intervening nucleobases between adjacent nucleobases).

"Individual" means a human or non-human animal selected for treatment or therapy.

"Inhibiting the expression or activity" refers to a reduction, blockade of the expression or activity relative to the expression or activity in an untreated or control sample, and does not necessarily indicate a total elimination of expression or activity.

"Internucleoside linkage" means a group or bond that forms a covalent linkage between adjacent nucleosides in an oligonucleotide. As used herein "modified internucleoside linkage" means any internucleoside linkage other than a naturally occurring, phosphate internucleoside linkage. Naturally occurring, non-phosphate linkages are referred to herein as modified internucleoside linkages. "Phosphorothioate linkage" means a linkage between nucleosides wherein the phosphodiester bond of a phosphate linkage is modified by replacing one of the non-bridging oxygen atoms with a sulfur atom. A phosphorothioate linkage is a modified internucleoside linkage.

"Lengthened" antisense oligonucleotides are those that have one or more additional nucleosides relative to an antisense oligonucleotide disclosed herein; e.g. a parent oligonucleotide.

"Linearly modified sugar" or "linearly modified sugar moiety" means a modified sugar moiety that comprises an acyclic or non-bridging modification. Such linear modifications are distinct from bicyclic sugar modifications.

"Linked deoxynucleoside" means a nucleic acid base (A, G, C, T, U) substituted by deoxyribose linked by a phosphate ester to form a nucleotide.

"Linked nucleosides" are nucleosides that are connected in a continuous sequence (*i.e.* no additional nucleosides are present between those that are linked).

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

hypoxanthine, are capable of hybridizing with at least one nucleobase but are still mismatched or non-complementary with respect to nucleobase to which it hybridized. As another example, a nucleobase of a first oligonucleotide that is not capable of hybridizing to the corresponding nucleobase of a second oligonucleotide or target nucleic acid when the first and second oligonucleotides are aligned is a mismatch or non-complementary nucleobase.

"Modified nucleobase" means any nucleobase other than adenine, cytosine, guanine, thymidine, or uracil. An "unmodified nucleobase" means the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). A "universal base" is a nucleobase that can pair with any one of the five unmodified nucleobases.

"Modified nucleoside" means a nucleoside having, independently, a modified sugar moiety and/or modified nucleobase.

"Modified nucleotide" means a nucleotide having, independently, a modified sugar moiety, modified internucleoside linkage, or modified nucleobase.

"Modified oligonucleotide" means an oligonucleotide comprising at least one modified internucleoside linkage, a modified sugar, and/or a modified nucleobase.

"Modulating" refers to changing or adjusting a feature in a cell, tissue, organ or organism. For example, modulating DGAT2 RNA can mean to increase or decrease the level of DGAT2 RNA and/or DGAT2 protein in a cell, tissue, organ or organism. A "modulator" effects the change in the cell, tissue, organ or organism. For example, a DGAT2 antisense compound can be a modulator that decreases the amount of DGAT2 RNA and/or DGAT2 protein in a cell, tissue, organ or organism.

"Monomer" refers to a single unit of an oligomer. Monomers include, but are not limited to, nucleosides and nucleotides, whether naturally occuring or modified.

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

"Natural" or "Naturally occurring" means found in nature. "Naturally occurring internucleoside linkage" means a 3' to 5' phosphodiester linkage. "Natural sugar moiety" means a sugar moiety found in DNA (2'-H) or RNA (2'-OH). "Naturally occurring nucleobase" means the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). "Non-complementary nucleobase" refers to a pair of nucleobases that do not form hydrogen bonds with one another or otherwise support hybridization.

"Nucleic acid" refers to molecules composed of monomeric nucleotides. A nucleic acid includes, but is not limited to, ribonucleic acids (RNA), deoxyribonucleic acids (DNA), single-stranded nucleic acids, and double-stranded nucleic acids.

"Nucleobase" means a heterocyclic moiety capable of pairing with a base of another nucleic acid.

"Nucleobase sequence" means the order of contiguous nucleobases independent of any sugar, linkage, and/or nucleobase modification.

"Nucleoside" means a compound comprising a nucleobase and a sugar moiety. The nucleobase and sugar moiety are each, independently, unmodified or modified.

"Nucleotide" means a nucleoside having a phosphate group covalently linked to the sugar portion of the nucleoside.

"Oligomeric compound" means a compound comprising an oligonucleotide and optionally one or more additional features, such as a conjugate group or terminal group. Examples of oligomeric compounds include single-stranded and double-stranded compounds, such as, antisense compounds, antisense oligonucleotides, ribozymes, siRNAs, shRNAs, ssRNAs, and occupancy-based compounds.

"Oligonucleoside" means an oligonucleotide in which the internucleoside linkages do not contain a phosphorus atom.

"Oligonucleotide" means a polymer of linked nucleosides each of which can be modified or unmodified, independent one from another.

"Parent oligonucleotide" means an oligonucleotide whose sequence is used as the basis of design for more oligonucleotides of similar sequence but with different lengths, motifs, and chemistries. The newly designed oligonucleotides may have the same or overlapping sequence as the parent oligonucleotide.

"Parenteral administration" means administration through injection or infusion. Parenteral administration includes subcutaneous administration, intravenous administration, intramuscular administration, intraarterial administration, intraperitoneal administration, or intracranial administration, e.g. intrathecal or intracerebroventricular administration.

"Pharmaceutically acceptable carrier or diluent" means a medium or diluent suitable for use in administering to an animal. For example, a pharmaceutically acceptable carrier can be a sterile aqueous solution, such as PBS or water-for-injection.

"Pharmaceutically acceptable salts" means physiologically and pharmaceutically acceptable salts of compounds, such as oligomeric compounds or antisense compounds, i.e., salts that retain the desired biological activity of the parent compound and do not impart undesired toxicological effects thereto.

"Pharmaceutical agent" means a compound that provides a therapeutic benefit when administered to an individual.

"Pharmaceutical composition" means a mixture of compounds suitable for administering to an individual. For example, a pharmaceutical composition may comprise one or more compounds or salts thereof and a sterile aqueous solution.

"Phosphorothioate linkage" means a modified internucleoside linkage between nucleosides where the phosphodiester bond is modified by replacing one of the non-bridging oxygen atoms with a sulfur atom.

"Phosphorus moiety" means a group of atoms comprising a phosphorus atom. In certain embodiments, a phosphorus moiety comprises a mono-, di-, or tri-phosphate, or phosphorothioate.

"Portion" means a defined number of contiguous (i.e., linked) nucleobases of a nucleic acid. In certain embodiments, a portion is a defined number of contiguous nucleobases of a target nucleic acid. In certain embodiments, a portion is a defined number of contiguous nucleobases of an oligomeric compound

"Prevent" refers to delaying or forestalling the onset, development or progression of a disease, disorder, or condition for a period of time from minutes to indefinitely. Prevent may also mean reducing the risk of developing a disease, disorder, or condition.

"Prodrug" means a form of a compound which, when administered to an individual, is metabolized to another form. In certain embodiments, the metabolized form is the active, or more active, form of the compound (e.g., drug).

"Prophylactically effective amount" refers to an amount of a pharmaceutical agent that provides a prophylactic or preventative benefit to an animal.

"RefSeq No." is a unique combination of letters and numbers assigned to a sequence to indicate the sequence is for a particular target transcript (e.g., target gene). Such sequence and information about the target gene (collectively, the gene record) can be found in a genetic sequence database. Genetic sequence databases include the NCBI Reference Sequence database, GenBank, the European Nucleotide Archive, and the DNA Data Bank of Japan (the latter three forming the International Nucleotide Sequence Database Collaboration or INSDC).

"Region" is defined as a portion of the target nucleic acid having at least one identifiable structure, function, or characteristic.

"Ribonucleotide" means a nucleotide having a hydroxy at the 2' position of the sugar portion of the nucleotide.

“RNAi compound” means an oligomeric compound that acts, at least in part, through RISC or Ago2 to modulate a target nucleic acid and/or protein encoded by a target nucleic acid. RNAi compounds include, but are not limited to double-stranded siRNA, single-stranded RNA (ssRNA), and microRNA, including microRNA mimics. The term RNAi compound excludes antisense oligonucleotides that act through RNase H.

“Segment” is defined as a smaller or sub-portion of region within an antisense compound, an oligonucleotide, or a target nucleic acid.

“Side effects” means physiological disease and/or conditions attributable to a treatment other than the desired effects. In certain embodiments, side effects include injection site reactions, liver function test abnormalities, renal function abnormalities, liver toxicity, renal toxicity, central nervous system abnormalities, myopathies, and malaise. For example, increased aminotransferase levels in serum may indicate liver toxicity or liver function abnormality. For example, increased bilirubin may indicate liver toxicity or liver function abnormality.

“Single-stranded” in reference to an antisense compound or oligomeric compound means there is one oligonucleotide in the compound. “Self-complementary” in reference to an antisense compound or oligomeric compound means a compound that at least partially hybridizes to itself. A compound consisting of one antisense or oligomeric compound, wherein the oligonucleotide of the compound is self-complementary, is a single-stranded compound. A single-stranded antisense or oligomeric compound may be capable of binding to a complementary compound to form a duplex.

“Sites,” as used herein, are defined as unique nucleobase positions within a target nucleic acid.

"Slows progression" means decrease in the development of the said disease.

“Specifically hybridizable” refers to an antisense compound having a sufficient degree of complementarity between an antisense oligonucleotide and a target nucleic acid to induce a desired effect, while exhibiting minimal or no effects on non-target nucleic acids.

“Specifically inhibit” a target nucleic acid means to reduce or block expression of the target nucleic acid while exhibiting fewer, minimal, or no effects on non-target nucleic acids reduction and does not necessarily indicate a total elimination of the target nucleic acid’s expression.

“Sugar moiety” means a group of atoms that can link a nucleobase to another group, such as an internucleoside linkage, conjugate group, or terminal group. In certain embodiments, a sugar moiety is attached to a nucleobase to form a nucleoside. As used herein, “unmodified sugar moiety” or “unmodified sugar” means a 2’-OH(H) furanosyl moiety, as found in RNA, or a 2’-H(H) moiety, as found in DNA. Unmodified sugar moieties have one hydrogen at each of the 1’, 3’, and 4’ positions, an oxygen at the 3’

position, and two hydrogens at the 5' position. As used herein, "modified sugar moiety" or "modified sugar" means a furanosyl moiety comprising a non-hydrogen substituent in place of at least one hydrogen of an unmodified sugar moiety, or a sugar surrogate. In certain embodiments, a modified sugar moiety is a 2'-substituted sugar moiety. Such modified sugar moieties include bicyclic sugars and linearly modified sugars.

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

10 "Synergy" or "synergize" refers to an effect of a combination that is greater than additive of the effects of each component alone.

"Target gene" refers to a gene encoding a target.

"Target nucleic acid," "target RNA," "target RNA transcript" and "nucleic acid target" mean a nucleic acid capable of being targeted by antisense compounds.

15 "Targeting" means the process of design and selection of an antisense compound that will specifically hybridize to a target nucleic acid and induce a desired effect.

"Target region" means a portion of a target nucleic acid to which one or more antisense compounds is targeted.

"Target segment" means the sequence of nucleotides of a target nucleic acid to which an antisense 20 compound is targeted. "5' target site" refers to the 5'-most nucleotide of a target segment. "3' target site" refers to the 3'-most nucleotide of a target segment.

"Terminal group" means a chemical group or group of atoms that is covalently linked to a terminus of an oligonucleotide.

"Therapeutically effective amount" means an amount of a compound, pharmaceutical agent, or 25 composition that provides a therapeutic benefit to an individual.

"Treat" refers to administering a compound or pharmaceutical composition to an animal in order to effect an alteration or improvement of a disease, disorder, or condition in the animal.

"Unmodified" nucleobases mean the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U).

"Unmodified nucleotide" means a nucleotide composed of naturally occuring nucleobases, sugar moieties, and internucleoside linkages. In certain embodiments, an unmodified nucleotide is an RNA nucleotide (i.e. β-D-ribonucleotides) or a DNA nucleotide (i.e. β-D-deoxyribonucleotide).

Certain Embodiments

Certain embodiments provide methods, compounds and compositions for inhibiting DGAT2 (DGAT2) expression.

Certain embodiments provide antisense compounds targeted to a DGAT2 nucleic acid. In certain embodiments, the DGAT2 nucleic acid has the sequence set forth in RefSeq No. NM_032564.3 (incorporated by reference, disclosed herein as SEQ ID NO: 1) or nucleotides 5669186 to 5712008 of RefSeq No. NT_033927.5 (incorporated by reference, disclosed herein as SEQ ID NO: 2). In certain embodiments, the antisense compound is a single-stranded oligonucleotide.

Certain embodiments provide an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the antisense compound is a single-stranded oligonucleotide.

Certain embodiments provide an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 9, at least 10, at least 11, or at least 12 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the antisense compound is a single-stranded oligonucleotide.

Certain embodiments provide an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the antisense compound is a single-stranded oligonucleotide.

Certain embodiments provide an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the antisense compound is a single-stranded oligonucleotide.

In certain embodiments, antisense compounds or antisense oligonucleotides target the 26711-26802 of a DGAT2 nucleic acid. In certain aspects, antisense compounds or antisense oligonucleotides target within nucleotides 26711-26802 of a DGAT2 nucleic acid having the nucleobase sequence of SEQ ID NO: 2 (nucleotides 5669186 to 5712008 of RefSeq No. NT_033927.5). In certain aspects, antisense compounds or antisense oligonucleotides have at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobase portion

complementary to an equal length portion within nucleotides 26711-26802 of a DGAT2 nucleic acid having the nucleobase sequence of SEQ ID NO: 2 (nucleotides 5669186 to 5712008 of RefSeq No. NT_033927.5).

In certain embodiments, antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid having the nucleobase sequence of SEQ ID NO: 2 within nucleobases 26711-26799, 26711-26730, 26721-26740, 26755-26744, 26778-26797, 26779-26798, 26755-26798, and 26780-26799. In certain aspects, antisense compounds or antisense oligonucleotides target at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobases within the aforementioned nucleobase regions.

In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 60% inhibition: 9930-9949, 9953-9973, 9959-9978, 9961-9981, 9970-9992, 9975-9994, 9984-10003, 10040-10059, 10043-10063, 10045-10064, 10046-10065, 10049-10068, 10054-10073, 10160-10179, 10209-10229, 10212-10231, 10214-10235, 10217-10236, 10218-10238, 10327-10346, 10389-10413, 10490-10511, 10522-10548, 10530-10549, 10531-10551, 10533-10553, 10645-10669, 10651-10670, 10653-10673, 10655-10674, 10656-10675, 10657-10676, 10658-10680, 10662-10681, 10663-10684, 10666-10685, 10667-10684, 10670-10689, 10702-10721, 10727-10747, 10729-10748, 10730-10750, 10733-10755, 10737-10756, 10742-10761, 10763-10782, 10814-10835, 10817-10836, 10818-10837, 10940-10964, 11008-11027, 11074-11097, 11123-11150, 11158-11182, 11168-11187, 11170-11190, 11171-11197, 11199-11218, 11200-11220, 11209-11228, 11318-11342, 11413-11432, 11559-11578, 11594-11618, 11707-11731, 11872-11891, 11920-11939, 12247-12266, 12285-12304, 12549-12573, 12671-12695, 12806-12826, 12839-12863, 12890-12909, 12927-12961, 13098-13117, 13212-13231, 13239-13258, 13441-13461, 13921-13945, 13962-13996, 14177-14201, 14194-14218, 14239-14258, 14385-14404, 14457-14522, 14504-14527, 14537-14556, 14648-14697, 14715-14790, 14715-14739, 14735-14764, 14746-14765, 14749-14774, 14756-14779, 14765-14789, 14771-14790, 14807-14831, 14852-14871, 14882-14901, 14953-15015, 14997-15065, 15041-15107, 15041-15092, 15083-15107, 15178-15197, 15214-15243, 15219-15243, 15248-15276, 15255-15276, 15292-15311, 15318-15338, 15321-15342, 15353-15372, 15368-15392, 15514-15533, 15573-15665, 15573-15597, 15729-15753, 15804-15828, 15814-15833, 15876-15900, 15876-15896, 15933-15962, 15933-15954, 15991-16010, 16046-16073, 16082-16124, 16237-16256, 16288-16314, 16288-16478, 16308-16329, 16428-16478, 16510-16529, 16808-16855, 16808-16828, 16811-16855, 16898-16921, 17007-17031, 17038-17057, 17207-17229, 17269-17298, 17273-17294, 17328-17357, 17420-17444, 17450-17471, 17530-17559, 17328-17559, 17960-17989, 18078-18097, 18155-18176, 18155-18198, 18177-18200, 18225-18305, 18306-18327, 18309-18330, 18312-18330, 18312-18332, 18315-18344, 18329-18355, 18379-18398, 18417-18446, 18430-18451, 1818450-18473, 18470-18494, 18581-18601, 18583-18605, 18581-18611, 18588-18611, 18821-18850, 18821-18847, 18836-18899, 18890-18914, 18898-18919, 19013-19037, 19013-19040, 19360-19411, 19363-19383, 19804-19823, 19909-19932, 19987-20009, 20232-20256, 20296-20325, 20462-20481, 20541-20560, 20668-20692, 20775-20797, 20779-20797, 20817-20841, 20828-20863, 20878-20897, 20956-20979, 21046-21120, 21091-21120, 21164-21203, 21164-21188, 21374-21403, 21659-21678,

21708-21727, 21765-21784, 21933-21955, 22153-22191, 22153-22175, 22158-22179, 22167-22191, 22439-22463, 22547-22567, 22770-22790, 22770-22795, 22775-22795, 22835-22870, 22841-22865, 22881-22901, 22885-22905, 22889-22910, 23095-23115, 23098-23119, 23099-23119, 23128-23157, 23179-23251, 23238-23258, 23240-23260, 23242-23262, 23429-23449, 23480-23566, 23547-23581, 23553-23573, 23555-23576, 23562-23586, 23597-23616, 23641-23670, 24123-24144, 24123-24147, 24202-24223, 24202-24241, 24799-25039, 24799-24847, 25018-2509, 25023-25053, 25026-25053, 25069-25092, 25069-25114, 25077-25104, 25088-25114, 25183-25205, 25183-25217, 25198-25217, 25226-25250, 25226-25265, 25236-25260, 25244-25291, 25312-25394, 25380-25400, 25717-25736, 25782-25860, 25845-25866, 25866-25935, 25919-25939, 25950-25971, 25954-25973, 25981-26030, 26102-26126, 26162-26220, 26300-26324, 26331-26372, 26363-26405, 26389-26409, 26396-26420, 26479-26504, 26516-26550, 26534-26555, 26534-26560, 26540-26560, 26610-26634, 26620-26640, 26626-26648, 26620-26664, 26633-26655, 26640-26664, 26716-26740, 26716-26799, 26755-26799, 26786-26807, 26789-26809, 26786-26809, 26811-26831, 26849-26869, 26869-26898, 26883-26903, 26926-26943, 27046-27075, 27106-27130, 27174-27230, 27221-27241, 27226-27258, 27241-27265, 27249-27269, 27367-27406, 27367-27402, 27386-27406, 27638-27664, 27769-27791, 27775-27810, 27852-27877, 28026-28049, 28128-28154, 28462-28492, 28475-28508, 28516-28542, 28584-28605, 28804-28826, 29010-29035, 29143-29167, 29151-29180, 29196-29218, 29244-29268, 29253-29282, 29361-29383, 29369-29391, 29450-29495, 29480-29504, 29538-29654, 29673-29697, 29681-29702, 29781-29801, 29804-29828, 29827-29847, 29832-29852, 29838-29858, 29844-29878, 30484-30504, 30524-30548, 30554-30588, 30669-30731, 30972-30997, 30984-31005, 31551-31571, 31554-31584, 31794-31818, 31932-31952, 31936-31956, 31939-31963, 31946-31971, 32115-32136, 32119-32140, 32130-32159, 32175-32201, 32428-32454, 32436-32467, 32459-32479, 32463-32489, 32474-32495, 32480-32529, 32586-32638, 32621-32641, 32756-32776, 32801-32825, 32816-32840, 33070-33180, 33176-33199, 33182-33202, 33411-33433, 33572-33601, 33729-33759, 33846-33876, 33860-33882, 33866-33886, 34063-34117, 34211-34232, 34686-34710, 34739-34887, 34901-34950, 35263-35292, 35277-35302, 35322-35346, 35408-35433, 35421-35441, 35436-35457, 35665-35685, 36246-36267, 36250-36270, 36253-36274, 36258-36281, 36268-36531, 36516-36537, 36573-36597, 36581-36603, 36632-36666, 36677-36698, 36682-36702, 36689-36757, 36742-36772, 36841-36874, 36846-36874, 36865-37041, 37054-37073, 37838-37858, 39668-39694, 39684-39705, 39820-39840, 39830-39852, and 40909-40933.

In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 70% inhibition: 9971-9991, 9975-9994, 9984-10003, 10040-10059, 10044-10063, 10045-10064, 10049-10068, 10054-10179, 10210-10229, 10214-10234, 10216-10235, 10217-10236, 10218-10237, 10327-10346, 10490-10509, 10491-10511, 10522-10541, 10528-10548, 10530-10549, 10531-10550, 10532-10551, 10533-10553, 10536-10555, 10537-10556, 10645-10664, 10647-10666, 10649-10669, 10653-10673, 10655-10674, 10656-10675, 10657-10676, 10658-10677, 10659-10679, 10661-10680, 10662-10681, 10663-10683, 10665-10684, 10666-10685, 10667-10686, 10668-10687,

10670-10689, 10672-10691, 10702-10721, 10727-10747, 10729-10748, 10730-10750, 10732-10751, 10733-10752, 10734-10753, 10735-10754, 10737-10756, 10742-10756, 10742-10761, 10763-10782, 10815-10835, 10817-10836, 10818-10837, 10819-10840, 10940-10959, 10941-10960, 10942-10961, 10944-10963, 11008-11027, 11074-11093, 11075-11094, 11076-11095, 11078-11097, 11124-11146, 11128-11147, 11129-11148, 11130-11149, 11131-11177, 11159-11178, 11160-11179, 11161-11180, 11168-11187, 11170-11190, 11172-11191, 11173-11192, 11174-11196, 11180-11218, 11200-11219, 11201-11221, 11203-11222, 11204-11220, 11209-11228, 11323-11342, 11413-11432, 11559-11578, 11599-11618, 11872-11891, 112285-12304, 12549-12568, 12806-12826, 12809-12828, 12927-12946, 12942-12961, 13441-13461, 13926-13945, 14182-14201, 14194-14213, 14196-14216, 14239-14258, 14385-14404, 14462-14522, 14504-14523, 14505-14524, 14506-14527, 14537-14556, 14648-14667, 14649-14668, 14650-14669, 14651-14670, 14658-14682, 14664-14683, 14665-14684, 14666-14686, 14668-14687, 14673-14739, 14741-14764, 14746-14765, 14749-14774, 14756-14775, 14757-14779, 14765-14784, 14767-14786, 14769-14789, 14771-14790, 14772-14793, 14807-14831, 14852-15005, 14992-15012, 14995-15015, 14997-15016, 14998-15017, 14999-15020, 15011-15040, 15073-15092, 15214-15233, 15219-15243, 15248-15269, 15248-15276, 15251-15270, 15252-15272, 15254-15273, 15255-15274, 15256-15276, 15321-15342, 15573-15595, 15578-15665, 15729-15748, 15809-15828, 15876-15895, 15881-15952, 15991-16066, 16051-16070, 16053-16102, 16289-16309, 16292-16312, 16310-16329, 16248-16448, 16432-16451, 16438-16457, 16808-16828, 16811-16830, 16813-16832, 16815-16835, 16828-16852, 16836-16855, 16898-16917, 16900-16921, 17007-17027, 17207-17227, 17210-17229, 17274-17294, 17328-17347, 17330-17352, 17450-17549, 17960-17979, 18155-18175, 18157-18176, 18160-15180, 18162-18181, 18163-18182, 18164-18183, 18165-18184, 18166-18185, 18172-18193, 18175-18194, 18176-18194, 18176-18195, 18178-18199, 18181-18200, 18225-18244, 18235-18305, 18307-18327, 18309-18328, 18310-18330, 18312-18332, 18315-18337, 18320-18340, 18322-18341, 18323-18342, 18324-18343, 18325-18347, 18330-18355, 18379-18436, 18418-18437, 18419-18438, 18420-18439, 18422-18441, 18431-18451, 18450-18469, 18451-18470, 18452-18471, 18470-18489, 18581-18600, 18582-18601, 18583-18602, 18584-18604, 18588-18610, 18828-18847, 18829-18848, 18831-18850, 18869-18888, 18870-18889, 18899-18919, 19013-19032, 19016-19035, 19018-19037, 19020-19039, 19360-19380, 19364-19383, 19911-19932, 19987-20008, 20232-20251, 20298-20317, 20300-20325, 20668-20689, 20672-20692, 20775-20796, 20780-20800, 20822-20841, 20829-20851, 20837-20857, 20840-20862, 20958-20979, 21164-21183, 21384-21403, 21933-21952, 22155-22175, 22439-22463, 22548-22567, 22549-22568, 22771-22790, 22772-22791, 22773-22792, 22846-22865, 22886-22905, 22888-22907, 22889-22908, 23095-23115, 23098-23117, 23099-23119, 23128-23147, 23138-23157, 23184-23251, 23238-23258, 23242-23261, 23243-23262, 23244-23263, 23245-23264, 23246-23262, 23305-23324, 23426-23446, 23430-23449, 23551-23570, 23552-23571, 23553-23572, 23554-23573, 23557-23576, 23562-23586, 23641-23665, 24123-24142, 24799-24897, 25019-25038, 25023-25042, 25026-25045, 25028-25092, 25075-25094, 25077-25101, 25085-25104, 25088-25202, 25186-25205, 25193-25212, 25198-25250, 25236-25255, 25245-25291, 25312-25394, 25380-25399, 25429-25448, 25717-25808,

25841-25860, 25846-25865, 25900-25928, 25911-25930, 25913-25935, 25920-25971, 25981-26026, 26010-26030, 26102-26121, 26165-26186, 26169-26219, 26300-26324, 26353-26372, 26358-26377, 26363-26404, 26389-26409, 26397-26416, 26479-26498, 26482-26503, 26516-26535, 26517-26536, 26518-26537, 26519-26538, 26520-26540, 26526-26550, 26535-26555, 26537-26556, 26538-26557, 26539-26558, 26615-26634, 26620-26640, 26626-26646, 26628-26647, 26629-26648, 26630-26649, 26631-26650, 26632-26651, 26633-26652, 26635-26654, 26640-26659, 26711-26730, 26721-26799, 26786-26807, 26811-26830, 26852-26871, 26854-26873, 26869-26898, 26883-26903, 26927-26946, 27050-27075, 27106-27125, 27221-27240, 27228-27247, 27231-27250, 27235-27257, 27241-27265, 27249-27268, 27367-27386, 27377-27396, 27379-27398, 27381-27401, 27383-27402, 27387-27406, 27438-27457, 27639-27658, 27642-27661, 27644-27664, 27769-27790, 27775-27799, 27782-27809, 27853-27877, 28026-28048, 28128-28154, 28463-28484, 28468-28489, 28475-28500, 28516-28542, 28806-28826, 29010-28033, 29140-29159, 29143-29165, 29148-29167, 29154-29177, 29160-29180, 29193-29212, 29196-29218, 29201-29220, 29245-29265, 29253-29272, 29255-29274, 29257-29278, 29262-29282, 26361-29382, 29369-29388, 29371-29390, 29485-29504, 29538-29557, 29548-29594, 29635-29654, 29673-29692, 29675-29695, 29678-29697, 29682-29702, 29781-29801, 29809-29828, 29827-59847, 29829-29848, 29830-29849, 29831-29850, 29832-29852, 29838-29858, 29840-29859, 29842-29861, 29843-29862, 29844-29873, 30483-30502, 30484-30503, 30514-30533, 30529-30548, 30559-30578, 30669-30693, 30972-30992, 30977-30996, 30982-31001, 30986-31005, 31554-31573, 31768-31787, 31797-31817, 31933-31952, 31936-31956, 31942-31961, 32116-32135, 32120-32140, 32131-32151, 32135-32158, 32177-32198, 32182-32201, 32336-32355, 32428-32447, 32429-32448, 32430-32449, 32431-32450, 32432-32451, 32433-32452, 32434-32450, 32435-32454, 32436-32455, 32446-32466, 32449-32468, 32450-32469, 32451-32470, 32452-32471, 32453-32472, 32454-32473, 32455-32474, 32456-32475, 32457-32476, 32459-32479, 32461-32480, 32462-32481, 32463-32483, 32465-32486, 32468-32489, 32475-32495, 32477-32496, 32478-32497, 32480-32500, 32510-32529, 32619-32638, 32621-32640, 32622-32641, 32623-32642, 32645-32664, 32670-32689, 32711-32730, 32752-32771, 32753-32772, 32755-32774, 32756-32776, 32816-32840, 33096-33125, 33161-33180, 33179-33199, 33181-33200, 33182-33201, 33412-33433, 33729-33750, 33861-33881, 33866-33885, 33918-33937, 34017-34036, 34211-34231, 34216-34235, 34350-34369, 34460-34479, 34739-34887, 34901-34950, 35278-35298, 35322-35346, 35362-35381, 35410-35430, 35414-35433, 35421-35440, 35436-35457, 35665-36685, 36246-36267, 36249-36268, 36250-36269, 36251-36270, 36252-36271, 36253-36272, 36258-36277, 36262-36281, 36268-36287, 36354-36428, 36512-36531, 36517-36536, 36573-36597, 36582-36602, 36617-36636, 36677-36698, 36680-36699, 36681-36700, 36682-36702, 36691-36754, 36738-36757, 36743-36772, 36758-36777, 36841-36860, 36846-36865, 36865-36942, 37054-37138, 37389-37408, 37497-37516, 37499-37518, 37501-37520, 37745-37764, 39670-39689, 39685-39704, 39820-39839, 39830-39849, 39832-39852, and 40333-40352.

In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 80% inhibition: 10040-10059, 10044-10063,

10045-10064, 10054-10073, 10210-10229, 10214-10234, 10217-10236, 10490-10509, 10531-10550, 10532-10551, 10533-10552, 10645-10664, 10650-10669, 10655-10674, 10656-10675, 10657-10676, 10659-10678, 10660-10679, 10661-10680, 10663-10682, 10664-10683, 10665-10684, 10666-10685, 10667-10686, 10670-10689, 10727-10746, 10730-10749, 10731-10750, 10732-10751, 10734-10753, 10735-10754, 10737-10756, 10816-10835, 10817-10836, 10818-10837, 10819-10838, 10820-10840, 10940-10959, 10941-10960, 10942-10961, 10944-10963, 11074-11093, 11075-11094, 11127-11146, 11128-11147, 11129-11148, 11130-11149, 11131-11177, 11159-11178, 11160-11179, 11170-11190, 11172-11191, 11173-11192, 11174-11193, 11175-11196, 11178-11197, 11199-11218, 11200-11219, 11201-11220, 11202-11221, 11203-11222, 11559-11578, 11599-11618, 12285-12304, 13442-13461, 14462-14481, 14503-14522, 14504-14523, 14505-14524, 14506-14527, 14648-14667, 14649-14668, 14650-14669, 14651-14670, 14658-14682, 14664-14683, 14666-14686, 14673-14697, 14741-14760, 14743-14764, 14746-14765, 14750-04769, 14752-14774, 14756-14775, 14757-14775, 14758-14777, 14759-14778, 14769-14789, 14771-14790, 14772-14791, 14773-14792, 14774-14793, 14807-14826, 14882-14901, 14986-15005, 14993-15012, 14995-15015, 14997-15016, 14998-15017, 14999-15018, 15000-15019, 15001-15020, 15016-15035, 15248-15268, 15250-15269, 15251-15270, 15252-15272, 15254-15273, 15319-15338, 15321-15342, 15574-15593, 15646-15665, 15881-15952, 16310-16329, 16813-16832, 16830-16852, 16900-16921, 17007-17026, 17208-17227, 17450-17470, 18156-18175, 18157-18176, 18161-18180, 18164-18183, 18166-18185, 18173-18193, 18175-18194, 18176-18195, 18180-18199, 18308-18327, 18310-18329, 18311-18330, 18312-18331, 18321-18340, 18323-18342, 18324-18343, 18325-18344, 18326-18345, 18327-18346, 18328-18347, 18331-18350, 18379-18436, 18432-18451, 18450-18469, 18581-18600, 18585-18604, 18828-18847, 18829-18848, 18900-18919, 19911-19930, 20300-20321, 20668-20687, 20830-20849, 20837-20857, 20958-20977, 22444-22463, 22548-22567, 22771-22790, 22772-22791, 22773-22792, 22886-22905, 23096-23115, 23100-23119, 23239-23258, 23242-23261, 23243-23262, 23244-23263, 23245-23264, 23246-23262, 23427-23446, 23551-23570, 23552-23571, 23557-23576, 24123-24142, 24878-24897, 25023-25042, 25028-25047, 25033-25088, 25073-25092, 25075-25094, 25078-25101, 25085-25104, 25183-25202, 25193-25212, 25246-25291, 25375-25394, 25380-25399, 25782-25804, 25787-25806, 25841-25860, 25846-25865, 25900-25919, 25905-25928, 25911-25930, 25915-25934, 25950-25970, 26005-26025, 26010-26029, 26162-26185, 26169-26191, 26174-26194, 26179-26219, 26300-26319, 26302-26321, 26304-26324, 26353-26372, 26358-26377, 26482-26501, 26517-26536, 26519-26538, 26520-26539, 26521-26540, 26536-26550, 26537-26556, 26538-26557, 26615-26634, 26620-26639, 26627-26646, 26629-26648, 26630-26649, 26631-26650, 26632-26651, 26635-26654, 26640-26659, 26711-26730, 26778-26798, 26788-26807, 26811-26830, 26884-26903, 27050-27070, 27053-27072, 27055-27075, 27221-27240, 27231-27250, 27236-27256, 27241-27260, 27382-27401, 27383-27402, 27387-27406, 27770-27789, 27775-27794, 27777-27796, 27779-27799, 27782-27804, 27787-27809, 27853-27877, 28026-28046, 28029-28048, 28128-28149, 28133-28152, 28463-28482, 28468-28488, 28476-28497, 28480-28500, 29011-29030, 29143-29163, 29160-29179, 29193-29212, 29245-29265, 26253-26272, 29369-29388, 29548-29589, 29678-29697, 29683-29702, 29782-

29801, 29827-29847, 29829-29848, 29830-29849, 29838-29858, 29840-29859, 29841-29860, 29842-29861, 29844-29863, 29854-29873, 30483-30502, 30484-30503, 30529-30548, 30674-30693, 30982-31001, 31554-31573, 32131-32151, 32135-32154, 32182-32201, 32431-32450, 32432-32451, 32433-32452, 32434-32453, 32446-32466, 32448-32467, 32449-32468, 32450-32469, 32451-32470, 32452-32471, 32453-32472, 32454-32473, 32455-32474, 32456-32475, 32459-32479, 32461-32480, 32462-32481, 32463-32482, 32464-32483, 32465-32484, 32466-32485, 32467-32486, 32468-32487, 32469-32488, 32470-32489, 32476-32495, 32477-32496, 32480-32499, 32619-32638, 32620-32639, 32621-32640, 32623-32642, 32645-32664, 32752-32771, 32753-32772, 32757-32776, 32816-32835, 33179-33199, 33181-33200, 33182-33201, 33412-33433, 33729-33749, 33866-33885, 34211-34231, 34739-34758, 34931-34950, 35436-35456, 35666-35685, 36247-36266, 36249-36268, 36250-36269, 36251-36270, 36252-36271, 36253-36272, 36258-36277, 36354-36373, 36409-36428, 36512-36531, 36517-36536, 36583-36602, 36680-36699, 36681-36700, 36841-36860, 36846-36865, 39670-39689, and 39832-39851.

In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 90% inhibition: 32447-32466, 32452-32471, 32460-32479, 32462-32481, 32464-32483, 32465-32484, 32466-32485, 32467-32486, 32468-32487, 32619-32638, 32620-32639, 32753-32772, 36250-36269, 36517-36536, 32432-32451, 32431-32450, 30483-30502, 29828-29847, 29011-29030, 28026-28045, 29011-29030, 29828-29847, 30483-30502, 32431-32450, 32432-32451, 32447-32466, 32452-32471, 32460-32479, 32462-32481, 32464-32483, 32465-32484, 32466-32485, 32467-32486, 32468-32487, 32619-32638, 32620-32639, 32753-32772, 36250-36269, 36252-36271, 36409-36428, and 36517-36536.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least a 60% inhibition of a DGAT2 mRNA, ISIS NOs: 413236, 413284, 413391, 413399, 413413, 413422, 413433, 413433, 413441, 413446, 423460-423466, 423520-423527, 423601-423604, 472182, 472188, 472189, 472194-472196, 472203-472206, 472208, 472347, 472349-472352, 472398, 483803, 483811-483814, 483816-483818, 483821-483823, 483825-483835, 483838-483842, 483846-483848, 483852, 483853, 483862, 483866, 483868-483875, 483879, 483886-483890, 483892, 483895, 483897-483903, 483906-483913, 483916-483929, 483932-483934, 483936, 483942, 483948-483950, 483952, 483954, 483956, 483961, 483968-483973, 483975-483979, 483981, 483983-483989, 483992-483997, 484001, 484002, 484004-484006, 484008-484013, 484015-484017, 484019, 484020, 484028, 484030, 484031, 484041, 484049, 484050, 484054-484057, 484063-484065, 484069-484073, 484081-484083, 484085, 484089, 484094, 484097-484107, 484110, 484111, 484114-484119, 484123, 484125-484127, 484129-484137, 484139-484142, 484145-484149, 484152, 484154, 484156-484159, 484161, 484162, 484164, 484165, 484167-484172, 484178-484182, 484184, 484185, 484188, 484190-484198, 484202-484204, 484209-484211, 484213, 484215, 484217-484221, 484227, 484231, 484232, 484234, 484235, 484237, 484240-484243, 484248-484250, 484257, 484263, 484265-

484271, 484273-484276, 484281-484285, 484290, 484292, 484293, 484298, 484299, 484301, 484302, 484310, 484319-484325, 484327, 484336, 484338, 484342-484344, 484346-484357, 484359, 484362-484365, 484368, 484370-484387, 484390, 484404, 484411, 495425, 495428, 495429, 495430, 495436, 495438, 495440-495459, 495461-495473, 495475, 495476, 495479-495492, 495495-495511, 495514-495545, 495548-495580, 495584, 495585, 495587-495594, 495596-495626, 495630-495639, 495641-495644, 495648-495651, 495656, 495657, 495660-495662, 495664-495667, 495669-495671, 495676, 495677, 495684-495689, 495692-495707, 495711, 495713, 495714, 495717-495732, 495734, 495736-495739, 495742-495757, 495762-495766, 495772-495774, 495781-495786, 495788, 495789, 495791, 495793-495797, 495799, 495800, 495804, 495808-495813, 495817-495844, 495847-495860, 495862-495870, 495873-495883, 495886, 495899-495904, 495909, 495911-495914, 495918, 495920-495923, 495955, 495957, 495958, 495983, 495992, 496004, 496009, 496010, 496012, 496033, 500841, 500843, 500844, 500852, 500859, 500866, 500867, 500870, 500871, 500892, 500895, 500912, 500913, 500928, 500929, 500934, 500935, 500942, 500944-500946, 500950, 500953, 500957, 500960, 500961, 500966, 500974, 500975, 500979, 500982, 500985, 500986, 500989, 500990, 500994, 500995, 500997, 500998, 501004, 501007, 501008, 501016, 501018-501020, 501025, 501026, 501029-501031, 501033-501035, 501037-501041, 501043, 501055, 501061, 501062, 501064, 501067-501070, 501076, 501093-501098, 501100, 501103, 501104, 501106, 501108, 501111, 501117-501119, 501122-501130, 501140, 501154, 501155, 501158, 501165, 501171, 501176, 501177, 501182-501184, 501193, 501194, 501199, 501200, 501209, 501210, 501212-501214, 501217, 501224, 501227-501230, 501240, 501241, 501244, 501247-501249, 501254, 501256, 501264, 501270, 501287, 501289, 501290, 501297, 501319, 501322, 501326, 501332, 501335, 501342, 501345, 501353, 501357, 501370, 501382-501406, 501410-501412, 501414, 501426-501431, 501434-501443, 501445-501457, 501831, 501835, 501837, 501838, 501849-501853, 501855, 501861, 501867, 501871, 501880, 501883, 501884, 501886-501890, 501900, 501903, 501916, 501932-501934, 501944, 501946, 501947, 501950, 501951, 501957, 501959, 501960, 501966, 501968, 501976, 501977, 501979, 501981-501983, 501991, 501996, 502011, 502013-502015, 502019, 502024-502028, 502031, 502034, 502036-502042, 502045, 502046, 502050, 502053, 502055, 502056, 502062, 502065, 502068-502070, 502083-502085, 502095-502100, 502102, 502106, 502110, 502113, 502114, 502117, 502119, 502120, 502122, 502124, 502127, 502131, 502135, 502144, 502146, 502149, 502150, 502154-502156, 502158, 502163, 502164, 502167, 502172-502176, 502179, 502186, 502189, 502191, 502192, 502194, 502204, 502206, 502215, 502220, 502223, 502228, 502236, 502314, 502319, 502320, 502322, 502334, 502336, 507663, 507665, 507667, 507669, 507675, 507677, 507679, 507684, 507689-507696, 507705, 507709-507719, 507724, 507726, 522363, 522365, 522366, 522368-522375, 522383-522386, 522389, 522391, 522395, 522396, 522398-522413, 522416-522422, 522424-522440, 522442-522452, 522454, 522456, 522457, 522461-522467, 522469-522474, 522478-522490, 522492-522513, 522516-522518, 522521, 522522, 522525, 522529, 522530, 522533-522535, 522540-522550, 522552-

522558, 522561-522565, 522573, 522577-522582, 522586-522593, 522597, 522598, 522602-522614, 522617-522625, 522627-522639, 522642-522645, 522657-522663, 522666-522668, 522671-522684, 522686-522702, 522704-522728, 522732, 522733, 522738-522740, 522744-522749, 522754, 522757-522761, 522763-522771, 522776-522778, 522780, 522782-522785, 522788-522797, 522801-522803, 522805, 522807-522809, 522813, 522821-522824, 522829-522831, 522835-522839, 522842, 522844, 522846-522850, 522852-522854, 522856, 522857, 522865-522873, 522875-522880, 522887-522897-522899, 522901, 522904-522906, 522909, 522913, 522914, 522917, 522924, 522925, 522927, 522931-522935, 522939-522943, 522945-522950, 522956, 522964, 522965, 522970, 522977-522982, 522986, 522987, 522996, 522997, 523000-523002, 523015, 523016, 523022, 523025-523027, 525388, 525391, 525394, 525395, 525399, 525401-525405, 525414-525416, 525419, 525420, 525423, 525424, 525431, 525434-525436, 525441-525444, 525450, 525461, 525468-525474, 525477, 525479, 525480, 525484, 525485, 525488-525491, 525498-525501, 525504-525507, 525511-525518, 525520, 525528, 525535-525537, 525539, 525541, 525542, 525544, 525547-525558, 525565, 525577-525579, 525606, 525609-525612, 525619, 525631, 525632, 525649, 525650, 525658, 525683, 525687, 525688, 525690, 525705-525711, 525733, 525737, 525740, 525741, and 525754.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least a 60% inhibition of a DGAT2 mRNA, SEQ ID NOs: 20, 38, 39, 41, 46-48, 61-64, 68, 69, 74, 75, 76, 103, 120, 121, 122, 131, 134, 144, 145, 150, 152, 153, 154, 181, 182, 183, 202-204, 221, 225, 226, 229, 236, 237, 246, 247, 251, 259, 262, 272, 277-280, 283, 383, 391, 405, 414, 425, 433, 438, 450, 452, 453, 455-479, 482-496, 504-507, 509-511, 514-516, 518-528, 531-535, 539-541, 545, 546, 555, 559, 561-568, 574, 575, 577, 578, 583, 584, 589, 594-596, 597, 601, 607, 608, 613-615, 622-625, 627, 652, 653, 660, 674, 706, 709-711, 718-720, 726, 738, 740-745, 749-752, 754-756, 758-769, 774, 789, 793, 794, 807-812, 815, 819, 820, 839, 841-846, 848-852, 878-880, 884, 885, 889, 890, 892-895, 897, 899, 900, 902, 904, 907, 910, 913-916, 923, 935-940, 960-964, 968, 972-977, 979-981, 983-985, 988, 991-1010, 1014, 1015, 1017, 1018, 1020, 1023-1025, 1032-1034, 1036-1038, 1040, 1043-1049, 1051-1054, 1057-1061, 1065, 1071-1073, 1078-1080, 1083, 1084, 1092-1098, 1103, 1107, 1108, 1117, 1118, 1136, 1141, 1142, 1148, 1149, 1153, 1155, 1159, 1165, 1172-1176, 1178, 1181, 1183-1189, 1192-1199, 1202-1215, 1218-1220, 1222, 1228, 1234-1236, 1238, 1240, 1242, 1247, 1254-1259, 1261-1265, 1267, 1269-1275, 1278-1283, 1287, 1288, 1290-1292, 1294-1299, 1301-1303, 1305, 1306, 1314, 1316, 1317, 1327, 1335, 1336, 1340-1343, 1349-1351, 1355-1359, 1367-1369, 1371, 1375, 1380, 1383-1393, 1396, 1397, 1400-1405, 1409, 1411-1413, 1415-1423, 1425-1428, 1431-1435, 1438, 1440, 1442-1445, 1447, 1448, 1450, 1451, 1453-1458, 1464-1468, 1470, 1471, 1474, 1476-1484, 1488-1490, 1495-1497, 1499, 1501, 1503-1507, 1513, 1517, 1518, 1520, 1521, 1523, 1526-1529, 1534-1536, 1543, 1549, 1551-1557, 1559-1562, 1567-1571, 1576, 1578, 1579, 1584, 1585, 1587, 1588, 1596, 1605-1611, 1613, 1622, 1624, 1628-1630, 1632-1643, 1645, 1648-1651, 1654, 1656-1673, 1676, 1677, 1690, 1697, 1698, 1701-1703, 1709, 1711, 1713-1746, 1748, 1749,

1752-1765, 1768-1784, 1787-1818, 1821-1853, 1857, 1858, 1860-1867, 1869-1899, 1903-1912, 1914-1917, 1921-1924, 1929, 1930, 1933-1935, 1937-1940, 1942-1944, 1949, 1950, 1957-1962, 1965-1980, 1984, 1986, 1987, 1990-2005, 2007, 2009-2012, 2015-2030, 2035-2039, 2045- 2047, 2054-2059, 2061, 2062, 2064, 2066-2070, 2072, 2073, 2077, 2081-2086, 2090-2117, 2120-2133, 2135-2143, 2146-2156, 2159, 2172-2177, 2182, 2184-2187, 2191, 2193-2196, 2228, 2230, 2231, 2256, 2265, 2277, 2282, 2283, 2285, 2306, 2308, 2310-2334, 2338-2340, 2342, 2350, 2351, 2354-2359, 2362-2371, 2373-2385, 2402, 2405, 2409, 2415, 2418, 2425, 2428, 2436, 2440, 2453, 2465-2468, 2478, 2479, 2482, 2485-2487, 2492, 2494, 2502, 2508, 2525, 2527, 2528, 2535, 2543, 2544, 2547, 2554, 2560, 2565, 2566, 2571-2573, 2582, 2583, 2588, 2589, 2598, 2599, 2601-2603, 2606, 2613, 2615, 2632-2637, 2639, 2642, 2643, 2645, 2647, 2650, 2656-2658, 2661-2669, 2679, 2691, 2692, 2694, 2695, 2701, 2704, 2705, 2713, 2715-2717, 2722, 2723, 2726, 2727, 2728, 2730-2732, 2734-2739, 2748, 2754, 2755, 2757, 2760-2763, 2779, 2780, 2785, 2786, 2793, 2795-2797, 2801, 2804, 2808, 2811, 2812, 2817, 2825, 2826, 2830, 2833, 2836, 2837, 2840, 2841, 2846, 2848, 2849, 2857, 2864, 2871, 2872, 2875, 2876, 2897, 2900, 2917, 2918, 2929, 2933, 2935, 2936-2951, 2953, 2959, 2965, 2969, 2978, 2981, 2982, 2984-2988, 2998, 3001, 3014, 3030-3032, 3042, 3044, 3045, 3048, 3049, 3055, 3057, 3058, 3064, 3066, 3074, 3075, 3077, 3079, 3080, 3081, 3089, 3094, 3109, 3111-3113, 3117, 3122-3126, 3129, 3132, 3134-3140, 3143, 3144, 3148, 3151, 3153, 3154, 3160, 3163, 3166-3168, 3172-3174, 3181-3183, 3193-3198, 3200, 3204, 3208, 3211, 3212, 3215, 3217, 3218, 3220, 3222, 3225, 3229, 3233, 3242, 3244, 3247, 3248, 3252-3254, 3256, 3261, 3262, 3265, 3270-3274, 3277, 3284, 3287, 3289, 3290, 3292, 3302, 3304, 3313, 3318, 3321, 3326, 3334, 3388, 3390, 3392, 3393, 3396, 3398, 3404, 3408, 3410, 3412, 3417, 3418, 3420, 3422-3429, 3432, 3434, 3438, 3442-3452, 3464, 3466, 3468, 3470, 3471, 3473-3480, 3488-3491, 3494, 3496, 3500, 3501, 3503-3518, 3521-3527, 3529-3545, 3547-3557, 3559, 3561, 3562, 3566-3572, 3574-3579, 3583-3595, 3597-3618, 3621-3623, 3626, 3627, 3630, 3634, 3635, 3638-3640, 3645-3655, 3657-3663, 3666-3670, 3678, 3682-3687, 3691-3698, 3702, 3703, 3707-3719, 3722-3730, 3732-3744, 3747-3750, 3762-3768, 3771-3773, 3776-3789, 3791-3807, 3809-3833, 3837, 3838, 3843-3845, 3849-3854, 3859, 3862-3866, 3868-3876, 3881-3883, 3885, 3887-3890, 3893-3902, 3906-3908, 3910, 3912-3914, 3918, 3926-3929, 3934-3936, 3940-3944, 3947, 3949, 3951-3955, 3957-3959, 3961, 3962, 3970-3978, 3980-3985, 3992-3995, 3997-4000, 4002-4004, 4006, 4009-4011, 4014, 4018, 4019, 4022, 4029, 4030, 4032, 4036-4040, 4044-4048, 4050-4055, 4061, 4069, 4070, 4075, 4082, 4083, 4085, 4086, 4092, 4095-4097, 4105-4109, 4113, 4114, 4123, 4124, 4127-4129, 4143, 4146, 4149, 4150, 4154, 4156-4160, 4169-4171, 4174, 4175, 4178, 4179, 4186, 4189-4191, 4196-4199, 4205, 4222, 4229-4235, 4238, 4240, 4241, 4245, 4246, 4249-4252, 4259-4262, 4265-4268, 4272-4279, 4281, 4289, 4296-4298, 4300, 4302, 4303, 4305, 4308-4319, 4326, 4338-4340, 4364, 4367, 4368, 4372, 4373, 4380, 4392, 4393, 4410, 4411, 4419, 4444, 4448, 4449, 4451, 4466-4472, 4494, 4498, 4501, 4502, 4515, 4526-4530, 4532-4535, 4537, 4538-4541, 4544-4546, 4556-4573, 4575-4578, 4580-4583, 4588, 4589, 4592-4594, 4596, 4597, 4599-4601, 4604, 4605, 4612-4614, 4616, 4620, 4622-4625, 4634-4636, 4644, 4652, 4655, 4656, 4667-4670, and 4672.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least a 70% inhibition of a DGAT2 mRNA, ISIS NOs: 413236, 413433, 413446, 423437, 423440-423445, 423447, 423449, 423450, 423452-423454, 423460-423465, 423522-423528, 423601-423604, 472204, 472205, 472208, 472349-472351, 483803, 483811-483814, 483816-483818, 483825, 483826, 483828-483835, 483838-483842, 483846, 483848, 483852, 483862, 483866, 483869, 483870, 483872-483875, 483879, 483887-483890, 483892, 483895, 483897-483903, 483908-483913, 483916-483921, 483923, 483924, 483926-483928, 483934, 483948-483950, 483952, 483954, 483968-483970, 483972, 483973, 483975, 483977-483979, 483984-483989, 483992-483994, 483996, 483997, 484001, 484004, 484006, 484010, 484012, 484017, 484019, 484020, 484030, 484031, 484041, 484049, 484056, 484064, 484069, 484070, 484071, 484073, 484082, 484083, 484085, 484089, 484094, 484099-484102, 484104, 484105, 484107, 484110, 484111, 484114-484118, 484126, 484127, 484129-484131, 484133, 484135-484137, 484139-484142, 484145-484148, 484156-484158, 484161, 484167, 484169-484172, 484178, 484180-484182, 484185, 484190, 484192-484194, 484198, 484202-484204, 484209, 484211, 484215, 484217-484220, 484231, 484232, 484235, 484241, 484248, 484249, 484263, 484265, 484267-484271, 484273, 484274, 484276, 484283-484285, 484290, 484292, 484293, 484301, 484302, 484320-484322, 484324, 484327, 484336, 484342-484344, 484346, 484348-484350, 484352, 484353, 484355-484357, 484359, 484368, 484370-484378, 484381-484383, 484390, 495425, 495429, 495430, 495440-495443, 495445-495454, 495456, 495458, 495461-495473, 495476, 495479-495485, 495487-495492, 495495-495499, 495501-495511, 495514-495531, 495533-495545, 495548-495556, 495558, 495560-495566, 495568-495580, 495584, 495585, 495588-495592, 495597-495600, 495602-495610, 495612-495614, 495616-495626, 495631-495633, 495636-495639, 495641-495643, 495649, 495650, 495656, 495657, 495661, 495664, 495666, 495669-495671, 495677, 495685, 495686, 495694, 495695, 495697, 495699-495702, 495705-495707, 495711, 495714, 495718-495720, 495724, 495730, 495731, 495736-495739, 495743-495746, 495748-495754, 495756, 495757, 495762, 495763, 495766, 495772, 495782, 495784, 495785, 495789, 495794, 495795, 495800, 495804, 495808-495813, 495817-495822, 495825-495833, 495835-495837, 495838-495844, 495848-495850, 495852-495857, 495859, 495860, 495867-495869, 495873-495878, 495882, 495899-495902, 495904, 495911, 495912, 495955, 495957, 495958, 495992, 500841, 500844, 500852, 500859, 500867, 500892, 500913, 500928, 500942, 500950, 500953, 500966, 500975, 500986, 500989, 500990, 500994, 500998, 501018-501020, 501025, 501030, 501033-501035, 501038-501041, 501062, 501064, 501067, 501069, 501093, 501094, 501097, 501098, 501100, 501103, 501111, 501118, 501122, 501123, 501127, 501128, 501154, 501165, 501171, 501176, 501183, 501184, 501199, 501200, 501210, 501212-501214, 501224, 501240, 501249, 501270, 501287, 501382-501385, 501387-501396, 501398-501402, 501404-501406, 501410-501412, 501414, 501426-501430, 501435, 501436, 501438-501443, 501445, 501447-501452, 501454-501457, 501849, 501850, 501852, 501855, 501861, 501871, 501883, 501884, 501886, 501890, 501916, 501932,

501944, 501946, 501950, 501951, 501959, 501960, 501966, 501968, 501981-501983, 502013, 502015, 502025, 502026, 502037, 502040, 502045, 502046, 502056, 502083, 502098, 502099, 502106, 502110, 502119, 502120, 502131, 502135, 502154-502156, 502163, 502164, 502175, 502179, 502189, 502191, 502194, 502220, 502319, 502322, 502334, 507663, 507679, 507684, 507692-507696, 507710, 507716-507718, 507724, 522363, 522366, 522368, 522370, 522373-522375, 522383-522385, 522399, 522404-522406, 522408, 522409, 522411, 522418, 522421, 522422, 522424, 522427, 522428, 522434-522437, 522440, 522442, 522444-522446, 522450, 522452, 522457, 522462-522467, 522470, 522473, 522474, 522478, 522479, 522482, 522484-522490, 522492, 522494-522496, 522501, 522503-522505, 522509, 522510, 522518, 522529, 522534, 522540, 522542-522550, 522552-522556, 522561, 522562, 522565, 522578-522582, 522587-522592, 522602-522610, 522612-522614, 522618, 522619, 522621, 522622, 522625, 522627, 522630-522638, 522642-522645, 522657, 522658, 522661-522663, 522666, 522667, 522671-522683, 522687-522694, 522696-522702, 522705, 522706, 522709, 522710, 522714-522719, 522722-522728, 522740, 522745-522748, 522754, 522757-522759, 522761, 522766-522771, 522776-522778, 522780, 522783, 522784, 522789, 522791, 522793, 522794, 522797, 522801, 522802, 522807, 522821, 522831, 522838, 522842, 522844, 522853, 522857, 522865, 522866, 522869-522872, 522877, 522878, 522888, 522889, 522894, 522897, 522898, 522905, 522913, 522917, 522924, 522925, 522932, 522939, 522940-522943, 522947, 522950, 522964, 522965, 522996, 523000, 523002, 523026, 525395, 525401, 525402, 525415, 525431, 525442, 525443, 525468-525472, 525474, 525477, 525479, 525480, 525499-525501, 525505, 525506, 525512, 525513, 525515, 525536, 525544, 525551-525554, 525578, 525612, 525631, 525688, 525705, 525708, 525711, 525733, and 525754.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least a 70% inhibition of a DGAT2 mRNA, SEQ ID NOs: 20, 38, 39, 46, 47, 62, 63, 103, 120, 121, 131, 144, 145, 150, 152, 153, 154, 182, 183, 202, 203, 204, 221, 225, 229, 246, 259, 283, 425, 438, 452, 453, 455-458, 460, 462-477, 479, 482-485, 487-496, 504-507, 509-511, 518, 519, 521-528, 531-535, 539, 541, 545, 555, 559, 562, 563, 565-568, 574, 575, 577, 594, 595, 597, 623, 624, 627, 653, 706, 710, 740, 742-744, 749-752, 754-756, 758, 760-766, 768, 769, 789, 808-811, 841-843, 845, 846, 848, 850-852, 880, 890, 893, 895, 897, 914-916, 939, 940, 960, 961, 973, 974, 981, 991-997, 1000, 1001, 1003-1008, 1015, 1020, 1024, 1032, 1034, 1036, 1043-1045, 1047-1049, 1052, 1059-1061, 1079, 1080, 1083, 1084, 1092, 1093, 1096, 1098, 1155, 1165, 1173-1176, 1178, 1181, 1183-1189, 1194-1199, 1202-1207, 1209, 1210, 1212-1214, 1220, 1234-1236, 1238, 1240, 1254-1256, 1258, 1259, 1261, 1263-1265, 1270-1275, 1278-1280, 1282, 1283, 1287, 1290, 1292, 1296, 1298, 1303, 1305, 1306, 1316, 1317, 1327, 1335, 1342, 1350, 1355-1357, 1359, 1368, 1369, 1371, 1375, 1380, 1385-1388, 1390, 1391, 1393, 1396, 1397, 1400-1404, 1412, 1413, 1415-1417, 1419, 1421-1423, 1425-1428, 1431-1434, 1442-1444, 1447, 1453, 1455-1458, 1464, 1466-1468, 1471, 1476, 1478-1480, 1484, 1488-1490, 1495, 1497, 1501, 1503-1506, 1517, 1518, 1521, 1527, 1534, 1535, 1549, 1551, 1553-1557, 1559, 1560, 1562, 1569-1571, 1576, 1578, 1579,

1587, 1588, 1606-1608, 1610, 1613, 1622, 1628-1630, 1632, 1634-1636, 1638, 1639, 1641-1643, 1645, 1654, 1656-1664, 1667-1669, 1676, 1677, 1698, 1702, 1703, 1713-1716, 1718-1727, 1729, 1731, 1734-1746, 1749, 1752-1758, 1760-1765, 1768-1772, 1774-1784, 1787-1804, 1806-1818, 1821-1829, 1831, 1833-1839, 1841-1853, 1857, 1858, 1861-1865, 1870-1873, 1875-1883, 1885-1887, 1889-1899, 1904-1906, 1909-1912, 1914-1916, 1922, 1923, 1929, 1930, 1934, 1937, 1939, 1942-1944, 1950, 1958, 1959, 1967, 1968, 1970, 1972-1975, 1978-1980, 1984, 1987, 1991-1993, 1997, 2003, 2004, 2009-2012, 2016-2019, 2021-2027, 2029, 2030, 2035, 2036, 2039, 2045, 2055, 2057, 2058, 2062, 2067, 2068, 2073, 2077, 2081-2086, 2090-2095, 2098-2106, 2108-2117, 2121-2123, 2125-2130, 2132, 2133, 2140-2142, 2146-2151, 2155, 2172-2175, 2177, 2184, 2185, 2228, 2230, 2231, 2265, 2308, 2310-2313, 2315-2324, 2326-2330, 2332-2334, 2338-2340, 2342, 2350, 2351, 2354-2358, 2363, 2364, 2366-2371, 2373, 2375-2380, 2382-2385, 2478, 2487, 2508, 2525, 2543, 2554, 2560, 2565, 2572, 2573, 2588, 2589, 2599, 2601-2603, 2613, 2632, 2633, 2636, 2637, 2639, 2642, 2650, 2657, 2661, 2662, 2666, 2667, 2691, 2695, 2715-2717, 2722, 2727, 2730-2732, 2735-2738, 2755, 2757, 2760, 2762, 2779, 2793, 2801, 2804, 2817, 2826, 2837, 2840, 2841, 2846, 2849, 2857, 2864, 2872, 2897, 2918, 2947, 2948, 2950, 2953, 2959, 2969, 2981, 2982, 2984, 2988, 3014, 3030, 3042, 3044, 3048, 3049, 3057, 3058, 3064, 3066, 3079-3081, 3111, 3113, 3123, 3124, 3135, 3138, 3143, 3144, 3154, 3173, 3181, 3196, 3197, 3204, 3208, 3217, 3218, 3229, 3233, 3252-3254, 3261, 3262, 3273, 3277, 3287, 3289, 3292, 3318, 3388, 3393, 3404, 3412, 3417, 3420, 3425-3429, 3432, 3443, 3449-3451, 3464, 3468, 3471, 3473, 3475, 3478-3480, 3488-3490, 3504, 3509-3511, 3513-3516, 3523, 3526, 3527, 3529, 3532, 3533, 3539-3542, 3545, 3547, 3549-3551, 3555, 3557, 3562, 3567-3572, 3575, 3578, 3579, 3583, 3584, 3587, 3589-3595, 3597, 3599-3601, 3606, 3608-3610, 3614, 3615, 3623, 3634, 3639, 3645, 3647-3655, 3657-3661, 3666, 3667, 3670, 3683-3687, 3692-3697, 3707-3715, 3717-3719, 3723, 3724, 3726, 3727, 3730, 3732, 3735-3743, 3747-3750, 3762, 3763, 3766-3768, 3771, 3772, 3776-3788, 3792-3799, 3801-3807, 3810, 3811, 3814, 3815, 3819-3824, 3827-3833, 3845, 3850-3853, 3859, 3862-3864, 3866, 3871-3876, 3881-3883, 3885, 3888, 3889, 3894, 3896, 3898, 3899, 3902, 3906, 3907, 3912, 3926, 3936, 3943, 3947, 3949, 3958, 3962, 3970, 3971, 3974-3977, 3982, 3983, 3993, 3994, 3999, 4002, 4003, 4010, 4018, 4022, 4029, 4030, 4037, 4044-4048, 4052, 4055, 4069, 4070, 4096, 4123, 4127, 4129, 4150, 4156, 4157, 4170, 4186, 4197, 4198, 4229-4233, 4235, 4238, 4240, 4241, 4260-4262, 4266, 4267, 4273, 4274, 4276, 4297, 4305, 4312-4315, 4339, 4373, 4392, 4449, 4466, 4469, 4472, 4494, 4515, 4526-4530, 4532, 4533, 4535, 4537-4540, 4545, 4546, 4558-4560, 4562-4570, 4573, 4575, 4576, 4578, 4580, 4582, 4588, 4589, 4592, 4596, 4600, 4601, 4604, 4612-4614, 4616, 4622-4625, 4634, 4635, 4652, 4667, and 4668.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least an 80% inhibition of a DGAT2 mRNA, ISIS NOs: 413433, 423463, 423464, 423523, 423524, 423526, 472351, 483817, 483825, 483826, 483828, 483830-483835, 483839-483841, 483848, 483852, 483866, 483869, 483870, 483873-483875, 483887, 483889, 483890, 483895, 483897, 483898, 483900, 483901, 483908-483910, 483913, 483916, 483919, 483921,

483923, 483924, 483927, 483952, 483968-483970, 483972, 483984, 483986-483988, 483992, 483993, 483996, 483997, 484004, 484017, 484031, 484041, 484049, 484064, 484070, 484085, 484094, 484099, 484100, 484115-484117, 484126, 484127, 484129-484131, 484133, 484137, 484139-484141, 484148, 484156-484158, 484167, 484169-484171, 484181, 484182, 484192, 484193, 484203, 484204, 484209, 484215, 484217, 484218, 484220, 484231, 484235, 484249, 484267-484271, 484273, 484283, 484284, 484292, 484293, 484301, 484327, 484336, 484343, 484344, 484348, 484350, 484353, 484357, 484368, 484377, 484378, 495425, 495429, 495440, 495442, 495446, 495449-495451, 495453, 495454, 495463, 495464, 495466, 495467, 495469-495472, 495481, 495482, 495484, 495485, 495488-495492, 495495-495498, 495505-495510, 495514-495531, 495533-495537, 495539-495541, 495543-495545, 495550-495556, 495560, 495561-495564, 495566, 495568-495578, 495585, 495591, 495598-495600, 495604, 495606, 495608, 495609, 495618-495622, 495639, 495649, 495650, 495685, 495686, 495697, 495702, 495705-495707, 495718, 495730, 495736, 495738, 495739, 495744, 495745, 495749, 495751-495753, 495756, 495785, 495808-495810, 495817-495820, 495822, 495825-495832, 495835-495844, 495849, 495852-495854, 495856, 495857, 495867-495869, 495874-495878, 495902, 495992, 500859, 500867, 500913, 500998, 501020, 501034, 501035, 501064, 501094, 501098, 501100, 501103, 501127, 501183, 501199, 501213, 501385, 501387-501393, 501396, 501398, 501404-501406, 501411, 501412, 501427-501430, 501435, 501436, 501438, 501440, 501442, 501443, 501447-501452, 501454-501855, 501861, 501884, 501944, 501950, 501983, 502040, 502046, 502056, 502083, 502099, 502119, 502154, 502164, 502175, 502179, 502189, 502191, 502319, 507692, 507694, 507696, 507717, 522366, 522373-522375, 522383, 522435-522437, 522444, 522445, 522450, 522465, 522473, 522484, 522485, 522495, 522501, 522509, 522529, 522546, 522550, 522553-522556, 522579-522582, 522587-522589, 522606-522610, 522618, 522621, 522627, 522630-522632, 522634, 522638, 522643, 522645, 522667, 522671, 522672, 522674-522683, 522687-522692, 522694, 522696-522700, 522705, 522709, 522715-522719, 522745, 522757, 522770, 522783, 522784, 522807, 522865, 522866, 522888, 522889, 522897, 522913, 522942, 522964, 523002, 525401, 525469, 525470, 525501, and 525612.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least a 80% inhibition of a DGAT2 mRNA, SEQ ID NOs: 103, 120, 121, 131, 144, 145, 150, 152, 153, 182, 204, 246, 259, 283, 425, 456, 457, 462, 463, 467-469, 487-490, 504, 506, 509, 510, 518, 519, 521, 523, 524-528, 532-534, 541, 545, 559, 562, 563, 566-568, 594, 742, 750, 751, 762, 808-810, 843, 845, 893, 915, 939, 973, 993-995, 997, 1000, 1001, 1005, 1006, 1008, 1034, 1060, 1061, 1079, 1084, 1173, 1175, 1176, 1181, 1183, 1184, 1186, 1187, 1194-1196, 1199, 1202, 1205, 1207, 1209, 1210, 1213, 1238, 1254-1256, 1258, 1270, 1272-1274, 1278, 1279, 1282, 1283, 1290, 1303, 1317, 1327, 1335, 1350, 1356, 1371, 1380, 1385, 1386, 1401-1403, 1412, 1413, 1415-1417, 1419, 1423, 1425-1427, 1434, 1442-1444, 1453, 1455-1457, 1467, 1468, 1478, 1479, 1489, 1490, 1495, 1501, 1503, 1504, 1506, 1517, 1521, 1535, 1553-1557, 1559, 1569, 1570, 1578, 1579, 1587, 1613, 1622, 1629, 1630, 1634,

1636, 1639, 1643, 1654, 1663, 1664, 1677, 1698, 1702, 1713, 1715, 1719, 1722-1724, 1726, 1727, 1736, 1737, 1739, 1740, 1742-1745, 1754, 1755, 1757, 1758, 1761-1765, 1768-1771, 1778-1783, 1787-1804, 1806-1810, 1812-1814, 1816-1818, 1823-1829, 1833-1837, 1839, 1841-1851, 1858, 1864, 1871-1873, 1877, 1879, 1881, 1882, 1891-1895, 1912, 1922, 1923, 1958, 1959, 1970, 1975, 1978-1980, 1991, 2003, 2009, 2011, 2012, 2017, 2018, 2022, 2024-2026, 2029, 2058, 2081-2083, 2090-2093, 2095, 2098-2105, 2108-2117, 2122, 2125-2127, 2129, 2130, 2140-2142, 2147-2151, 2175, 2265, 2313, 2315-2321, 2324, 2326, 2332-2334, 2339, 2340, 2355-2358, 2363, 2364, 2366, 2368, 2370, 2371, 2375-2380, 2382, 2383, 2572, 2588, 2602, 2633, 2637, 2639, 2642, 2666, 2695, 2717, 2731, 2732, 2757, 2864, 2872, 2918, 2953, 2959, 2982, 3042, 3048, 3081, 3138, 3144, 3154, 3181, 3197, 3217, 3252, 3262, 3273, 3277, 3287, 3289, 3404, 3417, 3425, 3427, 3429, 3450, 3471, 3478-3480, 3488, 3540-3542, 3549, 3550, 3555, 3570, 3578, 3589, 3590, 3600, 3606, 3614, 3634, 3651, 3655, 3658-3661, 3684-3687, 3692-3694, 3711-3715, 3723, 3726, 3732, 3735-3737, 3739, 3743, 3748, 3750, 3772, 3776, 3777, 3779-3788, 3792-3797, 3799, 3801-3803, 3805, 3810, 3814, 3820-3824, 3850, 3862, 3875, 3888, 3889, 3912, 3970, 3971, 3993, 3994, 4002, 4018, 4047, 4069, 4129, 4156, 4230, 4231, 4262, 4373, 4526, 4529, 4532, 4538, 4540, 4560, 4562-4564, 4566-4570, 4578, 4623, 4625, and 4667.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least a 90% inhibition of a DGAT2 mRNA, ISIS NOs: 413433, 423463, 483817, 483825, 483834, 483848, 483866, 483869, 483873, 483874, 483895, 483898, 483908, 483910, 483913, 483952, 484085, 484148, 484157, 484170, 484181, 484231, 484271, 484283, 484350, 484353, 495449, 495450, 495495, 495498, 495505, 495506, 495516-495520, 495522-495524, 495526, 495527, 495535, 495553-495555, 495562, 495563, 495570, 495571, 495575-495577, 495620, 495752, 495809, 495825, 495829, 495836, 495837, 495839-495842, 495853, 495857, 495876, 495878, 501385, 501387, 501404, 501412, 501427, 501430, 501442, 501443, 501447, 501448, 501450, 501452, 501861, 522632, 522688, and 522745.

In certain embodiments, the following antisense compounds or antisense oligonucleotides target a region of a DGAT2 nucleic acid and effect at least a 90% inhibition of a DGAT2 mRNA, SEQ ID NOs: 283, 425, 457, 467, 510, 518, 527, 541, 559, 562, 566, 567, 1181, 1184, 1194, 1196, 1199, 1238, 1371, 1434, 1443, 1456, 1467, 1517, 1557, 1569, 1636, 1639, 1722, 1723, 1768, 1771, 1778, 1779, 1789-1793, 1795-1797, 1799, 1800, 1808, 1826-1828, 1835, 1836, 1843, 1844, 1848-1850, 1893, 2025, 2082, 2098, 2102, 2109, 2110, 2112-2115, 2126, 2130, 2149, 2151, 2313, 2315, 2332, 2340, 2355, 2358, 2370, 2371, 2375, 2376, 2378, 2380, 2959, 3737, 3793, 3850, 4562, 4564, 4566, 4568, and 4569.

In certain embodiments, a compound comprises a modified oligonucleotide consisting of 8 to 80 linked nucleosides having at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobase portion complementary to an equal length portion within nucleotides 26778-26797, 23242-23261, 26630-26649,15251-15270, 28026-28045, 35436-35455, 10820-10836, 23246-23262 of SEQ ID NO: 2

In certain embodiments, a compound comprises a modified oligonucleotide consisting of 10 to 30 linked nucleosides complementary within nucleotides 26778-26797, 23242-23261, 26630-26649,15251-15270, 28026-28045, 35436-35455, 10820-10836, 23246-23262 of SEQ ID NO: 2.

In certain embodiments, a compound comprises a modified oligonucleotide consisting of 8 to 80 linked nucleosides having a nucleobase sequence comprising at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobase portion any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373.

In certain embodiments, a compound comprises a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373.

In certain embodiments, a compound comprises a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, a modified oligonucleotide targeted to DGAT2 is ISIS 484137, 484085, 484129, 495576, 501861, 502194, 525443, and 525612.

In certain embodiments, a modified oligonucleotide targeted to DGAT2 is ISIS 484137, 484085, 484129, 495576, 501861, 502194, 525443, and 525612. Out of about 5,000 antisense oligonucleotides that were screened as described in the Examples section below, ISIS 484137, 484085, 484129, 495576, 501861, 502194, 525443, and 525612 emerged as the top lead compounds. In particular, ISIS 484137 exhibited the best combination of properties in terms of potency and tolerability out of about 5,000 antisense oligonucleotides.

In certain embodiments, any of the foregoing compounds or oligonucleotides comprises at least one modified internucleoside linkage, at least one modified sugar, and/or at least one modified nucleobase.

In certain aspects, any of the foregoing compounds or oligonucleotides comprises at least one modified sugar. In certain aspects, at least one modified sugar comprises a 2'-O-methoxyethyl group. In certain aspects, at least one modified sugar is a bicyclic sugar, such as a 4'-$CH(CH_3)$-O-2' group, a 4'-CH_2-O-2' group, or a 4'-$(CH_2)_2$-O-2'group.

In certain aspects, the modified oligonucleotide comprises at least one modified internucleoside linkage, such as a phosphorothioate internucleoside linkage.

In certain embodiments, any of the foregoing compounds or oligonucleotides comprises at least one modified nucleobase, such as 5-methylcytosine.

In certain embodiments, any of the foregoing compounds or oligonucleotides comprises:

a gap segment consisting of linked 2'-deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar. In certain embodiments, the oligonucleotide consists of 8 to 80 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain aspects, the oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373.

In certain aspects, the modified oligonucleotide has a nucleobase sequence comprising the sequence recited in SEQ ID NO: 1423, 1371, 1415, 1849, 2959, or 3292, wherein the modified oligonucleotide comprises

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment, wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; wherein each internucleoside linkage is a phosphorothioate linkage and wherein each cytosine is a 5-methylcytosine. In certain embodiments, the modified oligonucleotide consists of 20-80 linked nucleosides. In certain embodiments, the modified oligonucleotide consists of 20-30 linked nucleosides.

In certain aspects, the modified oligonucleotide has a nucleobase sequence comprising the sequence recited in SEQ ID NO: 4198 or 4373, wherein the modified oligonucleotide comprises

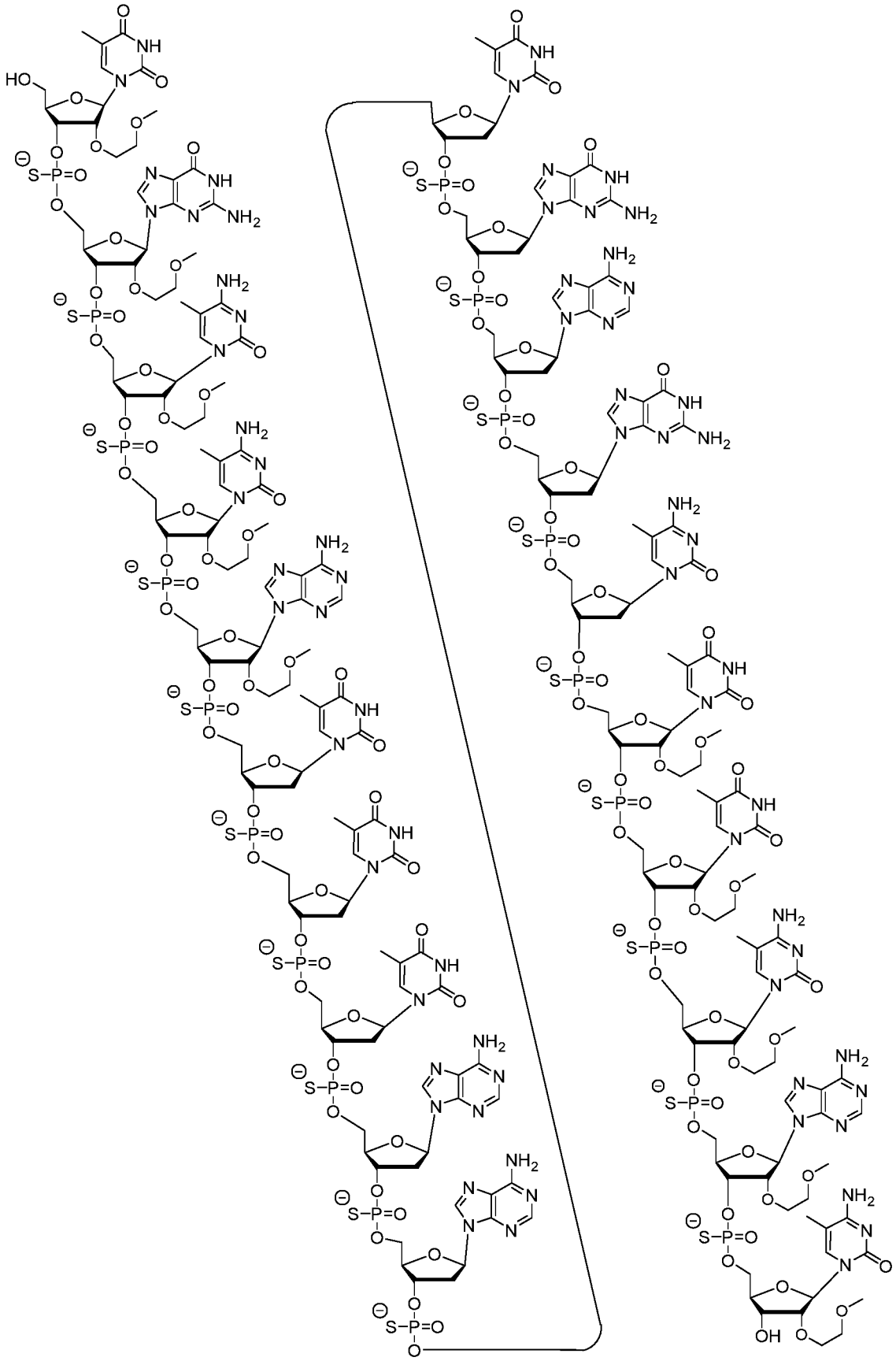
a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of three linked nucleosides; and

a 3' wing segment consisting of four linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment, wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; wherein each internucleoside linkage is a phosphorothioate linkage and wherein each cytosine is a 5-methylcytosine. In certain embodiments, the modified oligonucleotide consists of 17-80 linked nucleosides. In certain embodiments, the modified oligonucleotide consists of 17-30 linked nucleosides.

In certain embodiments, a compound comprises or consists of ISIS 484137 and has the following chemical structure or a salt thereof:



In certain embodiments, a compound comprises or consists of ISIS 484137, named by accepted oligonucleotide nomenclature, showing each 3′-*O* to 5′-*O*-linked phosphorothioate diester internucleotide linkage as follows:

2′-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl) -*P*-thioguanylyl-(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-5-methyl-*P*- thiocytidylyl -(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-*P*- thioadenylyl -(3′-*O*→5′-*O*)-*P*- thiothymidylyl -(3′-*O*→5′-*O*)-*P*- thiothymidylyl -(3′-*O*→5′-*O*)-*P*-thiothymidylyl-(3′-*O*→5′-*O*)-2′-deoxy-*P*- thioadenylyl -(3′-*O*→5′-*O*)-2′-deoxy-*P*- thioadenylyl -(3′-*O*→5′-*O*)-*P*-thiothymidylyl-(3′-*O*→5′-*O*)-2′-deoxy-*P*-thioguanylyl-(3′-*O*→5′-*O*)-2′-deoxy-*P*- thioadenylyl -(3′-*O*→5′-*O*)-2′-deoxy-*P*- thioguanylyl -(3′-*O*→5′-*O*)-2′-deoxy-5-methyl-*P*-thiocytidylyl-(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl -(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-5-methyl-*P*- thiouridylyl -(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-5-methyl-*P*- thiocytidylyl -(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-*P*- thioadenylyl -(3′-*O*→5′-*O*)-2′-*O*-(2-methoxyethyl)-5-methyl-cytidine, 19 sodium salt.

In any of the foregoing embodiments, the compound or oligonucleotide can be at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% complementary to a nucleic acid encoding DGAT2.

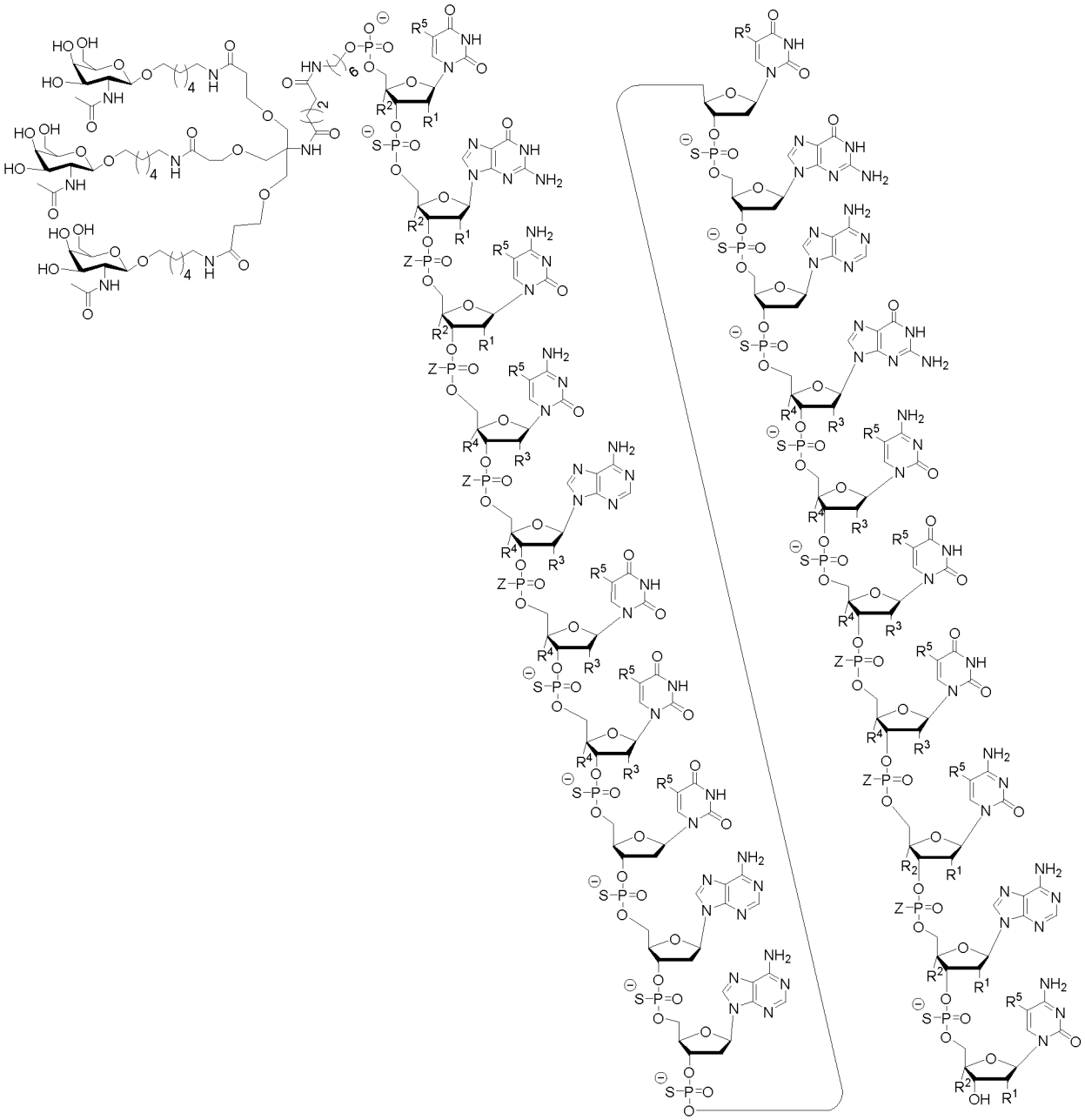
In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide.

In any of the foregoing embodiments, the oligonucleotide can consist of 8 to 80, 10 to 30, 12 to 50, 13 to 30, 13 to 50, 14 to 30, 14 to 50, 15 to 30, 15 to 50, 16 to 30, 16 to 50, 17 to 30, 17 to 50, 18 to 22, 18 to 24, 18 to 30, 18 to 50, 19 to 22, 19 to 30, 19 to 50, or 20 to 30 linked nucleosides.

In certain embodiments, compounds or compositions provided herein comprise a salt of the modified oligonucleotide. In certain embodiments, the salt is a sodium salt. In certain embodiments, the salt is a potassium salt.

In certain embodiments, a compound comprises a modified oligonucleotide described herein and a conjugate group. In certain embodiments, the conjugate group is linked to the modified oligonucleotide at the 5’ end of the modified oligonucleotide. In certain embodiments, the conjugate group is linked to the modified oligonucleotide at the 3’ end of the modified oligonucleotide. In certain embodiments, the conjugate group comprises at least one N- Acetylgalactosamine (GalNAc), at least two N- Acetylgalactosamines (GalNAcs), or at least three N- Acetylgalactosamines (GalNAcs).

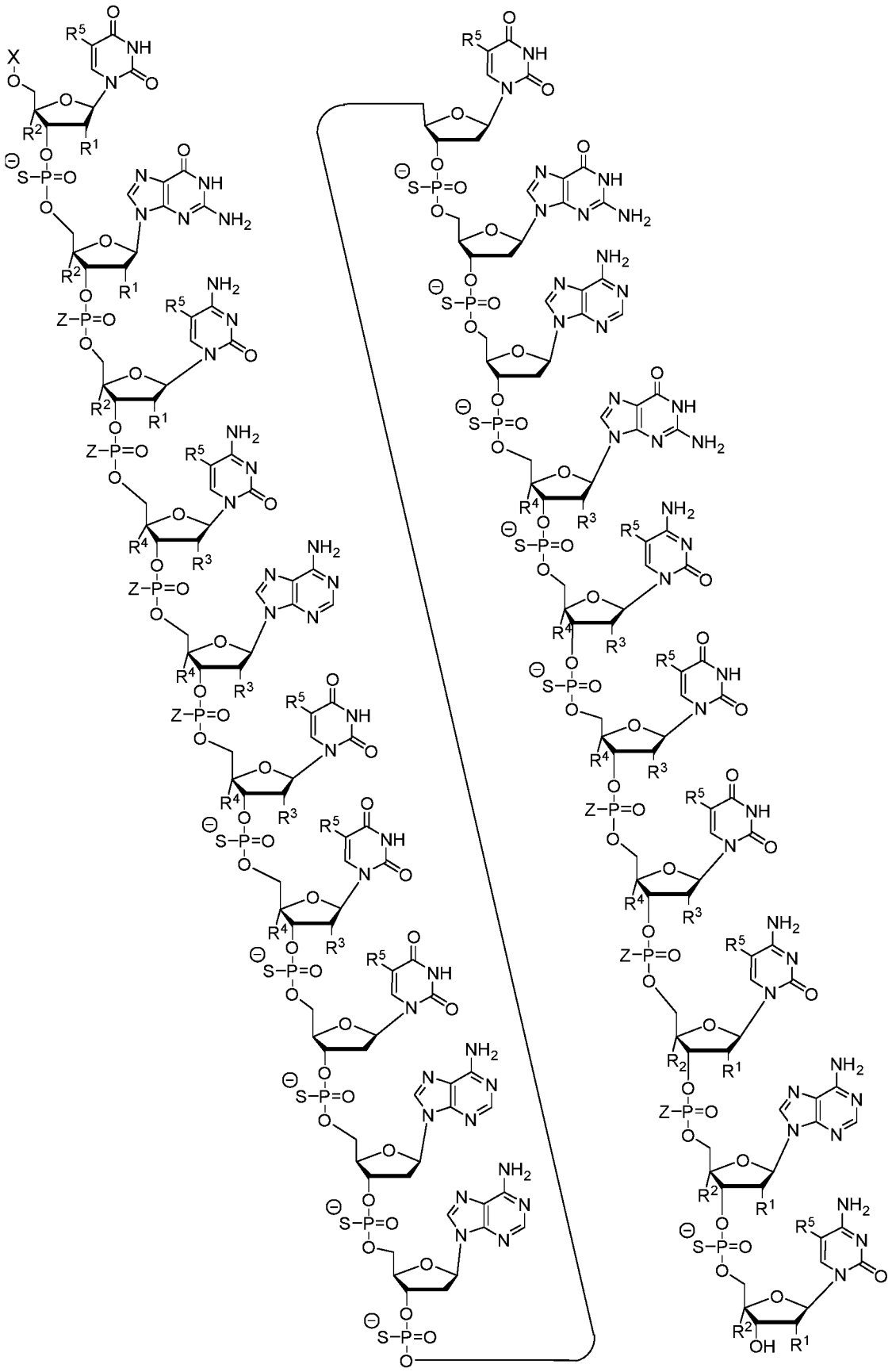
In certain embodiments, a compound having the following chemical structure comprises or consists of ISIS 484137 or salt thereof with a conjugate group comprising GalNAc as described herein:



wherein for each pair of R_1 and R_2 on the same ring, independently for each ring, either R_1 is –$OCH_2CH_2OCH_3$ (MOE) and R_2 is H; or R_1 and R_2 together form a bridge, wherein R_1 is –O- and R_2 is –CH_2-, -$CH(CH_3)$-, or -CH_2CH_2-, and R_1 and R_2 are directly connected such that the resulting bridge is selected from: -O-CH_2-, -O-$CH(CH_3)$-, and –O-CH_2CH_2-; and for each pair of R_3 and R_4 on the same ring, independently for each ring: either R_3 is selected from H and -$OCH_2CH_2OCH_3$ and R_4 is H; or R_3 and R_4 together form a bridge, wherein R_3 is –O-, and R_4 is –CH_2-, -$CH(CH_3)$-, or -CH_2CH_2-, and R_3 and R_4 are directly connected such that

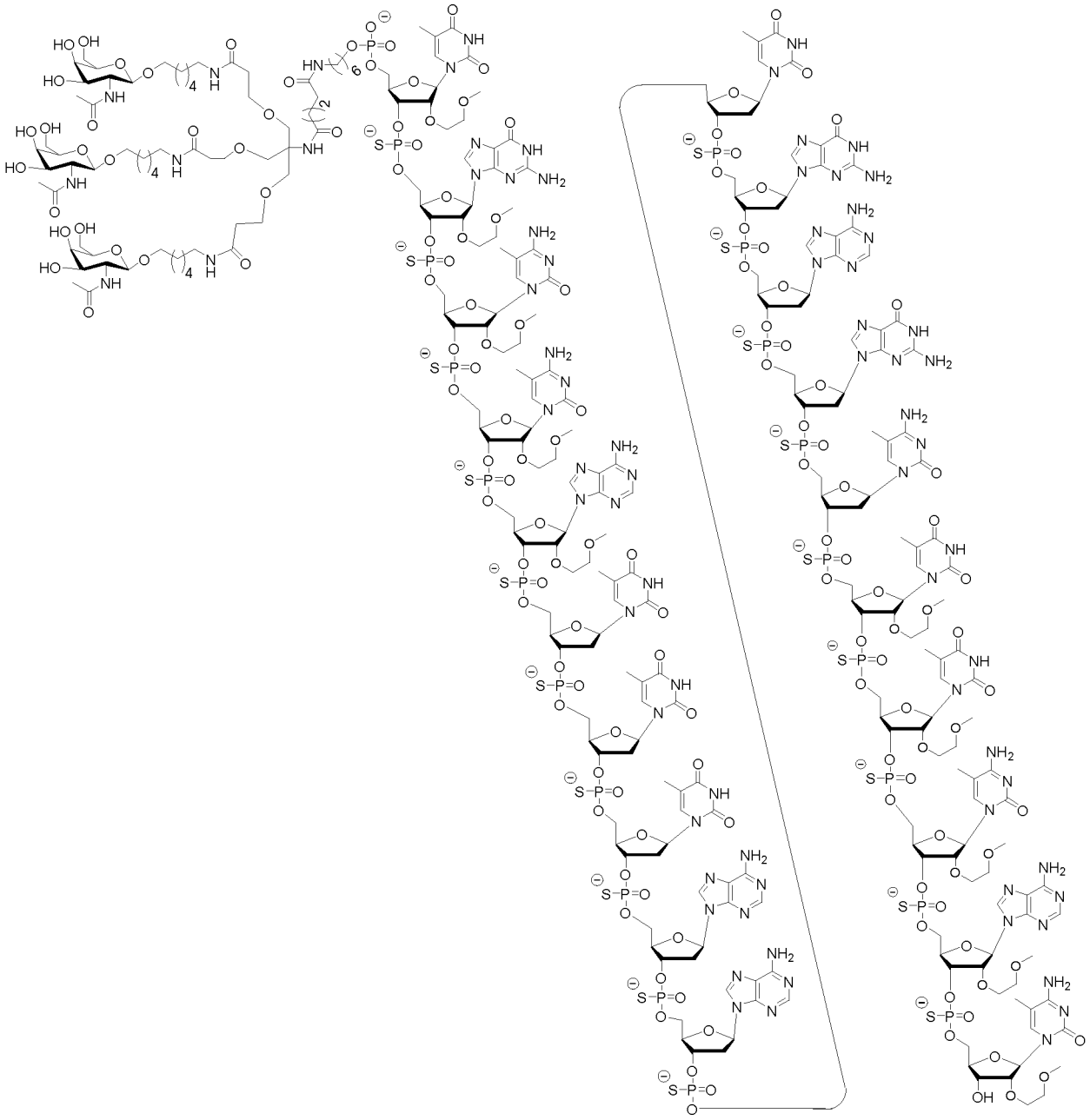
the resulting bridge is selected from: $-O-CH_2-$, $-O-CH(CH_3)-$, and $-O-CH_2CH_2-$; and each R_5 is independently selected from H and $-CH_3$; and each Z is independently selected from S- and O-.

In certain embodiments, a compound comprises or consists of SEQ ID NO: 1423, 5'-GalNAc, and chemical modifications as represented by the following chemical structure:

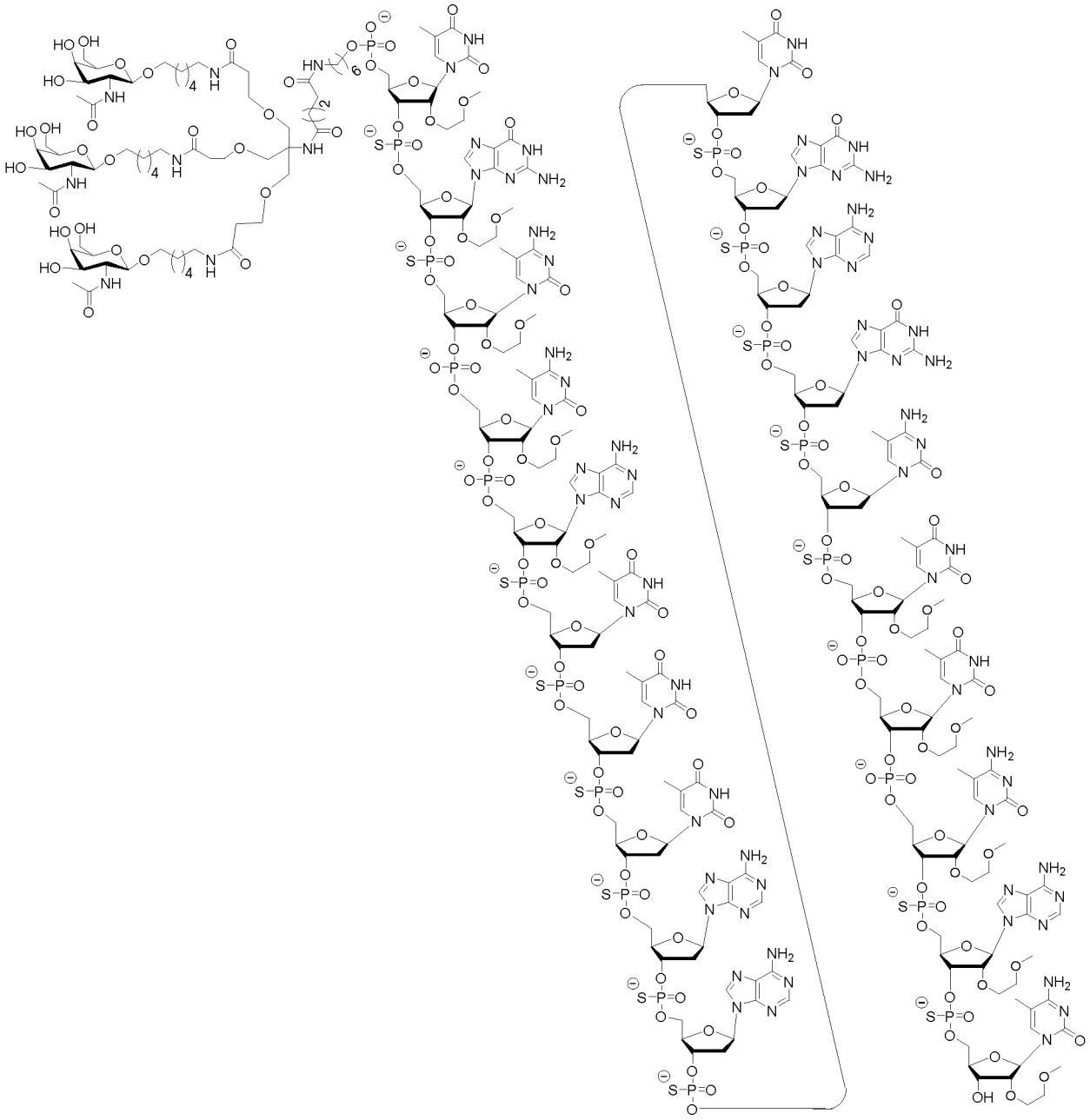


wherein for each pair of R_1 and R_2 on the same ring, independently for each ring, either R_1 is –$OCH_2CH_2OCH_3$ (MOE) and R_2 is H; or R_1 and R_2 together form a bridge, wherein R_1 is –O- and R_2 is –CH_2-, -$CH(CH_3)$-, or -CH_2CH_2-, and R_1 and R_2 are directly connected such that the resulting bridge is selected from: -O-CH_2-, -O-$CH(CH_3)$-, and –O-CH_2CH_2-; and for each pair of R_3 and R_4 on the same ring, independently for each ring: either R_3 is selected from H and -$OCH_2CH_2OCH_3$ and R_4 is H; or R_3 and R_4 together form a bridge, wherein R_3 is –O-, and R_4 is –CH_2-, -$CH(CH_3)$-, or -CH_2CH_2-, and R_3 and R_4 are directly connected such that the resulting bridge is selected from: -O-CH_2-, -O-$CH(CH_3)$-, and –O-CH_2CH_2-; and each R_5 is independently selected from H and –CH_3; and each Z is independently selected from S- and O-; and X is H or a conjugate group that optionally comprises a conjugate linker and/or cleavable moiety.

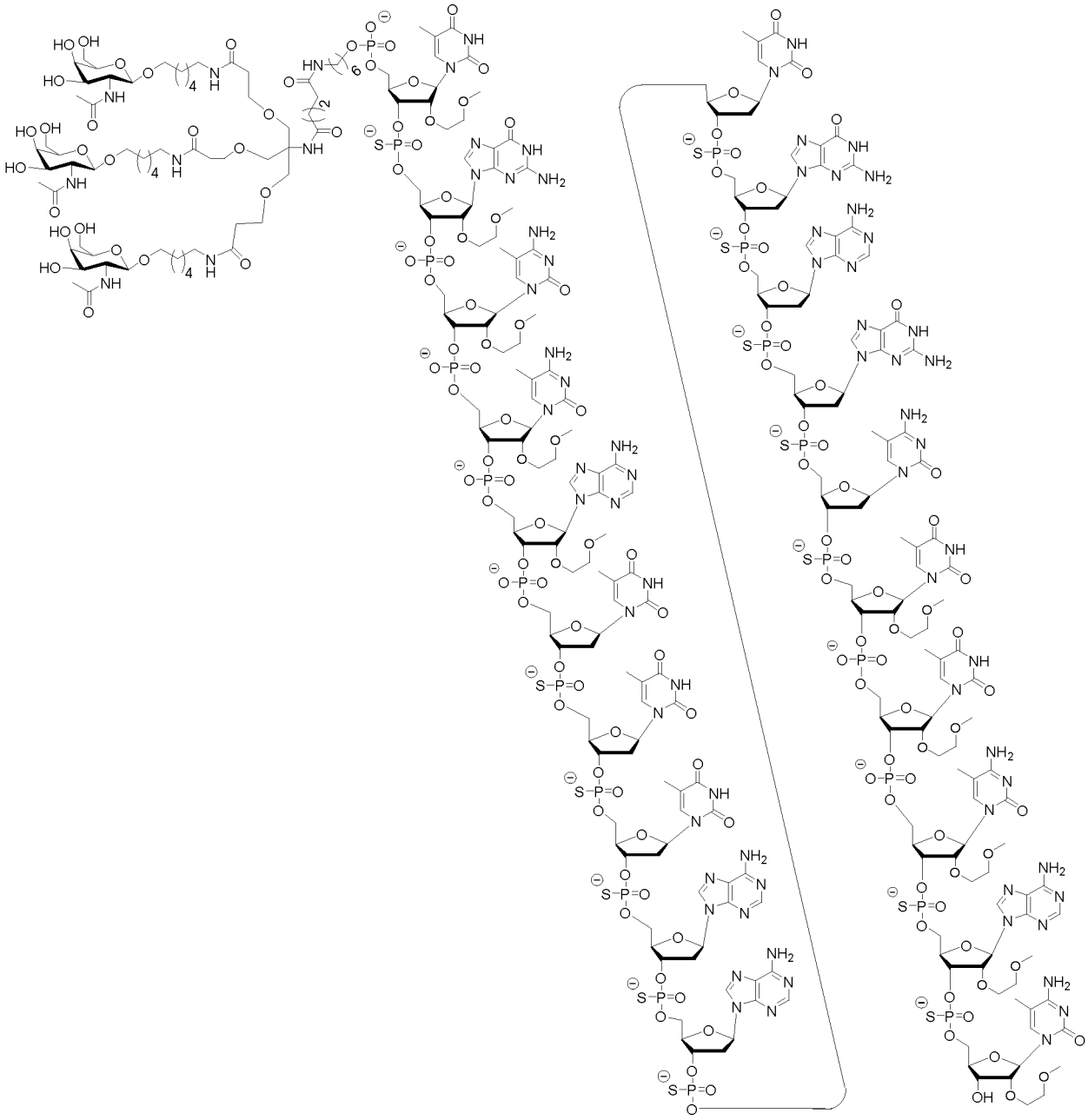
In certain embodiments, a compound comprises ISIS 769355 or salt thereof. In certain embodiments, a compound consists of ISIS 769355 or salt thereof. In certain embodiments, ISIS 769355 has the following chemical structure:



In certain embodiments, a compound comprises ISIS 769356 or salt thereof. In certain embodiments, a compound consists of ISIS 769356 or salt thereof. In certain embodiments, ISIS 769356 has the following chemical structure:



In certain embodiments, a compound comprises ISIS 769357 or salt thereof. In certain embodiments, a compound consists of ISIS 769357 or salt thereof. In certain embodiments, ISIS 769357 has the following chemical structure:



Certain embodiments provide compositions comprising any of the compounds comprising or consisting of a modified oligonucleotide targeted to DGAT2 or salt thereof and a conjugate group, and at least one of a pharmaceutically acceptable carrier or diluent.

In certain embodiments, the compounds or compositions as described herein are efficacious by virtue of having at least one of an *in vitro* IC_{50} of less than 2 nM, less than 3 nM, less than 4 nM, less than 5 nM,

less than 6 nM, less than 7 nM, less than 8 nM, less than 9 nM, less than 10 nM, less than 20 nM, less than 30 nM, less than 35 nM, less than 40 nM, less than 45 nM, less than 50 nM, less than 60 nM, less than 70 nM, less than 80 nM, less than 90 nM, less than 100 nM, less than 110 nM, less than 300 nM, less than 400 nM, less than 500 nM, less than 600 nM, less than 700 nM, less than 800 nM, less than 900 nM, less than 1 μM, less than 1.1 μM, less than 1.2 μM, less than 1.3 μM, less than 1.4 μM, less than 1.5 μM, less than 1.6 μM, less than 1.7 μM, less than 1.8 μM, less than 1.9 μM, less than 2 μM, less than 2.5 μM, less than 3 μM, less than 3.5 μM, less than 4 μM, less than 4.5 μM, less than 5 μM, less than 5.5 μM, less than 6 μM, less than 6.5 μM, or less than 10 μM.

In certain embodiments, the compounds or compositions as described herein are highly tolerable as demonstrated by having at least one of an increase an ALT or AST value of no more than 4 fold, 3 fold, or 2 fold over saline treated animals or an increase in liver, spleen, or kidney weight of no more than 30%, 20%, 15%, 12%, 10%, 5%, or 2%. In certain embodiments, the compounds or compositions as described herein are highly tolerable as demonstrated by having no increase of ALT or AST over saline treated animals. In certain embodiments, the compounds or compositions as described herein are highly tolerable as demonstrated by having no increase in liver, spleen, or kidney weight over saline treated animals.

Certain Indications

Certain embodiments provided herein relate to methods of treating, preventing, or ameliorating a disease associated with DGAT2 in an individual by administration of a DGAT2 specific inhibitor, such as an antisense compound targeted to DGAT2.

Examples of diseases associated with DGAT2 treatable, preventable, and/or ameliorable with the methods provided herein include nonalcoholic fatty liver diseases (NAFLD), nonalcoholic steatohepatitis (NASH), hepatic steatosis, fatty liver diseases, lipodystrophy syndromes, including congential generalized lipodystrophy (CGL), acquired generalized lipodystrophy (AGL), familial partial lipodystrophy (FPL), and acquired partial lipodystrophy (PL), metabolic syndrome and cardiovascular diseases.

In certain embodiments, a method of treating, preventing, or ameliorating a disease associated with NAFLD in an individual comprises administering to the individual a specific inhibitor of DGAT2, thereby treating, preventing, or ameliorating the disease. In certain embodiments, a method of treating, preventing, or ameliorating a disease associated with lipodystrophy syndrome in an individual comprises administering to the individual a specific inhibitor of DGAT2, thereby treating, preventing, or ameliorating the disease. In certain embodiments, the lipodystrophy syndrome is partial lipodystrophy. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or

consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide.

In certain embodiments, a method of treating, preventing, or ameliorating NAFLD/NASH comprises administering to the individual a DGAT2 specific inhibitor, thereby treating, preventing, or ameliorating NALFD/NASH. In certain embodiments, a method of treating, preventing, or ameliorating lipodystrophy comprises administering to the individual a DGAT2 specific inhibitor, thereby treating, preventing, or ameliorating lipodystrophy syndrome. In certain embodiments, the lipodystrophy syndrome is partial lipodystrophy. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific

inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide. In certain aspects, the antisense compound is administered to the individual parenterally. In certain aspects, administering the antisense compound results in specific reduction of DGAT2 expression, reduction in the rate of triglyceride synthesis, improvement of hepatic steatosis and blood lipid levels, reduction of hepatic lipids, reversal of diet-induced hepatic insulin resistance, and improvement in hepatic insulin sensitivity. In certain aspects, administering the antisense compound results in reduction in liver steatosis and fibrosis. In certain aspects, administering the antisense compound results in improvements in ALT levels. In certain aspects, administering the antisense compound results in decrease in NAFLD Activity Score (NAS). In certain aspects, administering the antisense compound results in reduction in serum total cholesterol and triglycerides. In certain aspects, administering the antisense compound results in neutral insulin sensitivity and glycemic control. In certain aspects, administering the antisense compound results in improved insulin sensitivity and glycemic control. In certain aspects, the individual is identified as having or at risk of having a disease associated with NAFLD. In certain aspects, the individual is identified as having or at risk of having a disease associated with lipodystrophy syndrome.

In certain embodiments, a method of inhibiting expression of DGAT2 in an individual having, or at risk of having, a disease associated with NAFLD comprises administering a DGAT2 specific inhibitor to the individual, thereby inhibiting expression of DGAT2 in the individual. In certain embodiments, a method of inhibiting expression of DGAT2 in an individual having, or at risk of having, a disease associated with lipodystrophy syndrome comprises administering a DGAT2 specific inhibitor to the individual, thereby inhibiting expression of DGAT2 in the individual. In certain aspects, administering the inhibitor inhibits

expression of DGAT2 in the liver. In certain aspects, administering the inhibitor inhibits expression of DGAT2 in adipose tissue. In certain aspects, the individual has, or is at risk of having lipodystrophy syndrome, partial lipodystrophy, liver steatosis, NAFLD, or NASH. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide.

In certain embodiments, a method of reducing or inhibiting triglyceride synthesis, hepatic lipid synthesis and insulin resistance in the liver of an individual having, or at risk of having, a disease associated with DGAT2 comprises administering a DGAT2 specific inhibitor to the individual, thereby reducing or inhibiting triglyceride synthesis, hepatic lipid synthesis and insulin resistance in the liver of the individual. In certain embodiments, a method of reducing or inhibiting triglyceride synthesis, lipid synthesis and insulin resistance in the adipose tissue of an individual having, or at risk of having, a disease associated with DGAT2 comprises administering a DGAT2 specific inhibitor to the individual, thereby reducing or inhibiting triglyceride synthesis, lipid synthesis and insulin resistance in the adipose tissue of the individual. In certain

aspects, administering the DGAT2 inhibitor leads to improvement in hepatic insulin signaling, hepatic insulin sensitivity and cardiovascular risk profile. In certain aspects, administering the DGAT2 specific inhibitor results in reduction in liver steatosis and fibrosis. In certain aspects, administering the DGAT2 specific inhibitor results in improvements in ALT levels. In certain aspects, administering the DGAT2 specific inhibitor results in decrease in NAFLD Activity Score (NAS). In certain aspects, administering the DGAT2 specific inhibitor results in reduction in serum total cholesterol and triglycerides. In certain aspects, administering the DGAT2 specific inhibitor results in neutral insulin sensitivity and glycemic control. In certain aspects, administering the antisense compound results in improved insulin sensitivity and glycemic control. In certain aspects, the individual has, or is at risk of having, NAFLD or NASH. In certain aspects, the individual has, or is at risk of having, lipodystrophy syndrome or partial lipodystrophy. In certain aspects, the inhibitor is an antisense compound targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can

be a single-stranded oligonucleotide. In certain aspects, the antisense compound is administered to the individual parenterally.

Certain embodiments are drawn to a DGAT2 specific inhibitor for use in treating a disease associated with NAFLD. In certain aspects, the disease is NASH. In certain aspects, the disease is hepatic steatosis. In certain aspects, the disease is liver cirrhosis. In certain aspects, the disease is hepatocellular carcinoma. Certain embodiments are drawn to a DGAT2 specific inhibitor for use in treating a disease associated with lipodystrophy syndromes. In certain aspects, the disease is partial lipodystrophy. In certain aspects, the inhibitor is an antisense compound targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide. In certain aspects, the antisense compound is administered to the individual parenterally.

Certain embodiments are drawn to a DGAT2 specific inhibitor for reducing or inhibiting triglyceride synthesis, hepatic lipid synthesis and insulin resistance in the liver of an individual having, or at risk of

having, a disease associated with NAFLD or lipodystrophy syndromes comprises administering a DGAT2 specific inhibitor to the individual, thereby reducing or inhibiting triglyceride synthesis, hepatic lipid synthesis and insulin resistance in the liver of the individual. Certain embodiments are drawn to a DGAT2 specific inhibitor for reducing or inhibiting triglyceride synthesis, lipid synthesis and insulin resistance in the adipose tissue of an individual having, or at risk of having, a disease associated with NAFLD or lipodystrophy syndromes comprises administering a DGAT2 specific inhibitor to the individual, thereby reducing or inhibiting triglyceride synthesis, lipid synthesis and insulin resistance in the adipose tissue of the individual. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide.

Certain embodiments are drawn to use of a DGAT2 specific inhibitor for the manufacture of a medicament for treating a disease associated with NAFLD. In certain aspects, the disease is NASH. In certain aspects, the disease is hepatic steatosis. In certain aspects, the disease is liver cirrhosis. In certain aspects, the disease is hepatocellular carcinoma. Certain embodiments are drawn to use of a DGAT2 specific

inhibitor for the manufacture of a medicament for treating a disease associated with lipodystrophy syndromes. In certain aspects, the disease is partial lipodystrophy. In certain aspects, the inhibitor is an antisense compound targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide. In certain aspects, the antisense compound is administered to the individual parenterally.

Certain embodiments are drawn to use of a DGAT2 specific inhibitor for the manufacture of a medicament for reducing or inhibiting triglyceride synthesis, hepatic lipid synthesis and insulin resistance in the liver of an individual having, or at risk of having, a disease associated with NAFLD or lipodystrophy syndromes. Certain embodiments are drawn to use of a DGAT2 specific inhibitor for the manufacture of a medicament for reducing or inhibiting triglyceride synthesis, hepatic lipid synthesis and insulin resistance in the liver of an individual having, or at risk of having, a disease associated with NAFLD or lipodystrophy syndromes. Certain embodiments are drawn to use of a DGAT2 specific inhibitor for the manufacture of a

medicament for reducing or inhibiting triglyceride synthesis, lipid synthesis and insulin resistance in the adipose tissue of an individual having, or at risk of having, a disease associated with NAFLD or lipodystrophy syndromes. Certain embodiments are drawn to use of a DGAT2 specific inhibitor for the manufacture of a medicament for reducing or inhibiting triglyceride synthesis, lipid synthesis and insulin resistance in the adipose tissue of an individual having, or at risk of having, a disease associated with NAFLD or lipodystrophy syndromes. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide.

In certain embodiments, a method of inhibiting expression of DGAT2 in a cell comprises contacting the cell with a DGAT2 specific inhibitor. In certain embodiments, the cell is a hepatocyte. In certain embodiments, the cell is in the liver of an individual. In certain embodiments, the cell is an adipose tissue cell of an individual. In certain embodiments, the cell is in the adipose tissue of an individual. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound targeted to DGAT2, such as an

antisense oligonucleotide targeted to DGAT2. In certain embodiments, the DGAT2 specific inhibitor is a compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising or consisting of a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is an antisense compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, and 4373. In certain embodiments, the DGAT2 specific inhibitor is ISIS 484137, ISIS 484085, ISIS 484129, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612. In certain embodiments the DGAT2 specific inhibitor is ISIS 769355, ISIS 769356, and ISIS 769357. In any of the foregoing embodiments, the antisense compound can be a single-stranded oligonucleotide. In certain aspects, the antisense compound is administered to the individual parenterally.

In any of the foregoing embodiments, the DGAT2 specific inhibitor can be an antisense compound targeted to DGAT2. In certain aspects, the antisense compound is an antisense oligonucleotide, for example an antisense oligonucleotide consisting of 8 to 80 linked nucleosides, 12 to 30 linked nucleosides, or 20 linked nucleosides. In certain aspects, the antisense oligonucleotide is at least 80%, 85%, 90%, 95% or 100% complementary to any of the nucleobase sequences recited in SEQ ID NOs: 1-4. In certain aspects, the antisense oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar and/or at least one modified nucleobase. In certain aspects, the modified internucleoside linkage is a phosphorothioate internucleoside linkage, the modified sugar is a bicyclic sugar or a 2'-O-methoxyethyl, and the modified nucleobase is a 5-methylcytosine. In certain aspects, the modified oligonucleotide comprises a gap segment consisting of linked 2'-deoxynucleosides; a 5' wing segment consisting of linked nucleosides; and a 3' wing segment consisting of linked nucleosides, wherein the gap segment is positioned immediately

adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

In any of the foregoing embodiments, the antisense oligonucleotide consists of 12 to 30, 15 to 30, 15 to 25, 15 to 24, 16 to 24, 17 to 24, 18 to 24, 19 to 24, 20 to 24, 19 to 22, 20 to 22, 16 to 20, or 17 or 20 linked nucleosides. In certain aspects, the antisense oligonucleotide is at least 80%, 85%, 90%, 95% or 100% complementary to any of the nucleobase sequences recited in SEQ ID NOs: 1-4. In certain aspects, the antisense oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar and/or at least one modified nucleobase. In certain aspects, the modified internucleoside linkage is a phosphorothioate internucleoside linkage, the modified sugar is a bicyclic sugar or a 2'-O-methoxyethyl, and the modified nucleobase is a 5-methylcytosine. In certain aspects, the modified oligonucleotide comprises a gap segment consisting of linked 2'-deoxynucleosides; a 5' wing segment consisting of linked nucleosides; and a 3' wing segment consisting of linked nucleosides, wherein the gap segment is positioned immediately adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 16-4679, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked 2'-deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising a conjugate group and a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 16-4679, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked 2'-deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 1423, 1371, 1415, 1849, 2959, 3292, 4198, or 4373, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked 2'-deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 16 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 1423, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 1423, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising a conjugate group and a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 1423, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 16 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 1371, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 1371, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 16 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 1415, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 1415, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 16 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 1849, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 1849, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 16 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 2959, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 2959, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 16 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 3292, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 3292, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 14 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 4198, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of three linked nucleosides; and

a 3' wing segment consisting of four linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 17 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 4198, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of three linked nucleosides; and

a 3' wing segment consisting of four linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 14 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 4373, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of three linked nucleosides; and

a 3' wing segment consisting of four linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor can be a compound comprising or consisting of a modified oligonucleotide consisting of 17 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 4373, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked 2'-deoxynucleosides;

a 5' wing segment consisting of three linked nucleosides; and

a 3' wing segment consisting of four linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a 2'MOE sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

In any of the foregoing methods or uses, the DGAT2 specific inhibitor is administered subcutaneously, such as by subcutaneous injection.

Antisense compounds

Oligomeric compounds include, but are not limited to, oligonucleotides, oligonucleosides, oligonucleotide analogs, antisense compounds, antisense oligonucleotides, and siRNAs. An oligomeric compound may be "antisense" to a target nucleic acid, meaning that is is capable of undergoing hybridization to a target nucleic acid through hydrogen bonding.

In certain embodiments, an antisense compound has a nucleobase sequence that, when written in the 5' to 3' direction, comprises the reverse complement of the target segment of a target nucleic acid to which it is targeted.

In certain embodiments, an antisense compound is 10 to 30 subunits in length. In certain embodiments, an antisense compound is 12 to 30 subunits in length. In certain embodiments, an antisense compound is 12 to 22 subunits in length. In certain embodiments, an antisense compound is 14 to 30 subunits in length. In certain embodiments, an antisense compound is 14 to 20 subunits in length. In certain embodiments, an antisense compoun is 15 to 30 subunits in length. In certain embodiments, an antisense compound is 15 to 20 subunits in length. In certain embodiments, an antisense compound is 16 to 30 subunits in length. In certain embodiments, an antisense compound is 16 to 20 subunits in length. In certain embodiments, an antisense compound is 17 to 30 subunits in length. In certain embodiments, an antisense compound is 17 to 20 subunits in length. In certain embodiments, an antisense compound is 18 to 30 subunits in length. In certain embodiments, an antisense compound is 18 to 21 subunits in length. In certain embodiments, an antisense compound is 18 to 20 subunits in length. In certain embodiments, an antisense compound is 20 to 30 subunits in length. In other words, such antisense compounds are from 12 to 30 linked subunits, 14 to 30 linked subunits, 14 to 20 subunits, 15 to 30 subunits, 15 to 20 subunits, 16 to 30 subunits, 16 to 20 subunits, 17 to 30 subunits, 17 to 20 subunits, 18 to 30 subunits, 18 to 20 subunits, 18 to 21 subunits, 20 to 30 subunits, or 12 to 22 linked subunits, respectively. In certain embodiments, an antisense compound is 14 subunits in length. In certain embodiments, an antisense compound is 16 subunits in length. In certain embodiments, an antisense compound is 17 subunits in length. In certain embodiments, an antisense compound is 18 subunits in length. In certain embodiments, an antisense compound is 19 subunits in length. In certain embodiments, an antisense compound is 20 subunits in length. In other embodiments, the antisense compound is 8 to 80, 12 to 50, 13 to 30, 13 to 50, 14 to 30, 14 to 50, 15 to 30, 15 to 50, 16 to 30, 16 to 50, 17

to 30, 17 to 50, 18 to 22, 18 to 24, 18 to 30, 18 to 50, 19 to 22, 19 to 30, 19 to 50, or 20 to 30 linked subunits. In certain such embodiments, the antisense compounds are 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 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, or 80 linked subunits in length, or a range defined by any two of the above values. In some embodiments the antisense compound is an antisense oligonucleotide, and the linked subunits are nucleotides, nucleosides, or nucleobases.

In certain embodiments, the antisense compound or oligomeric compound may further comprise additional features or elements, such as a conjugate group, that are attached to the oligonucleotide. In embodiments where a conjugate group comprises a nucleoside (*i.e.* a nucleoside that links the conjugate group to the oligonucleotide), the nucleoside of the conjugate group is not counted in the length of the oligonucleotide.

In certain embodiments antisense oligonucleotides may be shortened or truncated. For example, a single nucleoside may be deleted from the 5' end (5' truncation), or alternatively from the 3' end (3' truncation). A shortened or truncated antisense compound targeted to an DGAT2 nucleic acid may have two subunits deleted from the 5' end, or alternatively may have two subunits deleted from the 3' end, of the antisense compound. Alternatively, the deleted nucleosides may be dispersed throughout the antisense compound, for example, in an antisense compound having one nucleoside deleted from the 5' end and one nucleoside deleted from the 3' end.

When a single additional subunit is present in a lengthened antisense compound, the additional subunit may be located at the 5' or 3' end of the antisense compound. When two or more additional subunits are present, the added subunits may be adjacent to each other, for example, in an antisense compound having two subunits added to the 5' end (5' addition), or alternatively to the 3' end (3' addition), of the antisense compound. Alternatively, the added subunits may be dispersed throughout the antisense compound, for example, in an antisense compound having one subunit added to the 5' end and one subunit added to the 3' end.

It is possible to increase or decrease the length of an antisense compound, such as an antisense oligonucleotide, and/or introduce mismatch bases without eliminating activity (Woolf et al. (Proc. Natl. Acad. Sci. USA 89:7305-7309, 1992; Gautschi *et al. J. Natl. Cancer Inst.* 93:463-471, March 2001; Maher and Dolnick *Nuc. Acid. Res.* 16:3341-3358,1988). However, seemingly small changes in oligonucleotide sequence, chemistry and motif can make large differences in one or more of the many properties required for clinical development (Seth et al. *J. Med. Chem.* **2009**, *52*, 10; Egli et al. *J. Am. Chem. Soc.* **2011**, *133*, 16642).

In certain embodiments, antisense compounds are single-stranded, consisting of one oligomeric compound. The oligonucleotide of such single-stranded antisense compounds is an antisense oligonucleotide.

In certain embodiments, the antisense oligonucleotide of a single-stranded antisense compound is modified. In certain embodiments, the oligonucleotide of a single-stranded antisense compound or oligomeric compound comprises a self-complementary nucleobase sequence. In certain embodiments, antisense compounds are double-stranded, comprising two oligomeric compounds that form a duplex. In certain such embodiments, one oligomeric compound of a double-stranded antisense compound comprises one or more conjugate groups. In certain embodiments, each oligomeric compound of a double-stranded antisense compound comprises one or more conjugate groups. In certain embodiments, each oligonucleotide of a double-stranded antisense compound is a modified oligonucleotide. In certain embodiments, one oligonucleotide of a double-stranded antisense compound is a modified oligonucleotide. In certain embodiments, one oligonucleotide of a double-stranded antisense compound is an antisense oligonucleotide. In certain such embodiments, the antisense oligonucleotide is a modified oligonucleotide. Examples of single-stranded and double-stranded antisense compounds include but are not limited to antisense oligonucleotides, siRNAs, microRNA targeting oligonucleotides, and single-stranded RNAi compounds, such as small hairpin RNAs (shRNAs), single-stranded siRNAs (ssRNAs), and microRNA mimics.

In certain embodiments, antisense compounds are interfering RNA compounds (RNAi), which include double-stranded RNA compounds (also referred to as short-interfering RNA or siRNA) and single-stranded RNAi compounds (or ssRNA). Such compounds work at least in part through the RISC pathway to degrade and/or sequester a target nucleic acid (thus, include microRNA/microRNA-mimic compounds). As used herein, the term siRNA is meant to be equivalent to other terms used to describe nucleic acid molecules that are capable of mediating sequence specific RNAi, for example short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), short hairpin RNA (shRNA), short interfering oligonucleotide, short interfering nucleic acid, short interfering modified oligonucleotide, chemically modified siRNA, post-transcriptional gene silencing RNA (ptgsRNA), and others. In addition, as used herein, the term RNAi is meant to be equivalent to other terms used to describe sequence specific RNA interference, such as post transcriptional gene silencing, translational inhibition, or epigenetics.

In certain embodiments, a double-stranded compound can comprise any of the oligonucleotide sequences targeted to DGAT2 described herein. In certain embodiments, a double-stranded compound comprises a first strand comprising at least an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobase portion of any one of SEQ ID NOs: 16-4679 and a second strand. In certain embodiments, a double-stranded compound comprises a first strand comprising the nucleobase sequence of any one of SEQ ID NOs: 16-4679 and a second strand. In certain embodiments, the double-stranded compound comprises ribonucleotides in which the first strand has uracil (U) in place of thymine (T) in any one of SEQ ID NOs: 16-4679. In certain embodiments, a double-stranded compound comprises (i) a first strand comprising a nucleobase sequence complementary to the site on DGAT2 to which any of SEQ ID NOs: 16-4679 is targeted, and (ii) a second strand. In certain embodiments, the double-stranded compound comprises one or

more modified nucleotides in which the 2' position in the sugar contains a halogen (such as fluorine group; 2'-F) or contains an alkoxy group (such as a methoxy group; 2'-OMe). In certain embodiments, the double-stranded compound comprises at least one 2'-F sugar modification and at least one 2'-OMe sugar modification. In certain embodiments, the at least one 2'-F sugar modification and at least one 2'-OMe sugar modification are arranged in an alternating pattern for at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobases along a strand of the dsRNA compound. In certain embodiments, the double-stranded compound comprises one or more linkages between adjacent nucleotides other than a naturally-occurring phosphodiester linkage. Examples of such linkages include phosphoramide, phosphorothioate, and phosphorodithioate linkages. The double-stranded compounds may also be chemically modified nucleic acid molecules as taught in U.S. Pat. No. 6,673,661. In other embodiments, the dsRNA contains one or two capped strands, as disclosed, for example, by WO 00/63364, filed Apr. 19, 2000. In certain embodiments, the first strand of the double-stranded compound is an siRNA guide strand and the second strand of the double-stranded compound is an siRNA passenger strand. In certain embodiments, the second strand of the double-stranded compound is complementary to the first strand. In certain embodiments, each strand of the double-stranded compound consists of 16, 17, 18, 19, 20, 21, 22, or 23 linked nucleosides. In certain embodiments, the first or second strand of the double-stranded compound can comprise a conjugate group.

In certain embodiments, a single-stranded RNAi (ssRNAi) compound can comprise any of the oligonucleotide sequences targeted to DGAT2 described herein. In certain embodiments, an ssRNAi compound comprises at least an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobase portion of any one of SEQ ID NOs: 16-4679. In certain embodiments, an ssRNAi compound comprises the nucleobase sequence of any one of SEQ ID NOs: 16-4679. In certain embodiments, the ssRNAi compound comprises ribonucleotides in which uracil (U) is in place of thymine (T) in any one of SEQ ID NOs: 16-4679. In certain embodiments, an ssRNAi compound comprises a nucleobase sequence complementary to the site on DGAT2 to which any of SEQ ID NOs: 16-4679 is targeted. In certain embodiments, an ssRNAi compound comprises one or more modified nucleotides in which the 2' position in the sugar contains a halogen (such as fluorine group; 2'-F) or contains an alkoxy group (such as a methoxy group; 2'-OMe). In certain embodiments, an ssRNAi compound comprises at least one 2'-F sugar modification and at least one 2'-OMe sugar modification. In certain embodiments, the at least one 2'-F sugar modification and at least one 2'-OMe sugar modification are arranged in an alternating pattern for at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobases along a strand of the ssRNAi compound. In certain embodiments, the ssRNAi compound comprises one or more linkages between adjacent nucleotides other than a naturally-occurring phosphodiester linkage. Examples of such linkages include phosphoramide, phosphorothioate, and phosphorodithioate linkages. The ssRNAi compounds may also be chemically modified nucleic acid molecules as taught in U.S. Pat. No. 6,673,661. In other embodiments, the ssRNAi

contains a capped strand, as disclosed, for example, by WO 00/63364, filed Apr. 19, 2000. In certain embodiments, the ssRNAi compound consists of 16, 17, 18, 19, 20, 21, 22, or 23 linked nucleosides. In certain embodiments, the ssRNAi compound can comprise a conjugate group.

In certain embodiments, antisense compounds comprise modified oligonucleotides. Certain modified oligonucleotides have one or more asymmetric center and thus give rise to enantiomers, diastereomers, and other stereoisomeric configurations that may be defined, in terms of absolute stereochemistry, as (R) or (S), as α or β such as for sugar anomers, or as (D) or (L) such as for amino acids etc. Included in the modified oligonucleotides provided herein are all such possible isomers, including their racemic and optically pure forms, unless specified otherwise. Likewise, all cis- and trans-isomers and tautomeric forms are also included.

In certain embodiments, antisense compounds and oligomeric compounds described herein comprise modified oligonucleotides. Such modified oligonucleotides may contain any combination of the modified sugar moieites, modified nucleobases, modified internucleoside linkages, motifs, and/or lengths described herein.

Certain Antisense Compound Mechanisms

In certain embodiments, antisense compounds are capable of hybridizing to a target nucleic acid, resulting in at least one antisense activity. In certain embodiments, antisense compounds specifically affect one or more target nucleic acid. Such specific antisense compounds comprises a nucleobase sequence that hybridizes to one or more target nucleic acid, resulting in one or more desired antisense activity and does not hybridize to one or more non-target nucleic acid or does not hybridize to one or more non-target nucleic acid in such a way that results in an undesired antisense activity.

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

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

In certain embodiments, hybridization of an antisense compound to a target nucleic acid dose not result in recruitment of a protein that cleaves that target nucleic acid. In certain such embodiments, hybridization of the antisense compound to the target nucleic acid results in alteration of splicing of the target

nucleic acid. In certain embodiments, hybridization of an antisense compound to a target nucleic acid results in inhibition of a binding interaction between the target nucleic acid and a protein or other nucleic acid. In certain such embodiments, hybridization of an antisense compound to a target nucleic acid results in alteration of translation of the target nucleic acid.

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

In certain embodiments, modified oligonucleotides having a gapmer sugar motif described herein have desirable properties compared to non-gapmer oligonucleotides or to gapmers having other sugar motifs. In certain circumstances, it is desirable to identify motifs resulting in a favorable combination of potent antisense activity and relatively low toxicity. In certain embodiments, compounds of the present invention have a favorable therapeutic index (measure of activity divided by measure of toxicity).

Target Nucleic Acids, Target Regions and Nucleotide Sequences

In certain embodiments, antisense compounds comprise or consist of an oligonucleotide comprising a region that is complementary to a target nucleic acid. In certain embodiments, the target nucleic acid is an endogenous RNA molecule. In certain embodiments, the target nucleic acid encodes a protein. In certain such embodiments, the target nucleic acid is selected from: an mRNA and a pre-mRNA, including intronic, exonic and untranslated regions. In certain embodiments, the target RNA is an mRNA. In certain embodiments, the target nucleic acid is a pre-mRNA. In certain such embodiments, the target region is entirely within an intron. In certain embodiments, the target region spans an intron/exon junction. In certain embodiments, the target region is at least 50% within an intron.

Nucleotide sequences that encode DGAT2 include, without limitation, the following: RefSeq No. NM_032564.3 (incorporated herein by reference; designated herein as SEQ ID NO: 1), nucleotides 5669186 to 5712008 of RefSeq No. NT_033927.5 (incorporated herein by reference; designated herein as SEQ ID NO: 2), nucleotides 20780400 to 20823450 of RefSeq No. NT_167190.1 (incorporated herein by reference; designated herein as SEQ ID NO: 4878), RefSeq No. AK091870.1 (incorporated herein by reference; designated herein as SEQ ID NO: 4879), and nucleotides 1232000 to 1268000 of RefSeq No. NW_001100387.1 (incorporated herein by reference; designated herein as SEQ ID NO: 3).

Hybridization

In some embodiments, hybridization occurs between an antisense compound disclosed herein and a DGAT2 nucleic acid. The most common mechanism of hybridization involves hydrogen bonding (e.g., Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding) between complementary nucleobases of the nucleic acid molecules.

Hybridization can occur under varying conditions. Hybridization conditions are sequence-dependent and are determined by the nature and composition of the nucleic acid molecules to be hybridized.

Methods of determining whether a sequence is specifically hybridizable to a target nucleic acid are well known in the art. In certain embodiments, the antisense compounds provided herein are specifically hybridizable with a DGAT2 nucleic acid.

Complementarity

An oligonucleotide is said to be complementary to another nucleic acid when the nucleobase sequence of such oligonucleotide or one or more regions thereof matches the nucleobase sequence of another oligonucleotide or nucleic acid or one or more regions thereof when the two nucleobase sequences are aligned in opposing directions. Nucleobase matches or complementary nucleobases, as described herein, are limited to adenine (A) and thymine (T), adenine (A) and uracil (U), cytosine (C) and guanine (G), and 5-methyl cytosine (mC) and guanine (G) unless otherwise specified. Complementary oligonucleotides and/or nucleic acids need not have nucleobase complementarity at each nucleoside and may include one or more nucleobase mismatches. An oligonucleotide is fully complementary or 100% complementary when such oligonucleotides have nucleobase matches at each nucleoside without any nucleobase mismatches.

Non-complementary nucleobases between an antisense compound and a DGAT2 nucleic acid may be tolerated provided that the antisense compound remains able to specifically hybridize to a target nucleic acid. Moreover, an antisense compound may hybridize over one or more segments of a DGAT2 nucleic acid such that intervening or adjacent segments are not involved in the hybridization event (e.g., a loop structure, mismatch or hairpin structure).

In certain embodiments, the antisense compounds provided herein, or a specified portion thereof, are, or are at least, 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% complementary to a DGAT2 nucleic acid, a target region, target segment, or specified portion thereof. In certain such embodiments, the region of full complementarity is from 6 to 20 nucleobases in length. In certain such embodiments, the region of full complementarity is from 10 to 18 nucleobases in length. In certain such embodiments, the region of full complementarity is from 18 to 20 nucleobases in length. Percent complementarity of an antisense compound with a target nucleic acid can be determined using routine methods.

For example, an antisense compound in which 18 of 20 nucleobases of the antisense compound are complementary to a target region, and would therefore specifically hybridize, would represent 90 percent complementarity. In this example, the remaining noncomplementary nucleobases may be clustered or interspersed with complementary nucleobases and need not be contiguous to each other or to complementary nucleobases. As such, an antisense compound which is 18 nucleobases in length having four noncomplementary nucleobases which are flanked by two regions of complete complementarity with the

target nucleic acid would have 77.8% overall complementarity with the target nucleic acid and would thus fall within the scope of the present invention. Percent complementarity of an antisense compound with a region of a target nucleic acid can be determined routinely using BLAST programs (basic local alignment search tools) and PowerBLAST programs known in the art (Altschul *et al.*, *J. Mol. Biol.*, 1990, 215, 403 410; Zhang and Madden, Genome Res., 1997, 7, 649 656). Percent homology, sequence identity or complementarity, can be determined by, for example, the Gap program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, Madison Wis.), using default settings, which uses the algorithm of Smith and Waterman (Adv. Appl. Math., 1981, 2, 482 489).

In certain embodiments, the antisense compounds provided herein, or specified portions thereof, are fully complementary (i.e. 100% complementary) to a target nucleic acid, or specified portion thereof. For example, an antisense compound may be fully complementary to a DGAT2 nucleic acid, or a target region, or a target segment or target sequence thereof. As used herein, "fully complementary" means each nucleobase of an antisense compound is capable of precise base pairing with the corresponding nucleobases of a target nucleic acid. For example, a 20 nucleobase antisense compound is fully complementary to a target sequence that is 400 nucleobases long, so long as there is a corresponding 20 nucleobase portion of the target nucleic acid that is fully complementary to the antisense compound. Fully complementary can also be used in reference to a specified portion of the first and /or the second nucleic acid. For example, a 20 nucleobase portion of a 30 nucleobase antisense compound can be "fully complementary" to a target sequence that is 400 nucleobases long. The 20 nucleobase portion of the 30 nucleobase oligonucleotide is fully complementary to the target sequence if the target sequence has a corresponding 20 nucleobase portion wherein each nucleobase is complementary to the 20 nucleobase portion of the antisense compound. At the same time, the entire 30 nucleobase antisense compound may or may not be fully complementary to the target sequence, depending on whether the remaining 10 nucleobases of the antisense compound are also complementary to the target sequence.

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

The location of a non-complementary nucleobase may be at the 5' end or 3' end of the antisense compound. Alternatively, the non-complementary nucleobase or nucleobases may be at an internal position

of the antisense compound. When two or more non-complementary nucleobases are present, they may be contiguous (i.e. linked) or non-contiguous. In one embodiment, a non-complementary nucleobase is located in the wing segment of a gapmer antisense oligonucleotide.

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

In certain embodiments, antisense compounds that are, or are up to 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleobases in length comprise no more than 4, no more than 3, no more than 2, or no more than 1 non-complementary nucleobase(s) relative to a target nucleic acid, such as a DGAT2 nucleic acid, or specified portion thereof.

In certain embodiments, antisense compounds that are, or are up to 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleobases in length comprise no more than 6, no more than 5, no more than 4, no more than 3, no more than 2, or no more than 1 non-complementary nucleobase(s) relative to a target nucleic acid, such as a DGAT2 nucleic acid, or specified portion thereof.

The antisense compounds provided also include those which are complementary to a portion of a target nucleic acid. As used herein, "portion" refers to a defined number of contiguous (i.e. linked) nucleobases within a region or segment of a target nucleic acid. A "portion" can also refer to a defined number of contiguous nucleobases of an antisense compound. In certain embodiments, the antisense compounds, are complementary to at least an 8 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 9 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 10 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least an 11 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 12 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 13 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 14 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 15 nucleobase portion of a target segment. Also contemplated are antisense compounds that are complementary to at least a

9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more nucleobase portion of a target segment, or a range defined by any two of these values.

Identity

The antisense compounds provided herein may also have a defined percent identity to a particular nucleotide sequence, SEQ ID NO, or compound represented by a specific Isis number, or portion thereof. As used herein, an antisense compound is identical to the sequence disclosed herein if it has the same nucleobase pairing ability. For example, a RNA which contains uracil in place of thymidine in a disclosed DNA sequence would be considered identical to the DNA sequence since both uracil and thymidine pair with adenine. Shortened and lengthened versions of the antisense compounds described herein as well as compounds having non-identical bases relative to the antisense compounds provided herein also are contemplated. The non-identical bases may be adjacent to each other or dispersed throughout the antisense compound. Percent identity of an antisense compound is calculated according to the number of bases that have identical base pairing relative to the sequence to which it is being compared.

In certain embodiments, the antisense compounds, or portions thereof, are, or are at least, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to one or more of the antisense compounds or SEQ ID NOs, or a portion thereof, disclosed herein.

In certain embodiments, a portion of the antisense compound is compared to an equal length portion of the target nucleic acid. In certain embodiments, an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleobase portion is compared to an equal length portion of the target nucleic acid.

In certain embodiments, a portion of the antisense oligonucleotide is compared to an equal length portion of the target nucleic acid. In certain embodiments, an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleobase portion is compared to an equal length portion of the target nucleic acid.

Modifications

Modifications to antisense compounds encompass substitutions or changes to internucleoside linkages, sugar moieties, or nucleobases. Modified antisense compounds are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid target, increased stability in the presence of nucleases, or increased inhibitory activity.

Chemically modified nucleosides may also be employed to increase the binding affinity of a shortened or truncated antisense oligonucleotide for its target nucleic acid. Consequently, comparable results can often be obtained with shorter antisense compounds that have such chemically modified nucleosides.

Modified Internucleoside Linkages

The naturally occuring internucleoside linkage of RNA and DNA is a 3' to 5' phosphodiester linkage. Antisense compounds having one or more modified, i.e. non-naturally occurring, internucleoside

linkages are often selected over antisense compounds having naturally occurring internucleoside linkages because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for target nucleic acids, and increased stability in the presence of nucleases.

Oligonucleotides having modified internucleoside linkages include internucleoside linkages that retain a phosphorus atom as well as internucleoside linkages that do not have a phosphorus atom. Representative phosphorus containing internucleoside linkages include, but are not limited to, phosphodiesters, phosphotriesters, methylphosphonates, phosphoramidate, and phosphorothioates. Methods of preparation of phosphorous-containing and non-phosphorous-containing linkages are well known.

In certain embodiments, nucleosides of modified oligonucleotides may be linked together using any internucleoside linkage. The two main classes of internucleoside linking groups are defined by the presence or absence of a phosphorus atom. Representative phosphorus-containing internucleoside linkages include but are not limited to phosphates, which contain a phosphodiester bond ("P=O") (also referred to as unmodified or naturally occurring linkages), phosphotriesters, methylphosphonates, phosphoramidates, and phosphorothioates ("P=S"), and phosphorodithioates ("HS-P=S"). Representative non-phosphorus containing internucleoside linking groups include but are not limited to methylenemethylimino ($-CH_2-N(CH_3)-O-CH_2-$), thiodiester (-O-C(=O)-S-), thionocarbamate (-O-C(=O)(NH)-S-); siloxane ($-O-SiH_2-O-$); and N,N'-dimethylhydrazine ($-CH_2-N(CH_3)-N(CH_3)-$). Modified internucleoside linkages, compared to naturally occurring phosphate linkages, can be used to alter, typically increase, nuclease resistance of the oligonucleotide. In certain embodiments, internucleoside linkages having a chiral atom can be prepared as a racemic mixture, or as separate enantiomers. Representative chiral internucleoside linkages include but are not limited to alkylphosphonates and phosphorothioates. Methods of preparation of phosphorous-containing and non-phosphorous-containing internucleoside linkages are well known to those skilled in the art.

Neutral internucleoside linkages include, without limitation, phosphotriesters, methylphosphonates, MMI (3'-CH_2-N(CH_3)-O-5'), amide-3 (3'-CH_2-C(=O)-N(H)-5'), amide-4 (3'-CH_2-N(H)-C(=O)-5'), formacetal (3'-O-CH_2-O-5'), methoxypropyl, and thioformacetal (3'-S-CH_2-O-5'). Further neutral internucleoside linkages include nonionic linkages comprising siloxane (dialkylsiloxane), carboxylate ester, carboxamide, sulfide, sulfonate ester and amides (See for example: *Carbohydrate Modifications in Antisense Research*; Y.S. Sanghvi and P.D. Cook, Eds., ACS Symposium Series 580; Chapters 3 and 4, 40-65). Further neutral internucleoside linkages include nonionic linkages comprising mixed N, O, S and CH_2 component parts.

In certain embodiments, antisense compounds targeted to a DGAT2 nucleic acid comprise one or more modified internucleoside linkages. In certain embodiments, the modified internucleoside linkages are phosphorothioate linkages. In certain embodiments, each internucleoside linkage of an antisense compound is a phosphorothioate internucleoside linkage.

In certain embodiments, oligonucleotides comprise modified internucleoside linkages arranged along the oligonucleotide or region thereof in a defined pattern or modified internucleoside linkage motif. In

certain embodiments, internucleoside linkages are arranged in a gapped motif. In such embodiments, the internucleoside linkages in each of two wing regions are different from the internucleoside linkages in the gap region. In certain embodiments the internucleoside linkages in the wings are phosphodiester and the internucleoside linkages in the gap are phosphorothioate. The nucleoside motif is independently selected, so such oligonucleotides having a gapped internucleoside linkage motif may or may not have a gapped nucleoside motif and if it does have a gapped nucleoside motif, the wing and gap lengths may or may not be the same.

In certain embodiments, oligonucleotides comprise a region having an alternating internucleoside linkage motif. In certain embodiments, oligonucleotides of the present invention comprise a region of uniformly modified internucleoside linkages. In certain such embodiments, the oligonucleotide comprises a region that is uniformly linked by phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide is uniformly linked by phosphorothioate. In certain embodiments, each internucleoside linkage of the oligonucleotide is selected from phosphodiester and phosphorothioate. In certain embodiments, each internucleoside linkage of the oligonucleotide is selected from phosphodiester and phosphorothioate and at least one internucleoside linkage is phosphorothioate.

In certain embodiments, the oligonucleotide comprises at least 6 phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least 8 phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least 10 phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least one block of at least 6 consecutive phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least one block of at least 8 consecutive phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least one block of at least 10 consecutive phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least block of at least one 12 consecutive phosphorothioate internucleoside linkages. In certain such embodiments, at least one such block is located at the 3' end of the oligonucleotide. In certain such embodiments, at least one such block is located within 3 nucleosides of the 3' end of the oligonucleotide.

In certain embodiments, oligonucleotides comprise one or more methylphosponate linkages. In certain embodiments, oligonucleotides having a gapmer nucleoside motif comprise a linkage motif comprising all phosphorothioate linkages except for one or two methylphosponate linkages. In certain embodiments, one methylphosponate linkage is in the central gap of an oligonucleotide having a gapmer nucleoside motif.

In certain embodiments, it is desirable to arrange the number of phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages to maintain nuclease resistance. In certain embodiments, it is desirable to arrange the number and position of phosphorothioate internucleoside linkages and the number and position of phosphodiester internucleoside linkages to maintain nuclease resistance. In

certain embodiments, the number of phosphorothioate internucleoside linkages may be decreased and the number of phosphodiester internucleoside linkages may be increased. In certain embodiments, the number of phosphorothioate internucleoside linkages may be decreased and the number of phosphodiester internucleoside linkages may be increased while still maintaining nuclease resistance. In certain embodiments it is desirable to decrease the number of phosphorothioate internucleoside linkages while retaining nuclease resistance. In certain embodiments it is desirable to increase the number of phosphodiester internucleoside linkages while retaining nuclease resistance.

Modified Sugar Moieties

Antisense compounds can optionally contain one or more nucleosides wherein the sugar group has been modified. Such sugar modified nucleosides may impart enhanced nuclease stability, increased binding affinity, or some other beneficial biological property to the antisense compounds.

In certain embodiments, modified oligonucleotides comprise one or more modified nucleosides comprising a modified sugar moiety. Such modified oligonucleotides comprising one or more sugar-modified nucleosides may have desirable properties, such as enhanced nuclease stability or increased binding affinity with a target nucleic acid relative to oligonucleotides lacking such sugar-modified nucleosides. In certain embodiments, modified sugar moieties are linearly modified sugar moieties. In certain embodiments, modified sugar moieties are bicyclic or tricyclic sugar moieties. In certain embodiments, modified sugar moieties are sugar surrogates. Such sugar surrogates may comprise one or more substitutions corresponding to those of substituted sugar moieties.

In certain embodiments, modified sugar moieties are linearly modified sugar moieties comprising a furanosyl ring with one or more acyclic substituent, including but not limited to substituents at the 2' and/or 5' positions. Examples of 2'-substituent groups suitable for linearly modified sugar moieties include but are not limited to: 2'-F, 2'-OCH_3 ("OMe" or "O-methyl"), and 2'-$O(CH_2)_2OCH_3$ ("MOE"). In certain embodiments, 2'-substituent groups are selected from among: halo, allyl, amino, azido, SH, CN, OCN, CF_3, OCF_3, O-C_1-C_{10} alkoxy, O-C_1-C_{10} substituted alkoxy, O-C_1-C_{10} alkyl, O-C_1-C_{10} substituted alkyl, S-alkyl, N(R_m)-alkyl, O-alkenyl, S-alkenyl, N(R_m)-alkenyl, O-alkynyl, S-alkynyl, N(R_m)-alkynyl, O-alkylenyl-O-alkyl, alkynyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(R_m)(R_n)$ or $OCH_2C(=O)$-$N(R_m)(R_n)$, where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C_1-C_{10} alkyl. Certain embodiments of these 2'-substituent groups can be further substituted with one or more substituent groups independently selected from among: hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro (NO_2), thiol, thioalkoxy, thioalkyl, halogen, alkyl, aryl, alkenyl and alkynyl. Examples of 5'-substituent groups suitable for linearly modified sugar moieties include but are not limited to: 5'-methyl (R or S), 5'-vinyl, and 5'-methoxy. In certain embodiments, linearly modified sugars comprise more than one

non-bridging sugar substituent, for example, 2'-F-5'-methyl sugar moieties (*see*, e.g., PCT International Application WO 2008/101157, for additional 2', 5'-bis substituted sugar moieties and nucleosides).

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

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

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

Nucleosides comprising modified sugar moieties, such as linearly modified sugar moieties, are referred to by the position(s) of the substitution(s) on the sugar moiety of the nucleoside. For example, nucleosides comprising 2'-substituted or 2-modified sugar moieties are referred to as 2'-substituted nucleosides or 2-modified nucleosides.

Certain modifed sugar moieties comprise a bridging sugar substituent that forms a second ring resulting in a bicyclic sugar moiety. In certain such embodiments, the bicyclic sugar moiety comprises a bridge between the 4' and the 2' furanose ring atoms. Examples of such 4' to 2' bridging sugar substituents include but are not limited to: 4'-CH_2-2', 4'-$(CH_2)_2$-2', 4'-$(CH_2)_3$-2', 4'-CH_2-O-2' ("LNA"), 4'-CH_2-S-2', 4'-$(CH_2)_2$-O-2' ("ENA"), 4'-$CH(CH_3)$-O-2' (referred to as "constrained ethyl" or "cEt" when in the *S* configuration), 4'-CH_2-O-CH_2-2', 4'-CH_2-N(R)-2', 4'-$CH(CH_2OCH_3)$-O-2' ("constrained MOE" or "cMOE") and analogs thereof (*see, e.g.,* U.S. Patent 7,399,845), 4'-$C(CH_3)(CH_3)$-O-2' and analogs thereof (*see, e.g.,* WO2009/006478), 4'-CH_2-$N(OCH_3)$-2' and analogs thereof (*see, e.g.,* WO2008/150729), 4'-CH_2-O-$N(CH_3)$-2' (*see, e.g.,* US2004/0171570), 4'-CH_2-$C(H)(CH_3)$-2' (*see, e.g.,* Chattopadhyaya, *et al., J. Org. Chem.*,2009, *74*, 118-134), 4'-CH_2-$C(=CH_2)$-2' and analogs thereof (*see*, published PCT International Application WO 2008/154401), 4'-$C(R_aR_b)$-N(R)-O-2', 4'-$C(R_aR_b)$-O-N(R)-2', 4'-CH_2-O-N(R)-2', and 4'-CH_2-N(R)-O-2', wherein each R, R_a, and R_b is, independently, H, a protecting group, or C_1-C_{12} alkyl (*see, e.g.* U.S. Patent 7,427,672).

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

wherein:

x is 0, 1, or 2;

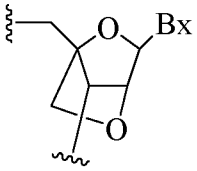
n is 1, 2, 3, or 4;

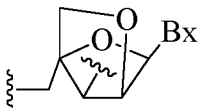
each R_a and R_b is, independently, H, a protecting group, hydroxyl, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, heterocycle radical, substituted heterocycle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

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

Additional bicyclic sugar moieties are known in the art, for example: Freier *et al., Nucleic Acids Research*, 1997, *25*(*22*), 4429-4443, Albaek *et al., J. Org. Chem.*, 2006, *71*, 7731-7740, Singh et al., *Chem. Commun.*, 1998, *4*, 455-456; Koshkin et al., *Tetrahedron*, 1998, *54*, 3607-3630; Wahlestedt et al., *Proc. Natl. Acad. Sci. U. S. A.*, 2000, *97*, 5633-5638; Kumar et al., *Bioorg. Med. Chem. Lett.*, 1998, *8*, 2219-2222; Singh et al., *J. Org. Chem.*, 1998, *63*, 10035-10039; Srivastava et al., *J. Am. Chem. Soc.*, 20017, *129,* 8362-8379; Elayadi *et al., Curr. Opinion Invens. Drugs,* 2001, *2*, 558-561; Braasch *et al., Chem. Biol.,* 2001, *8*, 1-7; Orum *et al., Curr. Opinion Mol. Ther.,* 2001, *3*, 239-243; U.S. Patent Nos. 7,053,207, 6,268,490, 6,770,748, 6,794,499, 7,034,133, 6,525,191, 6,670,461, and 7,399,845; WO 2004/106356, WO 1994/14226, WO 2005/021570, and WO 2007/134181; U.S. Patent Publication Nos. US2004/0171570, US2007/0287831, and US2008/0039618; U.S. Patent Serial Nos. 12/129,154, 60/989,574, 61/026,995, 61/026,998, 61/056,564, 61/086,231, 61/097,787, and 61/099,844; and PCT International Applications Nos. PCT/US2008/064591, PCT/US2008/066154, and PCT/US2008/068922.

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





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

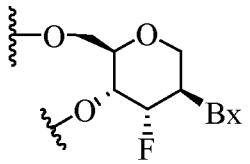
α-*L*-LNA (α-*L*-configuration) bridge = 4'-CH_2-O-2'

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

In certain embodiments, modified sugar moieties comprise one or more non-bridging sugar substituent and one or more bridging sugar substituent (e.g., 5'-substituted and 4'-2' bridged sugars). (*see, e.g.,* WO 2007/134181, wherein LNA nucleosides are further substituted with, for example, a 5'-methyl or a 5'-vinyl group, and *see, e.g.,* U.S. Patents 7,547,684; 7,750,131; 8,030,467; 8,268,980; 7,666, 854; and 8,088,746).

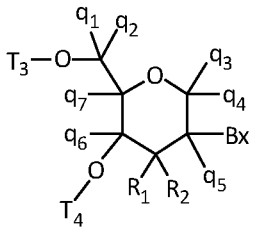
In certain embodiments, modified sugar moieties are sugar surrogates. In certain such embodiments, the oxygen atom of the sugar moiety is replaced, *e.g.,* with a sulfur, carbon or nitrogen atom. In certain such embodiments, such modified sugar moieties also comprise bridging and/or non-bridging substituents as described above. For example, certain sugar surrogates comprise a 4'-sulfur atom and a substitution at the 2'-position (*see*, *e.g.,* US2005/0130923) and/or the 5' position.

In certain embodiments, sugar surrogates comprise rings having other than 5 atoms. For example, in certain embodiments, a sugar surrogate comprises a six-membered tetrahydropyran ("THP"). Such tetrahydropyrans may be further modified or substituted. Nucleosides comprising such modified tetrahydropyrans include but are not limited to hexitol nucleic acid ("HNA"), anitol nucleic acid ("ANA"), manitol nucleic acid ("MNA") (*see* Leumann, CJ. *Bioorg. & Med. Chem.* 2002, *10*, 841-854), fluoro HNA:



F-HNA

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



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

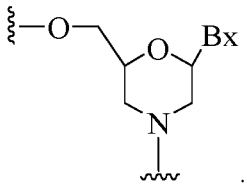
Bx is a nucleobase moiety;

T_3 and T_4 are each, independently, an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide or one of T_3 and T_4 is an internucleoside linking group

linking the modified THP nucleoside to the remainder of an oligonucleotide and the other of T_3 and T_4 is H, a hydroxyl protecting group, a linked conjugate group, or a 5' or 3'-terminal group; q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each, independently, H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl, or substituted C_2-C_6 alkynyl; and each of R_1 and R_2 is independently selected from among: hydrogen, halogen, substituted or unsubstituted alkoxy, NJ_1J_2, SJ_1, N_3, $OC(=X)J_1$, $OC(=X)NJ_1J_2$, $NJ_3C(=X)NJ_1J_2$, and CN, wherein X is O, S or NJ_1, and each J_1, J_2, and J_3 is, independently, H or C_1-C_6 alkyl.

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

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



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

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

Many other bicyclic and tricyclic sugar and sugar surrogate ring systems are known in the art that can be used in modified nucleosides (*see, e.g.,* Leumann, J. C, *Bioorganic & Medicinal Chemistry*, 2002, *10*, 841-854).

Modified Nucleobases

Nucleobase (or base) modifications or substitutions are structurally distinguishable from, yet functionally interchangeable with, naturally occurring or synthetic unmodified nucleobases. Both natural and

modified nucleobases are capable of participating in hydrogen bonding. Such nucleobase modifications can impart nuclease stability, binding affinity or some other beneficial biological property to antisense compounds.

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

In certain embodiments, modified nucleobases are selected from: 5-substituted pyrimidines, 6-azapyrimidines, alkyl or alkynyl substituted pyrimidines, alkyl substituted purines, and N-2, N-6 and O-6 substituted purines. In certain embodiments, modified nucleobases are selected from: 2-aminopropyladenine, 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-N-methylguanine, 6-N-methyladenine, 2-propyladenine , 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-propynyl (-C≡C-CH_3) uracil, 5-propynylcytosine, 6-azouracil, 6-azocytosine, 6-azothymine, 5-ribosyluracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl, 8-aza and other 8-substituted purines, 5-halo, particularly 5-bromo, 5-trifluoromethyl, 5-halouracil, and 5-halocytosine, 7-methylguanine, 7-methyladenine, 2-F-adenine, 2-aminoadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, 3-deazaadenine, 6-N-benzoyladenine, 2-N-isobutyrylguanine, 4-N-benzoylcytosine, 4-N-benzoyluracil, 5-methyl 4-N-benzoylcytosine, 5-methyl 4-N-benzoyluracil, universal bases, hydrophobic bases, promiscuous bases, size-expanded bases, and fluorinated bases. Further modified nucleobases include tricyclic pyrimidines, such as 1,3-diazaphenoxazine-2-one, 1,3-diazaphenothiazine-2-one and 9-(2-aminoethoxy)-1,3-diazaphenoxazine-2-one (G-clamp). Modified nucleobases may also include those in which the purine or pyrimidine base is replaced with other heterocycles, for example 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine and 2-pyridone. Further nucleobases include those disclosed in United States Patent No. 3,687,808, those disclosed in *The Concise Encyclopedia Of Polymer Science And Engineering*, Kroschwitz, J.I., Ed., John Wiley & Sons, 1990, 858-859; Englisch *et al.*, *Angewandte Chemie*, International Edition, 1991, *30*, 613; Sanghvi, Y.S., Chapter 15, *Antisense Research and Applications*, Crooke, S.T. and Lebleu, B., Eds., CRC Press, 1993, 273-288; and those disclosed in Chapters 6 and 15, *Antisense Drug Technology*, Crooke S.T., Ed., CRC Press, 2008, 163-166 and 442-443.

Representative United States patents that teach the preparation of certain of the above noted modified nucleobases as well as other modified nucleobases include without limitation, US2003/0158403, U.S. 3,687,808; 4,845,205; 5,130,302; 5,134,066; 5,175,273; 5,367,066; 5,432,272; 5,434,257; 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; 5,645,985; 5,681,941; 5,750,692; 5,763,588; 5,830,653 and 6,005,096.

In certain embodiments, antisense compounds targeted to a DGAT2 nucleic acid comprise one or more modified nucleobases. In certain embodiments, the modified nucleobase is 5-methylcytosine. In certain

embodiments, each cytosine is a 5-methylcytosine.

Certain Motifs

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

1. Certain Sugar Motifs

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

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

In certain embodiments, the wings of a gapmer comprise 1-5 nucleosides. In certain embodiments, the wings of a gapmer comprise 2-5 nucleosides. In certain embodiments, the wings of a gapmer comprise 3-5 nucleosides. In certain embodiments, the nucleosides of a gapmer are all modified nucleosides.

In certain embodiments, the gap of a gapmer comprises 7-12 nucleosides. In certain embodiments,

the gap of a gapmer comprises 7-10 nucleosides. In certain embodiments, the gap of a gapmer comprises 8-10 nucleosides. In certain embodiments, the gap of a gapmer comprises 10 nucleosides. In certain embodiment, each nucleoside of the gap of a gapmer is an unmodified 2'-deoxy nucleoside.

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

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

2. Certain Nucleobase Motifs

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

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

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

3. Certain Internucleoside Linkage Motifs

In certain embodiments, oligonucleotides comprise modified and/or unmodified internucleoside linkages arranged along the oligonucleotide or region thereof in a defined pattern or motif. In certain embodiments, essentially each internucleoside linking group is a phosphate internucleoside linkage (P=O). In certain embodiments, each internucleoside linking group of a modified oligonucleotide is a phosphorothioate (P=S). In certain embodiments, each internucleoside linking group of a modified oligonucleotide is independently selected from a phosphorothioate and phosphate internucleoside linkage. In certain embodiments, the sugar motif of a modified oligonucleotide is a gapmer and the internucleoside linkages within the gap are all modified. In certain such embodiments, some or all of the internucleoside linkages in the wings are unmodified phosphate linkages. In certain embodiments, the terminal internucleoside linkages are modified.

Certain Oligonucleotides

Oligonucleotides are characterized by their motifs and overall lengths. In certain embodiments, such parameters are each independent of one another. Thus, unless otherwise indicated, each internucleoside linkage of an oligonucleotide having a gapmer motif may be modified or unmodified and may or may not follow the gapmer modification pattern of the sugar modifications. For example, the internucleoside linkages within the wing regions of a gapmer may be the same or different from one another and may be the same or different from the internucleoside linkages of the gap region. Likewise, such gapmer oligonucleotides may comprise one or more modified nucleobase independent of the gapmer pattern of the sugar modifications. Furthermore, unless otherwise indicated, each internucleoside linkage and each nucleobase of a fully modified oligonucleotide may be modified or unmodified. One of skill in the art will appreciate that such motifs may be combined to create a variety of oligonucleotides. Herein, if a description of an oligonucleotide is silent with respect to one or more parameter, such parameter is not limited. Thus, a modified oligonucleotide described only as having a gapmer motif without further description may have any length, internucleoside linkage motif, and nucleobase motif. Unless otherwise indicated, all modifications are independent of nucleobase sequence.

In certain embodiments, oligonucleotides have a nucleobase sequence that is complementary to a second oligonucleotide or a target nucleic acid. In certain such embodiments, a region of an oligonucleotide has a nucleobase sequence that is complementary to a second oligonucleotide or a target nucleic acid. In certain embodiments, the nucleobase sequence of a region or entire length of an oligonucleotide is at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or 100% complementary to the second oligonucleotide or target nucleic acid. In certain embodiments, antisense compounds comprise two oligomeric compounds, wherein the two oligonucleotides of the oligomeric compounds are at least 80%, at least 90%, or 100% complementary to each other. In certain embodiments, one or both oligonucleotides of a double-stranded antisense compound comprise two nucleosides that are not complementary to the other

oligonucleotide.

Conjugated Groups and Terminal Groups

In certain embodiments, antisense compounds and oligomeric compounds comprise conjugate groups and/or terminal groups. In certain such embodiments, oligonucleotides are covalently attached to one or more conjugate group. In certain embodiments, conjugate groups modify one or more properties of the attached oligonucleotide, including but not limited to pharmacodynamics, pharmacokinetics, stability, binding, absorption, cellular distribution, cellular uptake, charge and clearance. In certain embodiments, conjugate groups impart a new property on the attached oligonucleotide, *e.g.*, fluorophores or reporter groups that enable detection of the oligonucleotide. Conjugate groups and/or terminal groups may be added to oligonucleotides having any of the modifications or motifs described above. Thus, for example, an antisense compound or oligomeric compound comprising an oligonucleotide having a gapmer motif may also comprise a conjugate group.

Conjugate groups include, without limitation, intercalators, reporter molecules, polyamines, polyamides, peptides, carbohydrates, vitamin moieties, polyethylene glycols, thioethers, polyethers, cholesterols, thiocholesterols, cholic acid moieties, folate, lipids, phospholipids, biotin, phenazine, phenanthridine, anthraquinone, adamantane, acridine, fluoresceins, rhodamines, coumarins, fluorophores, and dyes. Certain conjugate groups have been described previously, for example: cholesterol moiety (Letsinger et al., Proc. Natl. Acad. Sci. USA, 1989, 86, 6553-6556), cholic acid (Manoharan et al., *Bioorg. Med. Chem. Lett*., 1994, *4*, 1053-1060), a thioether, *e.g.*, hexyl-S-tritylthiol (Manoharan et al., *Ann. N.Y. Acad. Sci*., 1992, *660*, 306-309; Manoharan et al., *Bioorg. Med. Chem. Let.,* 1993, *3*, 2765-2770), a thiocholesterol (Oberhauser et al., *Nucl. Acids Res*., 1992, *20*, 533-538), an aliphatic chain, *e.g.*, do-decan-diol or undecyl residues (Saison-Behmoaras et al., *EMBO J.,* 1991, *10*, 1111-1118; Kabanov et al., *FEBS Lett*., 1990, *259*, 327-330; Svinarchuk et al., *Biochimie*, 1993, *75*, 49-54), a phospholipid, e.g., di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., *Tetrahedron Lett*., 1995, *36*, 3651-3654; Shea et al., *Nucl. Acids Res*., 1990, *18*, 3777-3783), a polyamine or a polyethylene glycol chain (Manoharan et al., *Nucleosides & Nucleotides*, 1995, *14*, 969-973), or adamantane acetic acid (Manoharan et al., *Tetrahedron Lett*., 1995, *36*, 3651-3654), a palmityl moiety (Mishra et al., *Biochim. Biophys. Acta*, 1995, *1264,* 229-237), an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke et al., *J. Pharmacol. Exp. Ther.,* 1996, *277*, 923-937), a tocopherol group (Nishina et al., *Molecular Therapy Nucleic Acids*, 2015, *4*, e220; doi:10.1038/mtna.2014.72 and Nishina et al., *Molecular Therapy,* 2008, *16*, 734-740), or a GalNAc cluster (*e.g*., WO2014/179620).

In certain embodiments, a conjugate group comprises an active drug substance, for example, aspirin, warfarin, phenylbutazone, ibuprofen, suprofen, fen-bufen, ketoprofen, (*S*)-(+)-pranoprofen, carprofen, dansylsarcosine, 2,3,5-triiodobenzoic acid, fingolimod, flufenamic acid, folinic acid, a benzothiadiazide,

chlorothiazide, a diazepine, indo-methicin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic.

Conjugate groups are attached directly or via an optional conjugate linker to a parent compound, such as an oligonucleotide. In certain embodiments, conjugate groups are directly attached to oligonucleotides. In certain embodiments, conjugate groups are indirectly attached to oligonucleotides via conjugate linkers. In certain embodiments, the conjugate linker comprises a chain structure, such as a hydrocarbyl chain, or an oligomer of repeating units such as ethylene glycol or amino acid units. In certain embodiments, conjugate groups comprise a cleavable moiety. In certain embodiments, conjugate groups are attached to oligonucleotides via a cleavable moiety. In certain embodiments, conjugate linkers comprise a cleavable moiety. In certain such embodiments, conjugate linkers are attached to oligonucleotides via a cleavable moiety. In certain embodiments, oligonucleotides comprise a cleavable moiety, wherein the cleavable moiety is a nucleoside is attached to a cleavable internucleoside linkage, such as a phosphate internucleoside linakge. In certain embodiments, a conjugate group comprises a nucleoside or oligonucleotide, wherein the nucleoside or oligonucleotide of the conjugate group is indirectly attached to a parent oligonucleotide.

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

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

Examples of conjugate linkers include but are not limited to pyrrolidine, 8-amino-3,6-dioxaoctanoic acid (ADO), succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) and 6-aminohexanoic acid (AHEX or AHA). Other conjugate linkers include but are not limited to substituted or unsubstituted C_1-C_{10} alkyl, substituted or unsubstituted C_2-C_{10} alkenyl or substituted or unsubstituted C_2-C_{10} alkynyl, wherein a

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

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

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

In certain embodiments, a cleavable moiety is a nucleoside. In certain such embodiments, the unmodified or modified nucleoside comprises an optionally protected heterocyclic base selected from a purine, substituted purine, pyrimidine or substituted pyrimidine. In certain embodiments, a cleavable moiety is a nucleoside selected from uracil, thymine, cytosine, 4-N-benzoylcytosine, 5-methylcytosine, 4-N-benzoyl-5-methylcytosine, adenine, 6-N-benzoyladenine, guanine and 2-N-isobutyrylguanine. In certain embodiments, a cleavable moiety is 2'-deoxy nucleoside that is attached to either the 3' or 5'-terminal nucleoside of an oligonucleotide by a phosphate internucleoside linkage and covalently attached to the conjugate linker or conjugate group by a phosphate or phosphorothioate linkage. In certain such embodiments, the cleavable moiety is 2'-deoxyadenosine.

Conjugate groups may be attached to either or both ends of an oligonucleotide and/or at any internal position. In certain embodiments, conjugate groups are attached to the 2'-position of a nucleoside of a modified oligonucleotide. In certain embodiments, conjugate groups that are attached to either or both ends of an oligonucleotide are terminal groups. In certain such embodiments, conjugate groups or terminal groups are attached at the 3’ and/or 5’-end of oligonucleotides. In certain such embodiments, conjugate groups (or terminal groups) are attached at the 3’-end of oligonucleotides. In certain embodiments, conjugate groups are attached near the 3’-end of oligonucleotides. In certain embodiments, conjugate groups (or terminal groups) are attached at the 5’-end of oligonucleotides. In certain embodiments, conjugate groups are attached near the 5’-end of oligonucleotides.

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

In certain embodiments, a conjugate group is a cell-targeting moiety. In certain embodiments, a conjugate group, optional conjugate linker, and optional cleavable moiety have the general formula:

$$\underbrace{[\text{Ligand}—\text{Tether}]_n—[\text{Branching group}]_m}_{\text{Cell-targeting moiety}}—[\text{Conjugate Linker}]_j—[\text{Cleavable Moiety}]_k—\}$$

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

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

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

In certain embodiments, the cell-targeting moiety comprises a branching group comprising one or more groups selected from alkyl, amino, oxo, amide, disulfide, polyethylene glycol, ether, thioether and hydroxylamino groups. In certain embodiments, the branching group comprises a branched aliphatic group comprising groups selected from alkyl, amino, oxo, amide, disulfide, polyethylene glycol, ether, thioether and hydroxylamino groups. In certain such embodiments, the branched aliphatic group comprises groups selected from alkyl, amino, oxo, amide and ether groups. In certain such embodiments, the branched aliphatic group comprises groups selected from alkyl, amino and ether groups. In certain such embodiments, the branched aliphatic group comprises groups selected from alkyl and ether groups. In certain embodiments, the branching group comprises a mono or polycyclic ring system.

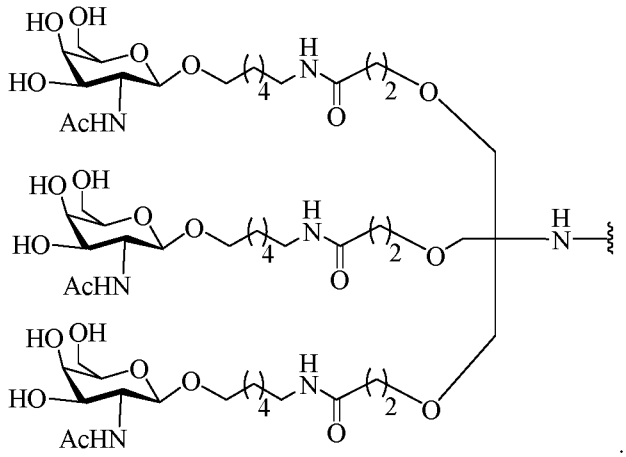
In certain embodiments, each tether of a cell-targeting moiety comprises one or more groups selected from alkyl, substituted alkyl, ether, thioether, disulfide, amino, oxo, amide, phosphodiester, and polyethylene glycol, in any combination. In certain embodiments, each tether is a linear aliphatic group comprising one or more groups selected from alkyl, ether, thioether, disulfide, amino, oxo, amide, and polyethylene glycol, in any combination. In certain embodiments, each tether is a linear aliphatic group comprising one or more groups selected from alkyl, phosphodiester, ether, amino, oxo, and amide, in any combination. In certain embodiments, each tether is a linear aliphatic group comprising one or more groups selected from alkyl,

ether, amino, oxo, and amid, in any combination. In certain embodiments, each tether is a linear aliphatic group comprising one or more groups selected from alkyl, amino, and oxo, in any combination. In certain embodiments, each tether is a linear aliphatic group comprising one or more groups selected from alkyl and oxo, in any combination. In certain embodiments, each tether is a linear aliphatic group comprising one or more groups selected from alkyl and phosphodiester, in any combination. In certain embodiments, each tether comprises at least one phosphorus linking group or neutral linking group. In certain embodiments, each tether comprises a chain from about 6 to about 20 atoms in length. In certain embodiments, each tether comprises a chain from about 10 to about 18 atoms in length. In certain embodiments, each tether comprises about 10 atoms in chain length.

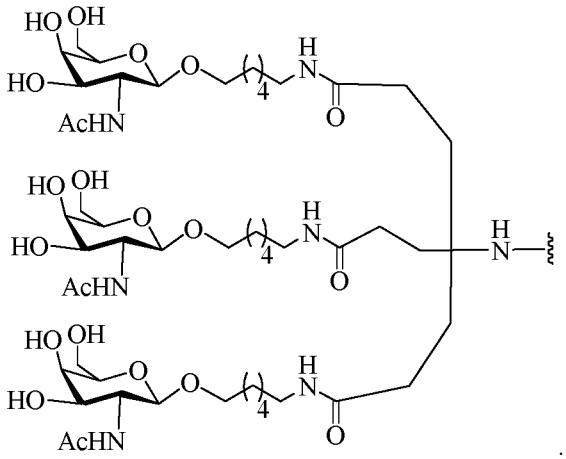
In certain embodiments, each ligand of a cell-targeting moiety has an affinity for at least one type of receptor on a target cell. In certain embodiments, each ligand has an affinity for at least one type of receptor on the surface of a mammalian liver cell. In certain embodiments, each ligand has an affinity for the hepatic asialoglycoprotein receptor (ASGP-R). In certain embodiments, each ligand is a carbohydrate. In certain embodiments, each ligand is, independently selected from galactose, N-acetyl galactoseamine (GalNAc), mannose, glucose, glucoseamine and fucose. In certain embodiments, each ligand is N-acetyl galactoseamine (GalNAc). In certain embodiments, the cell-targeting moiety comprises 3 GalNAc ligands. In certain embodiments, the cell-targeting moiety comprises 2 GalNAc ligands. In certain embodiments, the cell-targeting moiety comprises 1 GalNAc ligand.

In certain embodiments, each ligand of a cell-targeting moiety is a carbohydrate, carbohydrate derivative, modified carbohydrate, polysaccharide, modified polysaccharide, or polysaccharide derivative. In certain such embodiments, the conjugate group comprises a carbohydrate cluster (*see*, e.g., Maier et al., "Synthesis of Antisense Oligonucleotides Conjugated to a Multivalent Carbohydrate Cluster for Cellular Targeting," *Bioconjugate Chemistry*, 2003, *14*, 18-29, or Rensen et al., "Design and Synthesis of Novel *N*-Acetylgalactosamine-Terminated Glycolipids for Targeting of Lipoproteins to the Hepatic Asiaglycoprotein Receptor," *J. Med. Chem.* 2004, *47*, 5798-5808, which are incorporated herein by reference in their entirety). In certain such embodiments, each ligand is an amino sugar or a thio sugar. For example, amino sugars may be selected from any number of compounds known in the art, such as sialic acid, α-D-galactosamine, β-muramic acid, 2-deoxy-2-methylamino-L-glucopyranose, 4,6-dideoxy-4-formamido-2,3-di-*O*-methyl-D-mannopyranose, 2-deoxy-2-sulfoamino-D-glucopyranose and *N*-sulfo-D-glucosamine, and *N*-glycoloyl-α-neuraminic acid. For example, thio sugars may be selected from 5-Thio-β-D-glucopyranose, methyl 2,3,4-tri-*O*-acetyl-1-thio-6-*O*-trityl-α-D-glucopyranoside, 4-thio-β-D-galactopyranose, and ethyl 3,4,6,7-tetra-*O*-acetyl-2-deoxy-1,5-dithio-α-D-*gluco*-heptopyranoside.

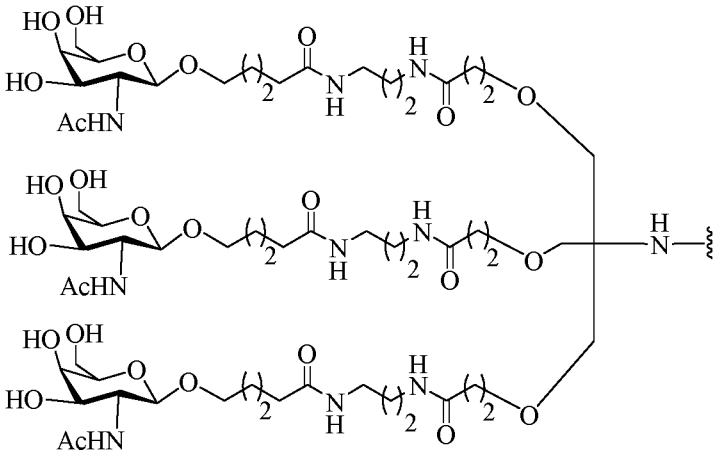
In certain embodiments, conjugate groups comprise a cell-targeting moiety having the formula:



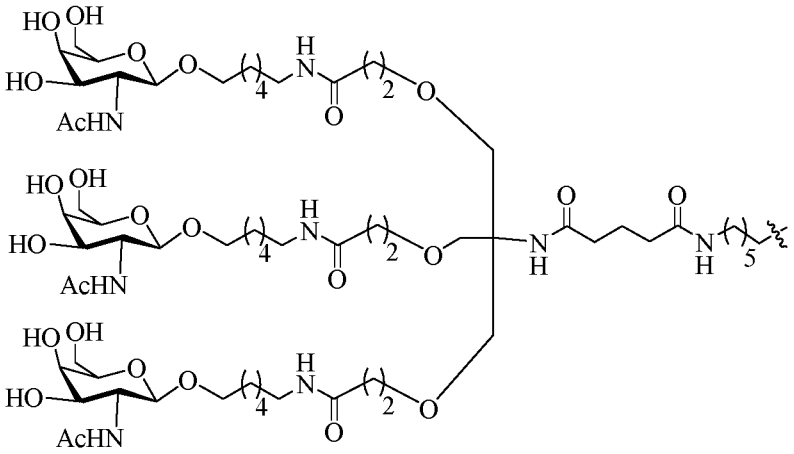
In certain embodiments, conjugate groups comprise a cell-targeting moiety having the formula:



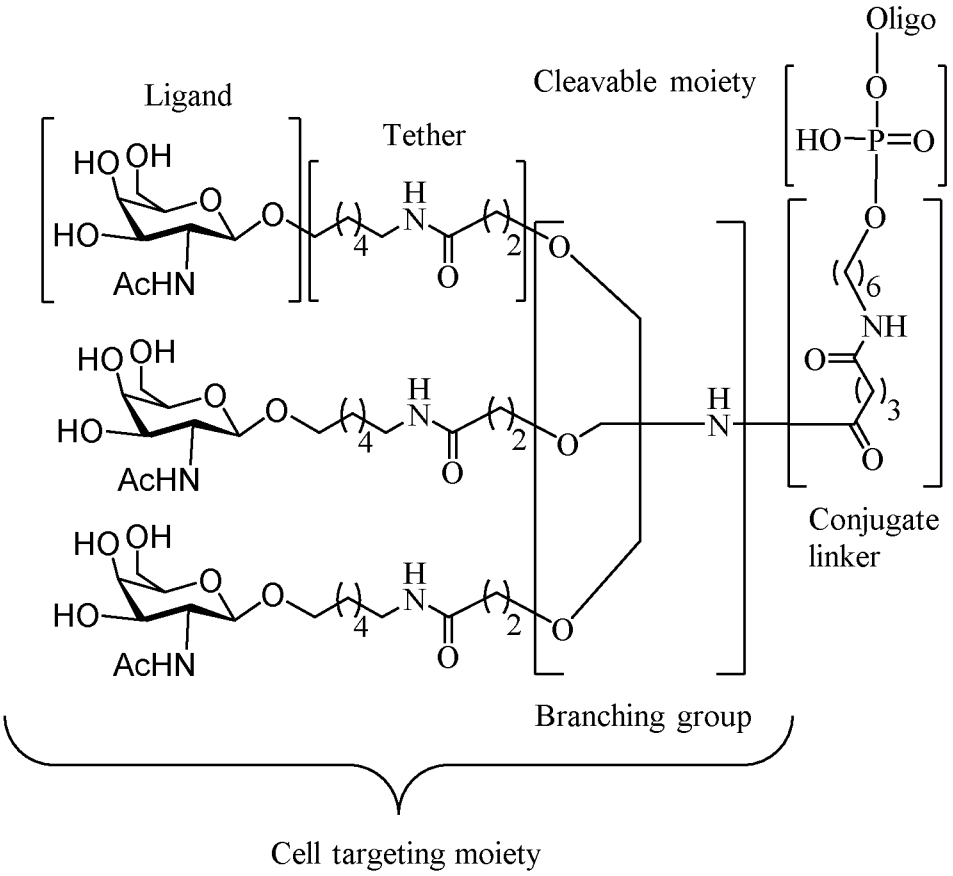
In certain embodiments, conjugate groups comprise a cell-targeting moiety having the formula:



In certain embodiments, antisense compounds and oligomeric compounds comprise a conjugate group and conjugate linker described herein as "LICA-1". LICA-1 has the formula:



In certain embodiments, antisense compounds and oligomeric compounds comprising LICA-1 have the formula:



wherein oligo is an oligonucleotide.

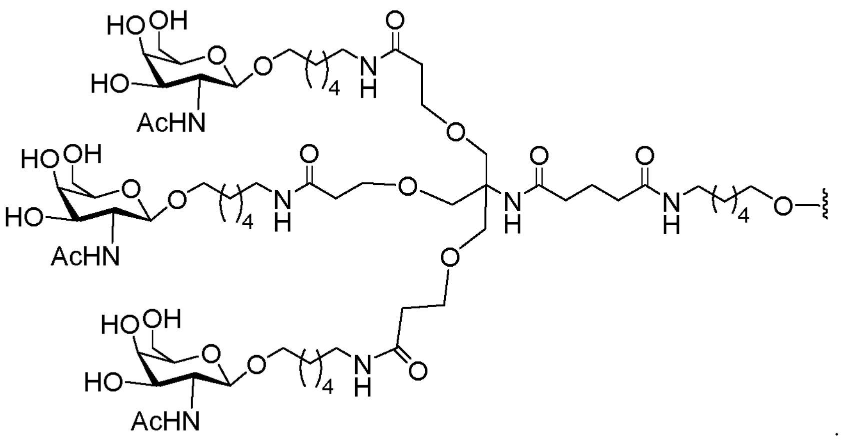
Representative United States patents, United States patent application publications, international patent application publications, and other publications that teach the preparation of certain of the above noted

conjugate groups, oligomeric compounds and antisense compounds comprising conjugate groups, tethers, conjugate linkers, branching groups, ligands, cleavable moieties as well as other modifications include without limitation, US 5,994,517, US 6,300,319, US 6,660,720, US 6,906,182, US 7,262,177, US 7,491,805, US 8,106,022, US 7,723,509, US 2006/0148740, US 2011/0123520, WO 2013/033230 and WO 2012/037254, Biessen et al., *J. Med. Chem.* 1995, *38*, 1846-1852, Lee et al., *Bioorganic & Medicinal Chemistry* 2011,*19*, 2494-2500, Rensen et al., *J. Biol. Chem.* 2001, *276*, 37577-37584, Rensen et al., *J. Med. Chem.* 2004, *47*, 5798-5808, Sliedregt et al., *J. Med. Chem.* 1999, *42*, 609-618, and Valentijn et al., *Tetrahedron,* 1997, *53,* 759-770, each of which is incorporated by reference herein in its entirety.

In certain embodiments, antisense compounds and oligomeric compounds comprise modified oligonucleotides comprising a gapmer or fully modified motif and a conjugate group comprising at least one, two, or three GalNAc ligands. In certain embodiments antisense compounds and oligomeric compounds comprise a conjugate group found in any of the following references: Lee, *Carbohydr Res*, 1978, 67, 509-514; Connolly et al., *J Biol Chem*, 1982, 257, 939-945; Pavia et al., *Int J Pep Protein Res*, 1983, 22, 539-548; Lee et al., *Biochem*, 1984, 23, 4255-4261; Lee et al., *Glycoconjugate J*, 1987, 4, 317-328; Toyokuni et al., *Tetrahedron Lett*, 1990, 31, 2673-2676; Biessen et al., *J Med Chem*, 1995, 38, 1538-1546; Valentijn et al., *Tetrahedron*, 1997, 53, 759-770; Kim et al., *Tetrahedron Lett*, 1997, 38, 3487-3490; Lee et al., *Bioconjug Chem*, 1997, 8, 762-765; Kato et al., *Glycobiol*, 2001, 11, 821-829; Rensen et al., *J Biol Chem*, 2001, 276, 37577-37584; Lee et al., *Methods Enzymol*, 2003, 362, 38-43; Westerlind et al., *Glycoconj J*, 2004, 21, 227-241; Lee et al., *Bioorg Med Chem Lett*, 2006, 16(19), 5132-5135; Maierhofer et al., *Bioorg Med Chem*, 2007, 15, 7661-7676; Khorev et al., *Bioorg Med Chem*, 2008, 16, 5216-5231; Lee et al., *Bioorg Med Chem*, 2011, 19, 2494-2500; Kornilova et al., Analyt Biochem, 2012, 425, 43-46; Pujol et al., *Angew Chemie Int Ed Engl*, 2012, 51, 7445-7448; Biessen et al., *J Med Chem*, 1995, 38, 1846-1852; Sliedregt et al., *J Med Chem*, 1999, 42, 609-618; Rensen et al., *J Med Chem*, 2004, 47, 5798-5808; Rensen et al., *Arterioscler Thromb Vasc Biol*, 2006, 26, 169-175; van Rossenberg et al., *Gene Ther*, 2004, 11, 457-464; Sato et al., *J Am Chem Soc*, 2004, 126, 14013-14022; Lee et al., *J Org Chem*, 2012, 77, 7564-7571; Biessen et al., *FASEB J*, 2000, 14, 1784-1792; Rajur et al., *Bioconjug Chem*, 1997, 8, 935-940; Duff et al., *Methods Enzymol*, 2000, 313, 297-321; Maier et al., *Bioconjug Chem*, 2003, 14, 18-29; Jayaprakash et al., *Org Lett*, 2010, 12, 5410-5413; Manoharan, *Antisense Nucleic Acid Drug Dev*, 2002, 12, 103-128; Merwin et al., *Bioconjug Chem*, 1994, 5, 612-620; Tomiya et al., Bioorg Med Chem, 2013, 21, 5275-5281; International applications WO1998/013381; WO2011/038356; WO1997/046098; WO2008/098788; WO2004/101619; WO2012/037254; WO2011/120053; WO2011/100131; WO2011/163121; WO2012/177947; WO2013/033230; WO2013/075035; WO2012/083185; WO2012/083046; WO2009/082607; WO2009/134487; WO2010/144740; WO2010/148013; WO1997/020563; WO2010/088537; WO2002/043771; WO2010/129709; WO2012/068187; WO2009/126933; WO2004/024757; WO2010/054406; WO2012/089352; WO2012/089602; WO2013/166121; WO2013/165816; U.S. Patents

4,751,219; 8,552,163; 6,908,903; 7,262,177; 5,994,517; 6,300,319; 8,106,022; 7,491,805; 7,491,805; 7,582,744; 8,137,695; 6,383,812; 6,525,031; 6,660,720; 7,723,509; 8,541,548; 8,344,125; 8,313,772; 8,349,308; 8,450,467; 8,501,930; 8,158,601; 7,262,177; 6,906,182; 6,620,916; 8,435,491; 8,404,862; 7,851,615; Published U.S. Patent Application Publications US2011/0097264; US2011/0097265; US2013/0004427; US2005/0164235; US2006/0148740; US2008/0281044; US2010/0240730; US2003/0119724; US2006/0183886; US2008/0206869; US2011/0269814; US2009/0286973; US2011/0207799; US2012/0136042; US2012/0165393; US2008/0281041; US2009/0203135; US2012/0035115; US2012/0095075; US2012/0101148; US2012/0128760; US2012/0157509; US2012/0230938; US2013/0109817; US2013/0121954; US2013/0178512; US2013/0236968; US2011/0123520; US2003/0077829; US2008/0108801; and US2009/0203132; each of which is incorporated by reference in its entirety.

In certain embodiments, a modified oligonucleotide targeting DGAT2 described herein further comprises a GalNAc conjugate group. In certain embodiments, the GalNAc conjugate group is 5'-Trishexylamino-(THA)-C6 GalNAc$_3$. In certain embodiments, the 5'-Trishexylamino-(THA)-C6 GalNAc$_3$ conjugate has the formula



In certain embodiments, the modified oligonucleotide is linked to the 5'-Trishexylamino-(THA)-C6 GalNAc$_3$ conjugate by a cleavable moiety. In certain embodiments, the cleavable moiety is a phosphate group.

Compositions and Methods for Formulating Pharmaceutical Compositions

In certain embodiments, the present invention provides pharmaceutical compositions comprising one or more antisense compound or a salt thereof. In certain such embodiments, the pharmaceutical composition comprises a suitable pharmaceutically acceptable diluent or carrier. In certain embodiments, a pharmaceutical composition comprises a sterile saline solution and one or more antisense compound. In certain embodiments, such pharmaceutical composition consists of a sterile saline solution and one or more antisense compound. In certain embodiments, the sterile saline is pharmaceutical grade saline. In certain

embodiments, a pharmaceutical composition comprises one or more antisense compound and sterile water. In certain embodiments, a pharmaceutical composition consists of one antisense compound and sterile water. In certain embodiments, the sterile water is pharmaceutical grade water. In certain embodiments, a pharmaceutical composition comprises one or more antisense compound and phosphate-buffered saline (PBS). In certain embodiments, a pharmaceutical composition consists of one or more antisense compound and sterile PBS. In certain embodiments, the sterile PBS is pharmaceutical grade PBS. Compositions and methods for the formulation of pharmaceutical compositions are dependent upon a number of criteria, including, but not limited to, route of administration, extent of disease, or dose to be administered.

An antisense compound targeted to DGAT2 nucleic acid can be utilized in pharmaceutical compositions by combining the antisense compound with a suitable pharmaceutically acceptable diluent or carrier. In certain embodiments, a pharmaceutically acceptable diluent is water, such as sterile water suitable for injection. Accordingly, in one embodiment, employed in the methods described herein is a pharmaceutical composition comprising an antisense compound targeted to DGAT2 nucleic acid and a pharmaceutically acceptable diluent. In certain embodiments, the pharmaceutically acceptable diluent is water. In certain embodiments, the antisense compound is an antisense oligonucleotide provided herein.

Pharmaceutical compositions comprising antisense compounds encompass any pharmaceutically acceptable salts, esters, or salts of such esters, or any other oligonucleotide which, upon administration to an animal, including a human, is capable of providing (directly or indirectly) the biologically active metabolite or residue thereof. Accordingly, for example, the disclosure is also drawn to pharmaceutically acceptable salts of antisense compounds, prodrugs, pharmaceutically acceptable salts of such prodrugs, and other bioequivalents. Suitable pharmaceutically acceptable salts include, but are not limited to, sodium and potassium salts.

A prodrug can include the incorporation of additional nucleosides at one or both ends of an antisense compound which are cleaved by endogenous nucleases within the body, to form the active antisense compound.

In certain embodiments, the compounds or compositions further comprise a pharmaceutically acceptable carrier or diluent.

Certain Compounds

In vitro screens in human HepG2 cells were performed with about 5,000 antisense oligonucleotides that exhibited 100% complementarity to a human DGAT2 gene sequence. The new compounds were compared with previously designed compounds, which have been previously determined to be some of the most potent antisense compounds in vitro (see, e.g. published PCT application WO 2005/019418). From these *in vitro* screens, several antisense oligonucleotides that exhibited the greatest potency in reducing the expression of human DGAT2 mRNA were selected for *in vivo* tolerability assays.

The selected oligonucleotides were tested for tolerability in a CD1 mouse model, as well as a Sprague-Dawley rat model. In these models, body weights and organ weights, liver function markers (such as alanine transaminase, aspartate transaminase, and bilirubin), and kidney function markers (such as BUN and creatinine) were measured.

Final evaluation of all studies (Examples 1-15) led to the selection of eight oligonucleotids having a nuclebase sequence of SEQ ID NO: 1371 (ISIS 484085), SEQ ID NO: 1415 (ISIS 484129), SEQ ID NO: 1423 (ISIS484137), SEQ ID NO: 1844 (ISIS 495576), SEQ ID NO: 2959 (ISIS 501861), SEQ ID NO: 3292 (ISIS 502194), SEQ ID NO: 4198 (ISIS 525443), and SEQ ID NO: 4373 (ISIS 525612). The compounds are complementary to the regions 23242-23261, 26630-26649, 26778-26797, 15251-15270, 28026-28045, 35436-35455, 10820-10836, and 23246-23262. In certain embodiments, the compounds targeting the listed regions, as further described herein, comprise a modified oligonucleotide having some nucleobase portion of the sequence recited in the SEQ ID Nos, as further described herein. In certain embodiments, the compounds targeting the listed regions or having a nucleobase portion of a sequence recited in the listed SEQ ID Nos can be of various lengths, as further described herein, and can have one of various motifs, as further described herein. In certain embodiments, a compound targeting a region or having a nucleobase portion of a sequence in the listed SEQ ID Nos has the specific length and motif, as indicated by the ISIS Nos: 484085, 484129, 484137, 495576, 501861, 502194, 525443, and 525612.

These eight compounds were tested for activity, pharmacokinetic profile and tolerability in cynomolgus monkeys (Example 16). Specifically, ISIS 484137 was found to be potent and the most tolerable in this monkey study. Further evaluation of ISIS 484137 in a separate monkey study (Example 17) confirmed this finding.

The nucleotide sequence of ISIS 484137 is fully homologous to the rhesus monkey DGAT2 mRNA transcript. The cynomolgus monkey is regarded as a relevant preclinical safety model system for oligonucleotide therapeutics and the demonstrated pharmacologic activity of ISIS 484137 in this species makes it an appropriate species for safety assessment. General toxicology studies were conducted with ISIS 484137 in monkeys for 13 weeks of treatment and it was well tolerated with no overt adverse effects and no changes in routine laboratory parameters. ISIS 484137 reduced the expression of hepatic DGAT2 by about 70%.

The findings observed in mice and monkey toxicology studies following 13-weeks of ISIS 484137 treatment were, in general, non-specific class effects that are typical for 2′-MOE ASOs. There was no drug-related mortality or changes in clinical signs up to the highest doses tested (100 mg/kg in mice and 40 mg/kg in monkeys). There were no toxicologically significant findings at doses up to 12 mg/kg/wk for 13 weeks in the mouse and monkey studies, and therefore there is sufficient therapeutic margin to support the safe clinical use of ISIS 484137 at the proposed clinical doses and regimen.

The pharmacokinetic results confirm continuous and dose-dependent exposure to ISIS 484137 in the

13-week mouse and monkey studies. Pharmacokinetics observed in monkeys for antisense oligonucleotides typically well predict the observed plasma (and expected tissue) exposure levels in humans on the basis of mg/kg equivalent doses (Geary et al. 2003; 31: 1419-1428; Yu et al. Drug Metab Dispos 2007; 35: 460-468).

Thus, reduction of DGAT2 expression with ISIS 484137 provides a mechanism to reduce hepatic steatosis, thereby potentially attenuating subsequent inflammation and fibrosis. This mechanism of action could offer an attractive treatment option for patients who have significant hepatic steatosis associated with NAFLD and NASH.

EXAMPLES

The Examples below describe the screening process to identify the lead compounds targeted to DGAT2. Out of about 5,000 antisense oligonucleotides screened, ISIS 484085, ISIS 484129, ISIS 484137, ISIS 495576, ISIS 501861, ISIS 502194, ISIS 525443, and ISIS 525612 emerged as the top lead compounds. In particular, ISIS 484137 exhibited the best combination of properties in terms of potency and tolerability for DGAT2 out of about 5,000 antisense oligonucleotides.

Non-limiting disclosure and incorporation by reference

Although the sequence listing accompanying this filing identifies each sequence as either “RNA” or “DNA” as required, in reality, those sequences may be modified with any combination of chemical modifications. One of skill in the art will readily appreciate that such designation as “RNA” or “DNA” to describe modified oligonucleotides is, in certain instances, arbitrary. For example, an oligonucleotide comprising a nucleoside comprising a 2’-OH sugar moiety and a thymine base could be described as a DNA having a modified sugar (2’-OH for the natural 2’-H of DNA) or as an RNA having a modified base (thymine (methylated uracil) for natural uracil of RNA).

Accordingly, nucleic acid sequences provided herein, including, but not limited to those in the sequence listing, are intended to encompass nucleic acids containing any combination of natural or modified RNA and/or DNA, including, but not limited to such nucleic acids having modified nucleobases. By way of further example and without limitation, an oligonucleotide having the nucleobase sequence “ATCGATCG” encompasses any oligonucleotides having such nucleobase sequence, whether modified or unmodified, including, but not limited to, such compounds comprising RNA bases, such as those having sequence “AUCGAUCG” and those having some DNA bases and some RNA bases such as “AUCGATCG”.

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

Example 1: Antisense inhibition of human diacylglycerol acyltransferase 2 in HepG2 cells by MOE gapmers

Antisense oligonucleotides were designed targeting a diacylglycerol acyltransferase 2 (DGAT2) nucleic acid and were tested for their effects on DGAT2 mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 10,000 cells per well were transfected using Lipofectin reagent with 120 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2367 (forward sequence GGCCTCCCGGAGACTGA, designated herein as SEQ ID NO: 4; reverse sequence AAGTGATTTGCAGCTGGTTCCT, designated herein as SEQ ID NO: 5; probe sequence AGGTGAACTGAGCCAGCCTTCGGG, designated herein as SEQ ID NO: 6) was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells.

ISIS oligonucleotides from an earlier published application, WO 2005/019418, were also included in this assay. These ISIS oligonucleotides are ISIS 217312-217322, ISIS 217324, ISIS 217325, ISIS 217328, ISIS 217333, ISIS 217336-217339, ISIS 217341-217343, ISIS 217346-217348, ISIS 217353-217355, ISIS 334177, ISIS 366710, ISIS 366714, ISIS 366722, ISIS 366728, ISIS 366730, ISIS 366741, ISIS 366746, ISIS 369220, ISIS 369221, ISIS 369255, ISIS 370727, ISIS 370747, ISIS 370784.

The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE gapmers. The gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted in the human gene sequence. Each gapmer listed in the Tables below is targeted to either the human DGAT2 mRNA, designated herein as SEQ ID NO: 1 (RefSeq No. NM_032564.3) or the human DGAT2 genomic sequence, designated herein as SEQ ID NO: 2 (RefSeq No. NT_033927.5 truncated from nucleotides 5669186 to 5712008). 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

Table 1
Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
381726	278	297	CGCAGGACCCCGGAGTAGGC	75	9899	9918	38
217312	668	687	TGGATGGGAAAGTAGTCTCG	40	31600	31619	16
411887	669	688	CTGGATGGGAAAGTAGTCTC	38	31601	31620	50
411888	670	689	GCTGGATGGGAAAGTAGTCT	22	n/a	n/a	51
411889	671	690	AGCTGGATGGGAAAGTAGTC	31	n/a	n/a	52
411890	672	691	CAGCTGGATGGGAAAGTAGT	21	n/a	n/a	53
217313	673	692	CCAGCTGGATGGGAAAGTAG	24	n/a	n/a	17
411891	674	693	ACCAGCTGGATGGGAAAGTA	21	n/a	n/a	54
380109	675	694	CACCAGCTGGATGGGAAAGT	31	n/a	n/a	35
411892	676	695	TCACCAGCTGGATGGGAAAG	22	n/a	n/a	55
411893	677	696	TTCACCAGCTGGATGGGAAA	26	n/a	n/a	56
217314	678	697	CTTCACCAGCTGGATGGGAA	36	n/a	n/a	18
369219	679	698	TCTTCACCAGCTGGATGGGA	50	n/a	n/a	32
411894	680	699	GTCTTCACCAGCTGGATGGG	42	n/a	n/a	57
411895	681	700	TGTCTTCACCAGCTGGATGG	55	n/a	n/a	58
411896	682	701	GTGTCTTCACCAGCTGGATG	49	n/a	n/a	59
217315	683	702	TGTGTCTTCACCAGCTGGAT	55	n/a	n/a	19
380110	684	703	GTGTGTCTTCACCAGCTGGA	53	n/a	n/a	36
411897	685	704	TGTGTGTCTTCACCAGCTGG	55	n/a	n/a	60
411873	686	705	TTGTGTGTCTTCACCAGCTG	63	37214	37233	46
411898	687	706	GTTGTGTGTCTTCACCAGCT	54	37215	37234	61
217316	688	707	GGTTGTGTGTCTTCACCAGC	64	37216	37235	20
381727	689	708	AGGTTGTGTGTCTTCACCAG	59	37217	37236	39
411899	690	709	CAGGTTGTGTGTCTTCACCA	68	37218	37237	62
411874	691	710	GCAGGTTGTGTGTCTTCACC	65	37219	37238	47
411900	692	711	AGCAGGTTGTGTGTCTTCAC	55	37220	37239	63
217317	693	712	CAGCAGGTTGTGTGTCTTCA	66	37221	37240	21
381728	694	713	TCAGCAGGTTGTGTGTCTTC	56	37222	37241	40
411901	695	714	GTCAGCAGGTTGTGTGTCTT	64	37223	37242	64
411875	696	715	GGTCAGCAGGTTGTGTGTCT	45	37224	37243	48
411902	697	716	TGGTCAGCAGGTTGTGTGTC	55	37225	37244	65
217318	698	717	GTGGTCAGCAGGTTGTGTGT	44	37226	37245	22
369220	699	718	GGTGGTCAGCAGGTTGTGTG	29	37227	37246	33
411903	700	719	TGGTGGTCAGCAGGTTGTGT	51	37228	37247	66
411904	701	720	CTGGTGGTCAGCAGGTTGTG	57	37229	37248	67
411905	702	721	CCTGGTGGTCAGCAGGTTGT	64	37230	37249	68

217319	703	722	TCCTGGTGGTCAGCAGGTTG	58	37231	37250	23
381729	704	723	TTCCTGGTGGTCAGCAGGTT	61	37232	37251	41
411906	705	724	GTTCCTGGTGGTCAGCAGGT	63	37233	37252	69
411907	706	725	AGTTCCTGGTGGTCAGCAGG	58	37234	37253	70
411908	707	726	TAGTTCCTGGTGGTCAGCAG	48	37235	37254	71
217320	708	727	ATAGTTCCTGGTGGTCAGCA	46	37236	37255	24
381730	709	728	TATAGTTCCTGGTGGTCAGC	56	37237	37256	42
411909	710	729	ATATAGTTCCTGGTGGTCAG	53	37238	37257	72
411876	711	730	GATATAGTTCCTGGTGGTCA	57	37239	37258	49
411910	712	731	AGATATAGTTCCTGGTGGTC	56	37240	37259	73
217321	713	732	AAGATATAGTTCCTGGTGGT	41	37241	37260	25
381731	714	733	AAAGATATAGTTCCTGGTGG	54	37242	37261	43
411911	715	734	CAAAGATATAGTTCCTGGTG	61	37243	37262	74
411912	716	735	CCAAAGATATAGTTCCTGGT	66	37244	37263	75
411913	717	736	TCCAAAGATATAGTTCCTGG	63	37245	37264	76
217322	718	737	ATCCAAAGATATAGTTCCTG	39	37246	37265	26
369221	719	738	TATCCAAAGATATAGTTCCT	13	37247	37266	34
411914	720	739	GTATCCAAAGATATAGTTCC	8	37248	37267	77
411915	721	740	GGTATCCAAAGATATAGTTC	43	37249	37268	78
411916	722	741	TGGTATCCAAAGATATAGTT	42	37250	37269	79
217324	752	771	AAGGCACCCAGGCCCATGAT	46	37280	37299	27
381732	753	772	GAAGGCACCCAGGCCCATGA	38	37281	37300	44
380114	754	773	AGAAGGCACCCAGGCCCATG	38	37282	37301	37
411917	755	774	CAGAAGGCACCCAGGCCCAT	33	37283	37302	80
217325	875	894	CCTCCAGACATCAGGTACTC	29	37403	37422	28
217333	992	1011	TTGCCAGGCATGGAGCTCAG	37	38145	38164	29
381733	993	1012	CTTGCCAGGCATGGAGCTCA	51	38146	38165	45
411918	994	1013	TCTTGCCAGGCATGGAGCTC	47	38147	38166	81
411919	995	1014	TTCTTGCCAGGCATGGAGCT	54	38148	38167	82
217336	1139	1158	TGGACCCATCGGCCCCAGGA	52	39186	39205	30
411920	1140	1159	CTGGACCCATCGGCCCCAGG	41	39187	39206	83
411921	1141	1160	TCTGGACCCATCGGCCCCAG	20	39188	39207	84
411922	1142	1161	TTCTGGACCCATCGGCCCCA	27	39189	39208	85
411923	1143	1162	CTTCTGGACCCATCGGCCCC	30	39190	39209	86
217337	1144	1163	TCTTCTGGACCCATCGGCCC	37	39191	39210	31
411924	1145	1164	TTCTTCTGGACCCATCGGCC	44	39192	39211	87
411925	1146	1165	CTTCTTCTGGACCCATCGGC	27	39193	39212	88
411926	1147	1166	ACTTCTTCTGGACCCATCGG	28	39194	39213	89
411927	1148	1167	AACTTCTTCTGGACCCATCG	28	39195	39214	90

Table 2
Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
217338	1149	1168	GAACTTCTTCTGGACCCATC	19	39196	39215	91
411928	1150	1169	GGAACTTCTTCTGGACCCAT	36	39197	39216	104
411929	1151	1170	TGGAACTTCTTCTGGACCCA	43	39198	39217	105
411930	1152	1171	CTGGAACTTCTTCTGGACCC	25	39199	39218	106
411931	1153	1172	TCTGGAACTTCTTCTGGACC	43	39200	39219	107
217339	1154	1173	TTCTGGAACTTCTTCTGGAC	37	39201	39220	92
217341	1226	1245	GGCACCAGCCCCCAGGTGTC	30	39273	39292	93
411932	1227	1246	GGGCACCAGCCCCCAGGTGT	34	39274	39293	108
411933	1228	1247	AGGGCACCAGCCCCCAGGTG	29	39275	39294	109
411934	1229	1248	TAGGGCACCAGCCCCCAGGT	32	39276	39295	110
411935	1230	1249	GTAGGGCACCAGCCCCCAGG	23	39277	39296	111
217342	1231	1250	AGTAGGGCACCAGCCCCCAG	0	39278	39297	94
411936	1232	1251	GAGTAGGGCACCAGCCCCCA	0	39279	39298	112
411937	1233	1252	GGAGTAGGGCACCAGCCCCC	17	39280	39299	113
411938	1234	1253	TGGAGTAGGGCACCAGCCCC	28	39281	39300	114
411939	1235	1254	TTGGAGTAGGGCACCAGCCC	16	39282	39301	115
217343	1236	1255	CTTGGAGTAGGGCACCAGCC	35	39283	39302	95
411940	1237	1256	GCTTGGAGTAGGGCACCAGC	45	39284	39303	116
411941	1238	1257	GGCTTGGAGTAGGGCACCAG	56	39285	39304	117
366741	1245	1264	GGTGATGGGCTTGGAGTAGG	36	39292	39311	102
411942	1246	1265	TGGTGATGGGCTTGGAGTAG	28	39293	39312	118
411943	1247	1266	GTGGTGATGGGCTTGGAGTA	23	39294	39313	119
217346	1338	1357	CAGGGCCTCCATGTACATGG	37	41309	41328	96
369255	1339	1358	CCAGGGCCTCCATGTACATG	38	41310	41329	103
411944	1340	1359	ACCAGGGCCTCCATGTACAT	52	41311	41330	120
411945	1341	1360	CACCAGGGCCTCCATGTACA	53	41312	41331	121
411946	1342	1361	TCACCAGGGCCTCCATGTAC	37	41313	41332	122
217347	1343	1362	TTCACCAGGGCCTCCATGTA	20	41314	41333	97
411947	1344	1363	CTTCACCAGGGCCTCCATGT	46	41315	41334	123
411948	1345	1364	GCTTCACCAGGGCCTCCATG	31	41316	41335	124
411949	1346	1365	AGCTTCACCAGGGCCTCCAT	42	41317	41336	125
411950	1347	1366	GAGCTTCACCAGGGCCTCCA	52	41318	41337	126
217348	1348	1367	AGAGCTTCACCAGGGCCTCC	46	41319	41338	98
411951	1349	1368	AAGAGCTTCACCAGGGCCTC	44	41320	41339	127
217353	1498	1517	AACCCACAGACACCCATGAC	4	41469	41488	99
411952	1499	1518	TAACCCACAGACACCCATGA	14	41470	41489	128

411953	1500	1519	ATAACCCACAGACACCCATG	24	41471	41490	129
411954	1501	1520	AATAACCCACAGACACCCAT	0	41472	41491	130
411955	1502	1521	AAATAACCCACAGACACCCA	10	41473	41492	131
217354	1503	1522	TAAATAACCCACAGACACCC	6	41474	41493	100
411956	1504	1523	TTAAATAACCCACAGACACC	0	41475	41494	132
411957	1505	1524	TTTAAATAACCCACAGACAC	14	41476	41495	133
411958	1506	1525	TTTTAAATAACCCACAGACA	10	41477	41496	134
411959	1507	1526	CTTTTAAATAACCCACAGAC	0	41478	41497	135
217355	1508	1527	TCTTTTAAATAACCCACAGA	10	41479	41498	101
411960	1509	1528	TTCTTTTAAATAACCCACAG	8	41480	41499	136
411961	1510	1529	TTTCTTTTAAATAACCCACA	1	41481	41500	137
411962	1511	1530	ATTTCTTTTAAATAACCCAC	1	41482	41501	138
411963	1512	1531	AATTTCTTTTAAATAACCCA	0	41483	41502	139
411964	1513	1532	TAATTTCTTTTAAATAACCC	0	41484	41503	140
411965	1514	1533	ATAATTTCTTTTAAATAACC	0	41485	41504	141
411966	1515	1534	TATAATTTCTTTTAAATAAC	0	41486	41505	142
411967	1516	1535	TTATAATTTCTTTTAAATAA	0	41487	41506	143

Table 3

Inhibition of DGAT2 mRNA by MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	Motif	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413166	254	273	ATGAGGGTCTTCATGGCTGA	5-10-5	7	9875	9894	156
413167	266	285	GAGTAGGCGGCTATGAGGGT	5-10-5	11	9887	9906	157
413168	269	288	CCGGAGTAGGCGGCTATGAG	5-10-5	37	9890	9909	158
413169	272	291	ACCCCGGAGTAGGCGGCTAT	5-10-5	46	9893	9912	159
334177	275	294	AGGACCCCGGAGTAGGCGGC	5-10-5	52	9896	9915	145
413170	304	323	GGTCAGCCTCGGCCTGACGC	5-10-5	11	9925	9944	160
413171	307	326	TCCGGTCAGCCTCGGCCTGA	5-10-5	20	9928	9947	161
413172	310	329	GGCTCCGGTCAGCCTCGGCC	5-10-5	0	9931	9950	162
413173	331	350	CAGGTCCTCCGTGAGAGCGC	5-10-5	29	9952	9971	163
413174	339	358	CGACAGCGCAGGTCCTCCGT	5-10-5	48	9960	9979	164
413175	348	367	CCCCTCGCGCGACAGCGCAG	5-10-5	25	9969	9988	165
413176	355	374	TCCCAGACCCCTCGCGCGAC	5-10-5	36	9976	9995	166
413177	361	380	CCCATCTCCCAGACCCCTCG	5-10-5	12	9982	10001	167
413178	367	386	CAGTGCCCCATCTCCCAGAC	5-10-5	0	n/a	n/a	168
413179	370	389	ATCCAGTGCCCCATCTCCCA	5-10-5	16	n/a	n/a	169
413180	376	395	TGCTGGATCCAGTGCCCCAT	5-10-5	44	n/a	n/a	170
413181	379	398	GGATGCTGGATCCAGTGCCC	5-10-5	32	n/a	n/a	171
413182	382	401	AGAGGATGCTGGATCCAGTG	5-10-5	45	25508	25527	172
413183	385	404	CGGAGAGGATGCTGGATCCA	5-10-5	47	25511	25530	173

413184	396	415	GTCCTGGAGGGCGGAGAGGA	5-10-5	32	25522	25541	174
413185	404	423	GAGAAGAGGTCCTGGAGGGC	5-10-5	10	25530	25549	175
366710	425	444	GACCTATTGAGCCAGGTGAC	5-10-5	36	25551	25570	146
370727	443	462	AGCTGCTTTTCCACCTTGGA	2-16-2	45	25569	25588	152
366714	445	464	GTAGCTGCTTTTCCACCTTG	5-10-5	43	25571	25590	147
413186	448	467	CCTGTAGCTGCTTTTCCACC	5-10-5	29	25574	25593	176
413187	451	470	TGACCTGTAGCTGCTTTTCC	5-10-5	35	25577	25596	177
413188	455	474	GAGATGACCTGTAGCTGCTT	5-10-5	34	25581	25600	178
413189	458	477	ACTGAGATGACCTGTAGCTG	5-10-5	33	25584	25603	179
413190	461	480	AGCACTGAGATGACCTGTAG	5-10-5	36	25587	25606	180
413191	467	486	CACTGGAGCACTGAGATGAC	5-10-5	27	25593	25612	181
413192	473	492	AGGACCCACTGGAGCACTGA	5-10-5	40	25599	25618	182
413193	476	495	GACAGGACCCACTGGAGCAC	5-10-5	44	25602	25621	183
380089	482	501	AGGAAGGACAGGACCCACTG	5-10-5	38	25608	25627	155
413194	494	513	ACTCCCAGTACAAGGAAGGA	5-10-5	3	n/a	n/a	184
413195	497	516	GCCACTCCCAGTACAAGGAA	5-10-5	0	n/a	n/a	185
413196	500	519	CAGGCCACTCCCAGTACAAG	5-10-5	1	n/a	n/a	186
413197	503	522	CTGCAGGCCACTCCCAGTAC	5-10-5	40	n/a	n/a	187
413198	506	525	GCACTGCAGGCCACTCCCAG	5-10-5	37	n/a	n/a	188
413199	510	529	GATGGCACTGCAGGCCACTC	5-10-5	28	31077	31096	189
366722	530	549	GTGCAGAATATGTACATGAG	5-10-5	43	31097	31116	148
413200	554	573	AGCACAGCGATGAGCCAGCA	5-10-5	35	31121	31140	190
413201	570	589	CAGCCAAGTGAAGTAGAGCA	5-10-5	41	31137	31156	191
413202	573	592	CACCAGCCAAGTGAAGTAGA	5-10-5	23	31140	31159	192
413203	576	595	AAACACCAGCCAAGTGAAGT	5-10-5	9	31143	31162	193
413204	579	598	GTCAAACACCAGCCAAGTGA	5-10-5	15	31146	31165	194
413205	585	604	GTTCCAGTCAAACACCAGCC	5-10-5	31	31152	31171	195
413206	588	607	TGTGTTCCAGTCAAACACCA	5-10-5	23	31155	31174	196
413207	591	610	GGGTGTGTTCCAGTCAAACA	5-10-5	6	31158	31177	197
413208	594	613	CTTGGGTGTGTTCCAGTCAA	5-10-5	5	31161	31180	198
413209	615	634	CTGTGACCTCCTGCCACCTT	5-10-5	25	31547	31566	199
413210	618	637	CCACTGTGACCTCCTGCCAC	5-10-5	30	31550	31569	200
413211	621	640	GACCCACTGTGACCTCCTGC	5-10-5	25	31553	31572	201
413212	625	644	TTCGGACCCACTGTGACCTC	5-10-5	38	31557	31576	202
413213	629	648	CAGTTTCGGACCCACTGTGA	5-10-5	39	31561	31580	203
413214	632	651	GCCCAGTTTCGGACCCACTG	5-10-5	51	31564	31583	204
413215	635	654	ACAGCCCAGTTTCGGACCCA	5-10-5	27	31567	31586	205
413216	638	657	CACACAGCCCAGTTTCGGAC	5-10-5	24	31570	31589	206
413217	642	661	GCGCCACACAGCCCAGTTTC	5-10-5	31	31574	31593	207
413218	658	677	AGTAGTCTCGAAAGTAGCGC	5-10-5	39	31590	31609	208
413219	661	680	GAAAGTAGTCTCGAAAGTAG	5-10-5	0	31593	31612	209
413220	665	684	ATGGGAAAGTAGTCTCGAAA	5-10-5	0	31597	31616	210
366728	757	776	TGCAGAAGGCACCCAGGCCC	5-10-5	46	37285	37304	149
413221	780	799	TTCTGTGGCCTCTGTGCTGA	5-10-5	25	37308	37327	211

413222	783	802	CACTTCTGTGGCCTCTGTGC	5-10-5	38	37311	37330	212
413223	786	805	GCTCACTTCTGTGGCCTCTG	5-10-5	41	37314	37333	213
413224	789	808	CTTGCTCACTTCTGTGGCCT	5-10-5	48	37317	37336	214
413225	792	811	CTTCTTGCTCACTTCTGTGG	5-10-5	25	37320	37339	215
413226	798	817	TGGGAACTTCTTGCTCACTT	5-10-5	43	37326	37345	216
413227	801	820	GCCTGGGAACTTCTTGCTCA	5-10-5	47	37329	37348	217
413228	804	823	TATGCCTGGGAACTTCTTGC	5-10-5	26	37332	37351	218
413229	808	827	GCCGTATGCCTGGGAACTTC	5-10-5	29	37336	37355	219
413230	811	830	AAGGCCGTATGCCTGGGAAC	5-10-5	25	37339	37358	220
413231	814	833	GGTAAGGCCGTATGCCTGGG	5-10-5	41	37342	37361	221
217328	938	957	GCATTGCCACTCCCATTCTT	5-10-5	41	38091	38110	144
366730	979	998	AGCTCAGAGACTCAGCCGCA	5-10-5	39	38132	38151	150
370747	982	1001	TGGAGCTCAGAGACTCAGCC	2-16-2	37	38135	38154	153
366746	1366	1385	TGGTCTTGTGCTTGTCGAAG	5-10-5	41	41337	41356	151
370784	2128	2147	GCTGCATCCATGTCATCAGC	2-16-2	53	42099	42118	154

Table 4

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413232	817	836	CCAGGTAAGGCCGTATGCCT	78	37345	37364	225
413233	820	839	TAGCCAGGTAAGGCCGTATG	56	37348	37367	226
413234	823	842	GTGTAGCCAGGTAAGGCCGT	50	37351	37370	227
413235	827	846	GCCAGTGTAGCCAGGTAAGG	9	37355	37374	228
413236	861	880	GTACTCCCTCAACACAGGCA	72	37389	37408	229
413237	864	883	CAGGTACTCCCTCAACACAG	52	37392	37411	230
413238	867	886	CATCAGGTACTCCCTCAACA	35	37395	37414	231
413239	870	889	AGACATCAGGTACTCCCTCA	35	37398	37417	232
413240	878	897	ATACCTCCAGACATCAGGTA	50	n/a	n/a	233
413241	881	900	CAGATACCTCCAGACATCAG	38	n/a	n/a	234
413242	887	906	ACAGGGCAGATACCTCCAGA	58	n/a	n/a	235
413243	910	929	AATAGTCTATGGTGTCCCGG	63	38063	38082	236
413244	913	932	GCAAATAGTCTATGGTGTCC	60	38066	38085	237
413245	916	935	AAAGCAAATAGTCTATGGTG	46	38069	38088	238
413246	919	938	TTGAAAGCAAATAGTCTATG	42	38072	38091	239
413247	922	941	TCTTTGAAAGCAAATAGTCT	40	38075	38094	240
413248	925	944	CATTCTTTGAAAGCAAATAG	15	38078	38097	241
413249	928	947	TCCCATTCTTTGAAAGCAAA	31	38081	38100	242
413250	932	951	CCACTCCCATTCTTTGAAAG	34	38085	38104	243
413251	935	954	TTGCCACTCCCATTCTTTGA	39	38088	38107	244
217328	938	957	GCATTGCCACTCCCATTCTT	70	38091	38110	144

413252	976	995	TCAGAGACTCAGCCGCACCC	43	38129	38148	245
413253	987	1006	AGGCATGGAGCTCAGAGACT	69	38140	38159	246
413254	1002	1021	GACTGCATTCTTGCCAGGCA	60	38155	38174	247
413255	1005	1024	GGTGACTGCATTCTTGCCAG	25	38158	38177	248
413256	1012	1031	TCCGCAGGGTGACTGCATTC	48	38165	38184	249
369241	1019	1038	TTGCGGTTCCGCAGGGTGAC	70	38172	38191	222
413257	1022	1041	CCCTTGCGGTTCCGCAGGGT	36	38175	38194	250
413258	1025	1044	AAGCCCTTGCGGTTCCGCAG	67	38178	38197	251
413259	1028	1047	ACAAAGCCCTTGCGGTTCCG	35	38181	38200	252
413260	1034	1053	AGTTTCACAAAGCCCTTGCG	25	38187	38206	253
413261	1037	1056	GCCAGTTTCACAAAGCCCTT	34	38190	38209	254
413262	1040	1059	AGGGCCAGTTTCACAAAGCC	33	38193	38212	255
413263	1043	1062	CGCAGGGCCAGTTTCACAAA	31	38196	38215	256
413264	1088	1107	TCATTCTCTCCAAAGGAGTA	18	39135	39154	257
413265	1091	1110	ACTTCATTCTCTCCAAAGGA	45	39138	39157	258
413266	1095	1114	GTACACTTCATTCTCTCCAA	82	39142	39161	259
413267	1101	1120	CTGCTTGTACACTTCATTCT	58	39148	39167	260
413268	1105	1124	TCACCTGCTTGTACACTTCA	40	39152	39171	261
413269	1111	1130	CGAAGATCACCTGCTTGTAC	63	39158	39177	262
413270	1114	1133	CCTCGAAGATCACCTGCTTG	53	39161	39180	263
413271	1117	1136	CCTCCTCGAAGATCACCTGC	49	39164	39183	264
413272	1120	1139	AGCCCTCCTCGAAGATCACC	39	39167	39186	265
413273	1123	1142	AGGAGCCCTCCTCGAAGATC	31	39170	39189	266
413274	1126	1145	CCCAGGAGCCCTCCTCGAAG	54	39173	39192	267
413275	1129	1148	GGCCCCAGGAGCCCTCCTCG	40	39176	39195	268
411877	1136	1155	ACCCATCGGCCCCAGGAGCC	59	39183	39202	223
413276	1157	1176	TATTTCTGGAACTTCTTCTG	22	39204	39223	269
413277	1160	1179	ATGTATTTCTGGAACTTCTT	45	39207	39226	270
413278	1171	1190	GGGCGAAACCAATGTATTTC	24	39218	39237	271
413279	1208	1227	TCGGAGGAGAAGAGGCCTCG	60	39255	39274	272
413280	1211	1230	GTGTCGGAGGAGAAGAGGCC	52	39258	39277	273
413281	1215	1234	CCAGGTGTCGGAGGAGAAGA	53	39262	39281	274
413282	1222	1241	CCAGCCCCCAGGTGTCGGAG	50	39269	39288	275
413283	1250	1269	ACAGTGGTGATGGGCTTGGA	52	39297	39316	276
413284	1273	1292	GGATGGTGATGGGCTCTCCC	67	41244	41263	277
411879	1330	1349	CCATGTACATGGTGTGGTAC	52	41301	41320	224
413285	1334	1353	GCCTCCATGTACATGGTGTG	63	41305	41324	278
413286	1363	1382	TCTTGTGCTTGTCGAAGAGC	62	41334	41353	279
413287	1399	1418	CCTCCAGGACCTCAGTCTCC	66	41370	41389	280
413288	1403	1422	TTCACCTCCAGGACCTCAGT	46	41374	41393	281
413289	1407	1426	TCAGTTCACCTCCAGGACCT	46	41378	41397	282
413290	1412	1431	CTGGCTCAGTTCACCTCCAG	90	41383	41402	283
413291	1537	1556	TGTAATGGTTTAGCAAAATT	26	41508	41527	284
413292	1555	1574	TTAAAAAAGACCTAACATTG	0	41526	41545	285

413293	1559	1578	CTTCTTAAAAAAGACCTAAC	26	41530	41549	286
413294	1563	1582	TTTCCTTCTTAAAAAAGACC	9	41534	41553	287
413295	1567	1586	ACTTTTTCCTTCTTAAAAAA	0	41538	41557	288
413296	1572	1591	TACTGACTTTTTCCTTCTTA	39	41543	41562	289
413297	1616	1635	CCACCACCTAGAACAGGGCA	55	41587	41606	290
413298	1653	1672	AGGTTAGCTGAGCCACCCAG	59	41624	41643	291
413299	1840	1859	GTCCTGCAGTTTCAGGACTA	54	41811	41830	292
413300	1844	1863	ACTGGTCCTGCAGTTTCAGG	55	41815	41834	293
413301	1860	1879	TCCCCTTGGCAGAGAAACTG	47	41831	41850	294
413302	1864	1883	CTCCTCCCCTTGGCAGAGAA	43	41835	41854	295
413303	1868	1887	CCAACTCCTCCCCTTGGCAG	28	41839	41858	296
413304	1872	1891	CTCTCCAACTCCTCCCCTTG	25	41843	41862	297
413305	1875	1894	GTGCTCTCCAACTCCTCCCC	34	41846	41865	298

Table 5

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413347	n/a	n/a	AGCCTGCCACAGGGCCCTTT	37	10050	10069	339
413348	n/a	n/a	AGGACAGGGCAGACACACCT	44	10396	10415	340
413349	n/a	n/a	GATTTGTACTTGAATCCAGG	34	10703	10722	341
413350	n/a	n/a	ACACGCAGACCAGGACAGCT	46	10747	10766	342
413351	n/a	n/a	TTTGGATAGTCGATTTACCA	41	10943	10962	343
413352	n/a	n/a	AAGATTCATAACTATATCTA	6	11045	11064	344
413353	n/a	n/a	AAAAACATGACAGCCAGGGT	31	11558	11577	345
413354	n/a	n/a	GACTTCCCTTCACAGAATCC	5	11983	12002	346
413355	n/a	n/a	CAGGCAGGTGTCAGAGGGCT	21	12250	12269	347
413356	n/a	n/a	TAGCCTGGCTTTGATAACCC	42	12892	12911	348
413357	n/a	n/a	CATAGGCCAGGAGGAAGAGT	35	13206	13225	349
413358	n/a	n/a	TTGCTTAAACAGATAAGCAC	17	13541	13560	350
413359	n/a	n/a	AATGTCACAAGTTCACAAAC	4	14428	14447	351
413360	n/a	n/a	CTGACCTCAGGGTGATCAAG	31	14721	14740	352
413361	n/a	n/a	CCAAGCAGGAGCTGGACAGA	19	15143	15162	353
413362	n/a	n/a	TCATTTCATAGATGAGGAGA	34	15215	15234	354
413363	n/a	n/a	AGGAGTTTGTGTTTCCCATT	39	15320	15339	355
413364	n/a	n/a	GGCAGGGCTTAGAATGGCTA	48	15359	15378	356
413365	n/a	n/a	ACCATTTTCACAAGGAGAAG	30	15572	15591	357
413366	n/a	n/a	TTCAAAAAGTAGCTACTGCA	47	15738	15757	358
413367	n/a	n/a	TCCAGGACCCTGGACATGAT	50	15813	15832	359
413368	n/a	n/a	AGAGCCAGCACACAGCTATG	20	16251	16270	360
413369	n/a	n/a	AGTCTAGTTGGAAAAGTAGA	16	16545	16564	361

413370	n/a	n/a	AGATGCCACTTCATCAAGGC	24	17722	17741	362
413371	n/a	n/a	GAAGTCAGGCCAAGTGCCAA	26	17744	17763	363
413372	n/a	n/a	TGATTCTTACCTGCAATGAG	22	18221	18240	364
413373	n/a	n/a	CCAAGTAAGCCTCGGTGTCC	32	18329	18348	365
413374	n/a	n/a	TGAGTAGTCAAAGGTGGCTT	30	19019	19038	366
413375	n/a	n/a	ATGCCTGAGGGCAGCAGTGT	45	19907	19926	367
413376	n/a	n/a	TGACCAGGAAGGCCACACCT	15	19967	19986	368
413377	n/a	n/a	GGCTTCACCGTCCCACAGCA	39	20409	20428	369
413378	n/a	n/a	CAGGACTTGGTACCTGATTC	35	20883	20902	370
413379	n/a	n/a	TGGCTGGGAGGAGTCCAGCA	10	21131	21150	371
413380	n/a	n/a	GGGTCAAGGTCACTCAGCCA	33	21660	21679	372
413381	n/a	n/a	TATTTGAAGATAAAGTCAGA	0	22021	22040	373
413382	n/a	n/a	GGGATGATAAACACTAAGGT	37	22093	22112	374
217328	938	957	GCATTGCCACTCCCATTCTT	59	38091	38110	144
413306	1992	2011	CTGGAGGCCAGTCCAGGCTC	23	41963	41982	299
413307	1995	2014	ATCCTGGAGGCCAGTCCAGG	18	41966	41985	300
413308	2006	2025	CCCCCATCCTCATCCTGGAG	7	41977	41996	301
413309	2010	2029	GCCACCCCCATCCTCATCCT	0	41981	42000	302
413310	2014	2033	CATTGCCACCCCCATCCTCA	9	41985	42004	303
413311	2040	2059	GGGCAGTCCTTTCCCCTGCA	37	42011	42030	304
413312	2081	2100	TAGCTCATGGTGGCGGCATC	35	42052	42071	305
413313	2087	2106	TCCACCTAGCTCATGGTGGC	21	42058	42077	306
413314	2091	2110	TTACTCCACCTAGCTCATGG	6	42062	42081	307
413315	2099	2118	AAAACCAGTTACTCCACCTA	0	42070	42089	308
413316	2102	2121	AGAAAAACCAGTTACTCCAC	4	42073	42092	309
413317	2113	2132	TCAGCCACCCAAGAAAAACC	0	42084	42103	310
413318	2120	2139	CATGTCATCAGCCACCCAAG	16	42091	42110	311
413319	2128	2147	GCTGCATCCATGTCATCAGC	43	42099	42118	154
413320	2131	2150	TGTGCTGCATCCATGTCATC	36	42102	42121	312
413321	2136	2155	GAGTCTGTGCTGCATCCATG	48	42107	42126	313
413322	2143	2162	CAAGGCTGAGTCTGTGCTGC	24	42114	42133	314
413323	2146	2165	GGCCAAGGCTGAGTCTGTGC	17	42117	42136	315
413324	2149	2168	CCAGGCCAAGGCTGAGTCTG	27	42120	42139	316
413325	2182	2201	AAGGTAAACTGAGGCCACCA	37	42153	42172	317
413326	2185	2204	GGGAAGGTAAACTGAGGCCA	32	42156	42175	318
413327	2236	2255	AGGCCCCTTCTGAAGAGGGA	43	42207	42226	319
413328	2239	2258	GCCAGGCCCCTTCTGAAGAG	36	42210	42229	320
413329	2242	2261	AAGGCCAGGCCCCTTCTGAA	32	42213	42232	321
413330	2246	2265	TCAGAAGGCCAGGCCCCTTC	20	42217	42236	322
413331	2252	2271	TGCTGCTCAGAAGGCCAGGC	42	42223	42242	323
413332	2257	2276	TAATCTGCTGCTCAGAAGGC	36	42228	42247	324
413333	2265	2284	TTTGGAACTAATCTGCTGCT	50	42236	42255	325
413334	2274	2293	GCCACCTGCTTTGGAACTAA	41	42245	42264	326
413335	2301	2320	ACAGAAAAGTGAGGCTTGGG	40	42272	42291	327

413336	2304	2323	GGCACAGAAAAGTGAGGCTT	32	42275	42294	328
413337	2307	2326	GAAGGCACAGAAAAGTGAGG	11	42278	42297	329
413338	2310	2329	CAGGAAGGCACAGAAAAGTG	28	42281	42300	330
413339	2313	2332	CCTCAGGAAGGCACAGAAAA	40	42284	42303	331
413340	2317	2336	ACCCCCTCAGGAAGGCACAG	25	42288	42307	332
413341	2323	2342	GGCCCAACCCCCTCAGGAAG	19	42294	42313	333
413342	2373	2392	TCTCATCAAGAGATAACAGA	6	42344	42363	334
413343	2376	2395	TGATCTCATCAAGAGATAAC	17	42347	42366	335
413344	2399	2418	TACAAAAGTCTGACATGGTG	40	42370	42389	336
413345	2402	2421	ATATACAAAAGTCTGACATG	21	42373	42392	337
413346	2406	2425	AGGCATATACAAAAGTCTGA	38	42377	42396	338

Table 6

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
413383	22161	22180	ACCCAGAGATGGTGATAAGG	53	375
413384	22521	22540	AAGTGAACCCTCACTTCCCA	35	376
413385	22840	22859	ACATATCCCCAACTGAAACA	21	377
413386	22849	22868	TCACTGATGACATATCCCCA	52	378
413387	22862	22881	GAGTATAGAAATTTCACTGA	44	379
413388	22877	22896	TGCAGCTTGGAGGAGGAGTA	36	380
413389	23153	23172	GCATTTTAACAAGATCCCCA	34	381
413390	23167	23186	CTGAATCAAAATCTGCATTT	28	382
413391	23182	23201	TCCAGACTGGATTTACTGAA	60	383
413392	23550	23569	TTATCCTTGAGGGTCTCATA	45	384
413393	23560	23579	CATCACATGCTTATCCTTGA	41	385
413394	23669	23688	TTCCCCAGAGCAGCTCTGAG	27	386
413395	23726	23745	GCGGCAGAGCCAGGACTGAA	35	387
413396	23812	23831	GTCATCCAGTATAGCCTAAT	44	388
413397	23956	23975	TAAAGAGGCTGGGCCATAGA	21	389
413398	24122	24141	TCAAACCTAGGTTCAGACTT	47	390
413399	24204	24223	AGGAAGGAAATGCTAGGCCT	64	391
413400	24642	24661	ACAGGAAGCCTGGTGACTGC	54	392
413401	24790	24809	CAGGCAGCCTGAAGGACACT	49	393
413402	25074	25093	AGGACAGAGGTTCAACATCC	53	394
413403	25234	25253	AGACCACATGAAGTATCTAA	50	395
413404	25376	25395	GCTATAGAATCAGACAGACC	46	396
413405	25488	25507	CCTACAGCAGAGGGAAGATG	13	397
413406	25493	25512	CAGTGCCTACAGCAGAGGGA	0	398
413407	25504	25523	GATGCTGGATCCAGTGCCTA	53	399
413408	25953	25972	GTGGGAAAGGCACAGGCTTT	53	400

413409	26393	26412	GATGGCAACCTAAGGAGTGA	37	401
413410	26893	26912	GTTCTTGGGCCTAAAGGTGA	34	402
413411	27564	27583	ATTAGCAGTAGCTCAGGAGA	48	403
413412	27677	27696	CTGGTCCAGGGAGAGACCAA	25	404
413413	27711	27730	AGAGGGTTCCATGGCACAAA	67	405
413414	28186	28205	AATTTCCTTACAGGGTATTG	46	406
413415	28461	28480	TCATGAGAAGCTTAGAAGGC	58	407
413416	28524	28543	CAACAGGCTCTGGTTCCATG	56	408
413417	28920	28939	CAGGCCCCACTGCTTAGAGG	48	409
413418	29446	29465	AAATGGTAGCCCCTTGTTGC	32	410
413419	29503	29522	TTTCCCATGGGAGAAGATAA	55	411
413420	30361	30380	AGCGCAGAGCCCATCAGCCT	48	412
413421	30620	30639	CAGGGTGACTTTGCCCCATT	43	413
413422	30974	30993	TGGCACTAAGCTAGGCACAC	62	414
413423	31184	31203	AGGGAGGCCTTGCACTTACC	13	415
413424	31240	31259	TGAGGCCCTTCAGCTTGTGC	49	416
413425	31370	31389	AAACCCTCGACTGAGTGTGA	37	417
413426	31531	31550	CCTTCCAGGGAATAAAATAC	3	418
413427	31534	31553	CCACCTTCCAGGGAATAAAA	22	419
413428	31537	31556	CTGCCACCTTCCAGGGAATA	27	420
413429	31620	31639	AACACTCACAGCACTTTACC	4	421
413430	31769	31788	TGGATACTCAGAAGAGCAGT	37	422
413431	31935	31954	CAGAGTTATCCTCAATTCAC	34	423
413432	32145	32164	ACACCAGGATCTCAGTCACT	42	424
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	70	425
413434	32528	32547	GAAACAGGCAGTAGGAAATC	23	426
413435	32644	32663	ATGGAGTGACAGGGCAGGAA	59	427
413436	32939	32958	AGGCCACAGTGGCAACAGAG	54	428
413437	33067	33086	GTTCTTTTGGAAGGGTGGAG	52	429
413438	33164	33183	GGAGCCCTCACAGGGCCAGG	38	430
413439	33364	33383	GGACAGGAGGGTCACACACA	45	431
413440	33671	33690	AGATGGACAGGTGATTCTAA	50	432
413441	33739	33758	TTAAGCTTTGTGACCTTGGG	67	433
413442	34101	34120	GGGAAGGATACCGCCAATGA	57	434
413443	34311	34330	CAGTGGGCCCCAGGTGGCTC	46	435
413444	34642	34661	GGTGGGAAACTTGGAAACTT	37	436
413445	35355	35374	ACAATTCCTGGATAACAAGG	41	437
413446	35362	35381	TAGAAATACAATTCCTGGAT	71	438
413447	35568	35587	TGTCCTTATCAAAATCCCTC	38	439
413448	36267	36286	GCTGAGAGAGACAATGAGTA	54	440
413449	36858	36877	GATTATTCTAAAACTCAAAT	0	441
413450	37202	37221	ACCAGCTGCAAGGATGACCT	49	442
413451	37457	37476	GAGGCTCAGGCCTTGACAAC	12	443
413452	37604	37623	TGTTATCCGAGTTGAATTCT	45	444

413453	37818	37837	GTTTTGGGAACTCATGCATT	50	445
413454	37837	37856	CAGCTAATGATACAAGGTTG	55	446
413455	37880	37899	GCTATTCATTTTTCTGAGCC	47	447
217328	38091	38110	GCATTGCCACTCCCATTCTT	67	144
413456	39033	39052	AGAGGCCCTGGACACTGGCC	32	448
413457	39040	39059	TCAGCCTAGAGGCCCTGGAC	26	449
413458	39300	39319	CCAACAGTGGTGATGGGCTT	60	450
413459	39305	39324	GCTTACCAACAGTGGTGATG	21	451

Example 2: Antisense inhibition of human diacylglycerol acyltransferase 2 in HepG2 cells by MOE gapmers

Antisense oligonucleotides were designed targeting a diacylglycerol acyltransferase 2 (DGAT2) nucleic acid and were tested for their effects on DGAT2 mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 10,000 cells per well were transfected using Lipofectin reagent with 120 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB (forward sequence AACTGGCCCTGCGTCATG, designated herein as SEQ ID NO: 7; reverse sequence CTTGTACACTTCATTCTCTCCAAAGG, designated herein as SEQ ID NO: 8; probe sequence CTGACCTGGTTCCC, designated herein as SEQ ID NO: 9) was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells.

ISIS oligonucleotides from an earlier published application, WO 2005/019418, were also included in this assay. These ISIS oligonucleotides are ISIS 217316, ISIS 217317, ISIS 217328, ISIS 217329, ISIS 334177, ISIS 334178, ISIS 366730, ISIS 366731, and ISIS 369255. As shown in the Tables below, several newly designed antisense oligonucleotides demonstrated similar or greater potency that any of these benchmark oligonucleotides.

The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE, 3-14-3 MOE, or 2-13-5 MOE gapmers. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 3-14-3 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of fourteen 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising three nucleosides each. The 2-13-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of thirteen 2'-

deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising two and three nucleosides respectively. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted in the human gene sequence. Each gapmer listed in the Tables below is targeted to either the human DGAT2 mRNA, designated herein as SEQ ID NO: 1 (RefSeq No. NM_032564.3) or the human DGAT2 genomic sequence, designated herein as SEQ ID NO: 2 (RefSeq No. NT_033927.5 truncated from nucleotides 5669186 to 5712008). 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

Table 8

Inhibition of DGAT2 mRNA by MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Motif	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
423460	n/a	n/a	5-10-5	TGGACAAGTCCTGCCCATCT	72	32428	32447	464
423520	n/a	n/a	3-14-3	TGGACAAGTCCTGCCCATCT	69	32428	32447	464
423598	n/a	n/a	2-13-5	TGGACAAGTCCTGCCCATCT	51	32428	32447	464
423461	n/a	n/a	5-10-5	CTGGACAAGTCCTGCCCATC	77	32429	32448	465
423521	n/a	n/a	3-14-3	CTGGACAAGTCCTGCCCATC	67	32429	32448	465
423599	n/a	n/a	2-13-5	CTGGACAAGTCCTGCCCATC	58	32429	32448	465
423462	n/a	n/a	5-10-5	CCTGGACAAGTCCTGCCCAT	73	32430	32449	466
423522	n/a	n/a	3-14-3	CCTGGACAAGTCCTGCCCAT	70	32430	32449	466
423600	n/a	n/a	2-13-5	CCTGGACAAGTCCTGCCCAT	59	32430	32449	466
413433	n/a	n/a	5-10-5	GCCTGGACAAGTCCTGCCCA	86	32431	32450	425
423523	n/a	n/a	3-14-3	GCCTGGACAAGTCCTGCCCA	84	32431	32450	425
423601	n/a	n/a	2-13-5	GCCTGGACAAGTCCTGCCCA	78	32431	32450	425
423463	n/a	n/a	5-10-5	AGCCTGGACAAGTCCTGCCC	79	32432	32451	467
423524	n/a	n/a	3-14-3	AGCCTGGACAAGTCCTGCCC	82	32432	32451	467
423602	n/a	n/a	2-13-5	AGCCTGGACAAGTCCTGCCC	75	32432	32451	467
423464	n/a	n/a	5-10-5	CAGCCTGGACAAGTCCTGCC	84	32433	32452	468
423525	n/a	n/a	3-14-3	CAGCCTGGACAAGTCCTGCC	72	32433	32452	468
423603	n/a	n/a	2-13-5	CAGCCTGGACAAGTCCTGCC	72	32433	32452	468
423465	n/a	n/a	5-10-5	GCAGCCTGGACAAGTCCTGC	70	32434	32453	469
423526	n/a	n/a	3-14-3	GCAGCCTGGACAAGTCCTGC	83	32434	32453	469

423604	n/a	n/a	2-13-5	GCAGCCTGGACAAGTCCTGC	77	32434	32453	469
423466	n/a	n/a	5-10-5	TGCAGCCTGGACAAGTCCTG	67	32435	32454	470
423527	n/a	n/a	3-14-3	TGCAGCCTGGACAAGTCCTG	77	32435	32454	470
413191	467	486	5-10-5	CACTGGAGCACTGAGATGAC	48	25593	25612	181
423502	467	486	3-14-3	CACTGGAGCACTGAGATGAC	55	25593	25612	181
423580	467	486	2-13-5	CACTGGAGCACTGAGATGAC	61	25593	25612	181
423449	468	487	5-10-5	CCACTGGAGCACTGAGATGA	71	25594	25613	452
423503	468	487	3-14-3	CCACTGGAGCACTGAGATGA	62	25594	25613	452
423581	468	487	2-13-5	CCACTGGAGCACTGAGATGA	54	25594	25613	452
423450	469	488	5-10-5	CCCACTGGAGCACTGAGATG	78	25595	25614	453
423504	469	488	3-14-3	CCCACTGGAGCACTGAGATG	75	25595	25614	453
423582	469	488	2-13-5	CCCACTGGAGCACTGAGATG	70	25595	25614	453
334178	470	489	5-10-5	ACCCACTGGAGCACTGAGAT	72	25596	25615	454
423505	470	489	3-14-3	ACCCACTGGAGCACTGAGAT	59	25596	25615	454
423583	470	489	2-13-5	ACCCACTGGAGCACTGAGAT	52	25596	25615	454
423451	471	490	5-10-5	GACCCACTGGAGCACTGAGA	69	25597	25616	455
423506	471	490	3-14-3	GACCCACTGGAGCACTGAGA	56	25597	25616	455
423584	471	490	2-13-5	GACCCACTGGAGCACTGAGA	70	25597	25616	455
423452	472	491	5-10-5	GGACCCACTGGAGCACTGAG	84	25598	25617	456
423507	472	491	3-14-3	GGACCCACTGGAGCACTGAG	82	25598	25617	456
423585	472	491	2-13-5	GGACCCACTGGAGCACTGAG	86	25598	25617	456
413192	473	492	5-10-5	AGGACCCACTGGAGCACTGA	70	25599	25618	182
423508	473	492	3-14-3	AGGACCCACTGGAGCACTGA	82	25599	25618	182
423586	473	492	2-13-5	AGGACCCACTGGAGCACTGA	75	25599	25618	182
423453	474	493	5-10-5	CAGGACCCACTGGAGCACTG	80	25600	25619	457
423509	474	493	3-14-3	CAGGACCCACTGGAGCACTG	71	25600	25619	457
423587	474	493	2-13-5	CAGGACCCACTGGAGCACTG	78	25600	25619	457
423454	475	494	5-10-5	ACAGGACCCACTGGAGCACT	79	25601	25620	458
423510	475	494	3-14-3	ACAGGACCCACTGGAGCACT	61	25601	25620	458
423588	475	494	2-13-5	ACAGGACCCACTGGAGCACT	68	25601	25620	458
413193	476	495	5-10-5	GACAGGACCCACTGGAGCAC	69	25602	25621	183
423511	476	495	3-14-3	GACAGGACCCACTGGAGCAC	58	25602	25621	183
423589	476	495	2-13-5	GACAGGACCCACTGGAGCAC	73	25602	25621	183
413212	625	644	5-10-5	TTCGGACCCACTGTGACCTC	75	31557	31576	202
423512	625	644	3-14-3	TTCGGACCCACTGTGACCTC	64	31557	31576	202
423590	625	644	2-13-5	TTCGGACCCACTGTGACCTC	71	31557	31576	202

423455	626	645	5-10-5	TTTCGGACCCACTGTGACCT	65	31558	31577	459
423513	626	645	3-14-3	TTTCGGACCCACTGTGACCT	61	31558	31577	459
423591	626	645	2-13-5	TTTCGGACCCACTGTGACCT	68	31558	31577	459
423456	627	646	5-10-5	GTTTCGGACCCACTGTGACC	65	31559	31578	460
423514	627	646	3-14-3	GTTTCGGACCCACTGTGACC	71	31559	31578	460
423592	627	646	2-13-5	GTTTCGGACCCACTGTGACC	70	31559	31578	460
423457	628	647	5-10-5	AGTTTCGGACCCACTGTGAC	63	31560	31579	461
423515	628	647	3-14-3	AGTTTCGGACCCACTGTGAC	60	31560	31579	461
423593	628	647	2-13-5	AGTTTCGGACCCACTGTGAC	64	31560	31579	461
413213	629	648	5-10-5	CAGTTTCGGACCCACTGTGA	74	31561	31580	203
423516	629	648	3-14-3	CAGTTTCGGACCCACTGTGA	58	31561	31580	203
423594	629	648	2-13-5	CAGTTTCGGACCCACTGTGA	77	31561	31580	203
423458	630	649	5-10-5	CCAGTTTCGGACCCACTGTG	83	31562	31581	462
423517	630	649	3-14-3	CCAGTTTCGGACCCACTGTG	82	31562	31581	462
423595	630	649	2-13-5	CCAGTTTCGGACCCACTGTG	80	31562	31581	462
423459	631	650	5-10-5	CCCAGTTTCGGACCCACTGT	85	31563	31582	463
423518	631	650	3-14-3	CCCAGTTTCGGACCCACTGT	76	31563	31582	463
423596	631	650	2-13-5	CCCAGTTTCGGACCCACTGT	70	31563	31582	463
413214	632	651	5-10-5	GCCCAGTTTCGGACCCACTG	89	31564	31583	204
423519	632	651	3-14-3	GCCCAGTTTCGGACCCACTG	81	31564	31583	204
423597	632	651	2-13-5	GCCCAGTTTCGGACCCACTG	82	31564	31583	204
217328	938	957	5-10-5	GCATTGCCACTCCCATTCTT	82	38091	38110	144

Table 9

Inhibition of DGAT2 mRNA by MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Motif	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
334177	275	294	5-10-5	AGGACCCCGGAGTAGGCGGC	76	9896	9915	145
423528	275	294	3-14-3	AGGACCCCGGAGTAGGCGGC	76	9896	9915	145
423606	275	294	2-13-5	AGGACCCCGGAGTAGGCGGC	81	9896	9915	145
423467	276	295	5-10-5	CAGGACCCCGGAGTAGGCGG	75	9897	9916	471
423529	276	295	3-14-3	CAGGACCCCGGAGTAGGCGG	53	9897	9916	471
423607	276	295	2-13-5	CAGGACCCCGGAGTAGGCGG	76	9897	9916	471
423468	277	296	5-10-5	GCAGGACCCCGGAGTAGGCG	58	9898	9917	472

423530	277	296	3-14-3	GCAGGACCCCGGAGTAGGCG	70	9898	9917	472
423608	277	296	2-13-5	GCAGGACCCCGGAGTAGGCG	68	9898	9917	472
381726	278	297	5-10-5	CGCAGGACCCCGGAGTAGGC	70	9899	9918	38
423531	278	297	3-14-3	CGCAGGACCCCGGAGTAGGC	65	9899	9918	38
423609	278	297	2-13-5	CGCAGGACCCCGGAGTAGGC	71	9899	9918	38
423469	279	298	5-10-5	GCGCAGGACCCCGGAGTAGG	79	9900	9919	473
423532	279	298	3-14-3	GCGCAGGACCCCGGAGTAGG	71	9900	9919	473
423610	279	298	2-13-5	GCGCAGGACCCCGGAGTAGG	72	9900	9919	473
423470	280	299	5-10-5	CGCGCAGGACCCCGGAGTAG	74	9901	9920	474
423533	280	299	3-14-3	CGCGCAGGACCCCGGAGTAG	69	9901	9920	474
423611	280	299	2-13-5	CGCGCAGGACCCCGGAGTAG	67	9901	9920	474
423471	281	300	5-10-5	CCGCGCAGGACCCCGGAGTA	75	9902	9921	475
423534	281	300	3-14-3	CCGCGCAGGACCCCGGAGTA	71	9902	9921	475
411873	686	705	5-10-5	TTGTGTGTCTTCACCAGCTG	73	37214	37233	46
423542	686	705	3-14-3	TTGTGTGTCTTCACCAGCTG	60	37214	37233	46
423620	686	705	2-13-5	TTGTGTGTCTTCACCAGCTG	71	37214	37233	46
411898	687	706	5-10-5	GTTGTGTGTCTTCACCAGCT	68	37215	37234	61
423543	687	706	3-14-3	GTTGTGTGTCTTCACCAGCT	56	37215	37234	61
423621	687	706	2-13-5	GTTGTGTGTCTTCACCAGCT	65	37215	37234	61
217316	688	707	5-10-5	GGTTGTGTGTCTTCACCAGC	70	37216	37235	20
423544	688	707	3-14-3	GGTTGTGTGTCTTCACCAGC	70	37216	37235	20
423622	688	707	2-13-5	GGTTGTGTGTCTTCACCAGC	68	37216	37235	20
381727	689	708	5-10-5	AGGTTGTGTGTCTTCACCAG	74	37217	37236	39
423545	689	708	3-14-3	AGGTTGTGTGTCTTCACCAG	61	37217	37236	39
423623	689	708	2-13-5	AGGTTGTGTGTCTTCACCAG	61	37217	37236	39
411899	690	709	5-10-5	CAGGTTGTGTGTCTTCACCA	76	37218	37237	62
423546	690	709	3-14-3	CAGGTTGTGTGTCTTCACCA	68	37218	37237	62
423624	690	709	2-13-5	CAGGTTGTGTGTCTTCACCA	62	37218	37237	62
411874	691	710	5-10-5	GCAGGTTGTGTGTCTTCACC	73	37219	37238	47
423547	691	710	3-14-3	GCAGGTTGTGTGTCTTCACC	69	37219	37238	47
423625	691	710	2-13-5	GCAGGTTGTGTGTCTTCACC	56	37219	37238	47
411900	692	711	5-10-5	AGCAGGTTGTGTGTCTTCAC	77	37220	37239	63
423548	692	711	3-14-3	AGCAGGTTGTGTGTCTTCAC	63	37220	37239	63
423626	692	711	2-13-5	AGCAGGTTGTGTGTCTTCAC	44	37220	37239	63
217317	693	712	5-10-5	CAGCAGGTTGTGTGTCTTCA	75	37221	37240	21
423549	693	712	3-14-3	CAGCAGGTTGTGTGTCTTCA	47	37221	37240	21

423627	693	712	2-13-5	CAGCAGGTTGTGTGTCTTCA	57	37221	37240	21
381728	694	713	5-10-5	TCAGCAGGTTGTGTGTCTTC	56	37222	37241	40
423550	694	713	3-14-3	TCAGCAGGTTGTGTGTCTTC	54	37222	37241	40
423628	694	713	2-13-5	TCAGCAGGTTGTGTGTCTTC	57	37222	37241	40
411901	695	714	5-10-5	GTCAGCAGGTTGTGTGTCTT	59	37223	37242	64
423551	695	714	3-14-3	GTCAGCAGGTTGTGTGTCTT	61	37223	37242	64
423629	695	714	2-13-5	GTCAGCAGGTTGTGTGTCTT	58	37223	37242	64
411875	696	715	5-10-5	GGTCAGCAGGTTGTGTGTCT	62	37224	37243	48
423552	696	715	3-14-3	GGTCAGCAGGTTGTGTGTCT	57	37224	37243	48
423630	696	715	2-13-5	GGTCAGCAGGTTGTGTGTCT	45	37224	37243	48
411902	697	716	5-10-5	TGGTCAGCAGGTTGTGTGTC	43	37225	37244	65
423553	697	716	3-14-3	TGGTCAGCAGGTTGTGTGTC	57	37225	37244	65
423631	697	716	2-13-5	TGGTCAGCAGGTTGTGTGTC	57	37225	37244	65
413231	814	833	5-10-5	GGTAAGGCCGTATGCCTGGG	71	37342	37361	221
423535	814	833	3-14-3	GGTAAGGCCGTATGCCTGGG	51	37342	37361	221
423613	814	833	2-13-5	GGTAAGGCCGTATGCCTGGG	53	37342	37361	221
423472	815	834	5-10-5	AGGTAAGGCCGTATGCCTGG	72	37343	37362	476
423536	815	834	3-14-3	AGGTAAGGCCGTATGCCTGG	67	37343	37362	476
423614	815	834	2-13-5	AGGTAAGGCCGTATGCCTGG	63	37343	37362	476
423473	816	835	5-10-5	CAGGTAAGGCCGTATGCCTG	63	37344	37363	477
423537	816	835	3-14-3	CAGGTAAGGCCGTATGCCTG	72	37344	37363	477
423615	816	835	2-13-5	CAGGTAAGGCCGTATGCCTG	59	37344	37363	477
413232	817	836	5-10-5	CCAGGTAAGGCCGTATGCCT	76	37345	37364	225
423538	817	836	3-14-3	CCAGGTAAGGCCGTATGCCT	71	37345	37364	225
423616	817	836	2-13-5	CCAGGTAAGGCCGTATGCCT	64	37345	37364	225
423474	818	837	5-10-5	GCCAGGTAAGGCCGTATGCC	68	37346	37365	478
423539	818	837	3-14-3	GCCAGGTAAGGCCGTATGCC	61	37346	37365	478
423617	818	837	2-13-5	GCCAGGTAAGGCCGTATGCC	66	37346	37365	478
423475	819	838	5-10-5	AGCCAGGTAAGGCCGTATGC	70	37347	37366	479
423540	819	838	3-14-3	AGCCAGGTAAGGCCGTATGC	51	37347	37366	479
423618	819	838	2-13-5	AGCCAGGTAAGGCCGTATGC	67	37347	37366	479
413233	820	839	5-10-5	TAGCCAGGTAAGGCCGTATG	60	37348	37367	226
423541	820	839	3-14-3	TAGCCAGGTAAGGCCGTATG	49	37348	37367	226
423619	820	839	2-13-5	TAGCCAGGTAAGGCCGTATG	51	37348	37367	226
217328	938	957	5-10-5	GCATTGCCACTCCCATTCTT	82	38091	38110	144

Table 10
Inhibition of DGAT2 mRNA by MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Motif	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413251	935	954	5-10-5	TTGCCACTCCCATTCTTTGA	57	38088	38107	244
423476	935	954	3-14-3	TTGCCACTCCCATTCTTTGA	59	38088	38107	244
423554	935	954	2-13-5	TTGCCACTCCCATTCTTTGA	57	38088	38107	244
423435	936	955	5-10-5	ATTGCCACTCCCATTCTTTG	35	38089	38108	480
423477	936	955	3-14-3	ATTGCCACTCCCATTCTTTG	40	38089	38108	480
423555	936	955	2-13-5	ATTGCCACTCCCATTCTTTG	53	38089	38108	480
423436	937	956	5-10-5	CATTGCCACTCCCATTCTTT	44	38090	38109	481
423478	937	956	3-14-3	CATTGCCACTCCCATTCTTT	46	38090	38109	481
423556	937	956	2-13-5	CATTGCCACTCCCATTCTTT	40	38090	38109	481
217328	938	957	5-10-5	GCATTGCCACTCCCATTCTT	85	38091	38110	144
423479	938	957	3-14-3	GCATTGCCACTCCCATTCTT	85	38091	38110	144
423557	938	957	2-13-5	GCATTGCCACTCCCATTCTT	61	38091	38110	144
380133	939	958	5-10-5	AGCATTGCCACTCCCATTCT	74	38092	38111	482
423480	939	958	3-14-3	AGCATTGCCACTCCCATTCT	67	38092	38111	482
423558	939	958	2-13-5	AGCATTGCCACTCCCATTCT	50	38092	38111	482
423437	940	959	5-10-5	TAGCATTGCCACTCCCATTC	71	38093	38112	483
423481	940	959	3-14-3	TAGCATTGCCACTCCCATTC	68	38093	38112	483
423559	940	959	2-13-5	TAGCATTGCCACTCCCATTC	60	38093	38112	483
423438	941	960	5-10-5	ATAGCATTGCCACTCCCATT	57	38094	38113	484
423482	941	960	3-14-3	ATAGCATTGCCACTCCCATT	71	38094	38113	484
423560	941	960	2-13-5	ATAGCATTGCCACTCCCATT	57	38094	38113	484
423439	942	961	5-10-5	GATAGCATTGCCACTCCCAT	66	38095	38114	485
423483	942	961	3-14-3	GATAGCATTGCCACTCCCAT	75	38095	38114	485
423561	942	961	2-13-5	GATAGCATTGCCACTCCCAT	62	38095	38114	485
217329	943	962	5-10-5	TGATAGCATTGCCACTCCCA	64	38096	38115	486
423484	943	962	3-14-3	TGATAGCATTGCCACTCCCA	66	38096	38115	486
423562	943	962	2-13-5	TGATAGCATTGCCACTCCCA	69	38096	38115	486
413252	976	995	5-10-5	TCAGAGACTCAGCCGCACCC	55	38129	38148	245
423485	976	995	3-14-3	TCAGAGACTCAGCCGCACCC	41	38129	38148	245

423563	976	995	2-13-5	TCAGAGACTCAGCCGCACCC	56	38129	38148	245
423440	977	996	5-10-5	CTCAGAGACTCAGCCGCACC	80	38130	38149	487
423486	977	996	3-14-3	CTCAGAGACTCAGCCGCACC	70	38130	38149	487
423564	977	996	2-13-5	CTCAGAGACTCAGCCGCACC	43	38130	38149	487
423441	978	997	5-10-5	GCTCAGAGACTCAGCCGCAC	86	38131	38150	488
423487	978	997	3-14-3	GCTCAGAGACTCAGCCGCAC	69	38131	38150	488
423565	978	997	2-13-5	GCTCAGAGACTCAGCCGCAC	82	38131	38150	488
366730	979	998	5-10-5	AGCTCAGAGACTCAGCCGCA	85	38132	38151	150
423488	979	998	3-14-3	AGCTCAGAGACTCAGCCGCA	77	38132	38151	150
423566	979	998	2-13-5	AGCTCAGAGACTCAGCCGCA	86	38132	38151	150
423442	980	999	5-10-5	GAGCTCAGAGACTCAGCCGC	81	38133	38152	489
423489	980	999	3-14-3	GAGCTCAGAGACTCAGCCGC	89	38133	38152	489
423567	980	999	2-13-5	GAGCTCAGAGACTCAGCCGC	89	38133	38152	489
423443	981	1000	5-10-5	GGAGCTCAGAGACTCAGCCG	73	38134	38153	490
423490	981	1000	3-14-3	GGAGCTCAGAGACTCAGCCG	81	38134	38153	490
423568	981	1000	2-13-5	GGAGCTCAGAGACTCAGCCG	65	38134	38153	490
423444	982	1001	5-10-5	TGGAGCTCAGAGACTCAGCC	77	38135	38154	153
423491	982	1001	3-14-3	TGGAGCTCAGAGACTCAGCC	76	38135	38154	153
423569	982	1001	2-13-5	TGGAGCTCAGAGACTCAGCC	82	38135	38154	153
423445	983	1002	5-10-5	ATGGAGCTCAGAGACTCAGC	78	38136	38155	491
423492	983	1002	3-14-3	ATGGAGCTCAGAGACTCAGC	71	38136	38155	491
423570	983	1002	2-13-5	ATGGAGCTCAGAGACTCAGC	73	38136	38155	491
366731	984	1003	5-10-5	CATGGAGCTCAGAGACTCAG	65	38137	38156	492
423493	984	1003	3-14-3	CATGGAGCTCAGAGACTCAG	62	38137	38156	492
423571	984	1003	2-13-5	CATGGAGCTCAGAGACTCAG	71	38137	38156	492
423446	985	1004	5-10-5	GCATGGAGCTCAGAGACTCA	69	38138	38157	493
423494	985	1004	3-14-3	GCATGGAGCTCAGAGACTCA	51	38138	38157	493
423572	985	1004	2-13-5	GCATGGAGCTCAGAGACTCA	77	38138	38157	493
423447	986	1005	5-10-5	GGCATGGAGCTCAGAGACTC	77	38139	38158	494
423495	986	1005	3-14-3	GGCATGGAGCTCAGAGACTC	74	38139	38158	494
423573	986	1005	2-13-5	GGCATGGAGCTCAGAGACTC	77	38139	38158	494
413253	987	1006	5-10-5	AGGCATGGAGCTCAGAGACT	83	38140	38159	246
423496	987	1006	3-14-3	AGGCATGGAGCTCAGAGACT	66	38140	38159	246
423574	987	1006	2-13-5	AGGCATGGAGCTCAGAGACT	78	38140	38159	246
423448	988	1007	5-10-5	CAGGCATGGAGCTCAGAGAC	57	38141	38160	495

423497	988	1007	3-14-3	CAGGCATGGAGCTCAGAGAC	76	38141	38160	495
423575	988	1007	2-13-5	CAGGCATGGAGCTCAGAGAC	70	38141	38160	495
369255	1339	1358	5-10-5	CCAGGGCCTCCATGTACATG	83	41310	41329	103
423498	1339	1358	3-14-3	CCAGGGCCTCCATGTACATG	86	41310	41329	103
423576	1339	1358	2-13-5	CCAGGGCCTCCATGTACATG	69	41310	41329	103
411944	1340	1359	5-10-5	ACCAGGGCCTCCATGTACAT	85	41311	41330	120
423499	1340	1359	3-14-3	ACCAGGGCCTCCATGTACAT	84	41311	41330	120
423577	1340	1359	2-13-5	ACCAGGGCCTCCATGTACAT	50	41311	41330	120
411945	1341	1360	5-10-5	CACCAGGGCCTCCATGTACA	80	41312	41331	121
423500	1341	1360	3-14-3	CACCAGGGCCTCCATGTACA	41	41312	41331	121
423578	1341	1360	2-13-5	CACCAGGGCCTCCATGTACA	69	41312	41331	121
411946	1342	1361	5-10-5	TCACCAGGGCCTCCATGTAC	65	41313	41332	122
423501	1342	1361	3-14-3	TCACCAGGGCCTCCATGTAC	68	41313	41332	122
423579	1342	1361	2-13-5	TCACCAGGGCCTCCATGTAC	3	41313	41332	122

Example 3: Antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Antisense oligonucleotides were designed targeting a DGAT2 nucleic acid and were tested for their effects on DGAT2 mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. Previously dislosed oligonucleotides, ISIS 217317, 217328, ISIS 366722, ISIS 366710, ISIS 366714, ISIS 366728, ISIS 366746, and ISIS 369255 were included in this study as benchmark oligonucleotides. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 4,500 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. The potency of some oligonucleotides was measured with human primer probe set RTS2367 (forward sequence GGCCTCCCGGAGACTGA, designated herein as SEQ ID NO: 4; reverse sequence AAGTGATTTGCAGCTGGTTCCT, designated herein as SEQ ID NO: 5; probe sequence AGGTGAACTGAGCCAGCCTTCGGG, designated herein as SEQ ID NO: 6). DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. The results show several antisense oligonucleotides demonstrate greater potency than the benchmark oligonucleotides.

The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE gapmers. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in

the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted in the human gene sequence. Each gapmer listed in the Tables below is targeted to SEQ ID NO: 1, SEQ ID NO: 2, or both. 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity. In case the sequence alignment for a target gene sequence in a particular table is not shown, it is understood that none of the oligonucleotides presented in that table align with 100% complementarity with that target gene sequence.

Table 7
Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
334177	9896	9915	AGGACCCCGGAGTAGGCGGC	76	145
366710	25551	25570	GACCTATTGAGCCAGGTGAC	60	146
366722	31097	31116	GTGCAGAATATGTACATGAG	50	148
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	80	425
523014	35670	35689	TTCTACTCAAAAATATACAT	23	4084
495875	36249	36268	TAAGGGTATTCTGCTCATAA	73	2148
495876	36250	36269	GTAAGGGTATTCTGCTCATA	83	2149
495877	36251	36270	AGTAAGGGTATTCTGCTCAT	82	2150
495878	36252	36271	GAGTAAGGGTATTCTGCTCA	89	2151
523015	36254	36273	ATGAGTAAGGGTATTCTGCT	68	4085
523016	36255	36274	AATGAGTAAGGGTATTCTGC	65	4086
523017	36256	36275	CAATGAGTAAGGGTATTCTG	39	4087
523018	36257	36276	ACAATGAGTAAGGGTATTCT	25	4088
495879	36259	36278	AGACAATGAGTAAGGGTATT	64	2152
495880	36260	36279	GAGACAATGAGTAAGGGTAT	62	2153
495881	36261	36280	AGAGACAATGAGTAAGGGTA	64	2154
495882	36262	36281	GAGAGACAATGAGTAAGGGT	66	2155
523019	36513	36532	CAGCCCTGTGCCAGCCAGCC	37	4089
523020	36514	36533	ACAGCCCTGTGCCAGCCAGC	17	4090
523021	36515	36534	GACAGCCCTGTGCCAGCCAG	52	4091
523022	36516	36535	CGACAGCCCTGTGCCAGCCA	62	4092
495886	36518	36537	AGCGACAGCCCTGTGCCAGC	57	2159
495887	36519	36538	AAGCGACAGCCCTGTGCCAG	46	2160
495888	36520	36539	CAAGCGACAGCCCTGTGCCA	28	2161
495889	36521	36540	ACAAGCGACAGCCCTGTGCC	46	2162

523023	36579	36598	ACTTTCCCACAGTCAGCTGG	59	4093
523024	36580	36599	AACTTTCCCACAGTCAGCTG	51	4094
523025	36581	36600	AAACTTTCCCACAGTCAGCT	68	4095
523026	36582	36601	GAAACTTTCCCACAGTCAGC	73	4096
523027	36584	36603	TGGAAACTTTCCCACAGTCA	68	4097
523028	36585	36604	ATGGAAACTTTCCCACAGTC	52	4098
523029	36586	36605	AATGGAAACTTTCCCACAGT	23	4099
523030	36587	36606	AAATGGAAACTTTCCCACAG	36	4100
523031	36842	36861	AAATCCAACCCTTGTCACTC	28	4101
523032	36843	36862	CAAATCCAACCCTTGTCACT	22	4102
523033	36844	36863	TCAAATCCAACCCTTGTCAC	21	4103
523034	36845	36864	CTCAAATCCAACCCTTGTCA	38	4104
523035	37120	37139	TGGATGTGTCATTTCCCCTG	69	4105
217328	38091	38110	GCATTGCCACTCCCATTCTT	73	144
423444	38135	38154	TGGAGCTCAGAGACTCAGCC	56	153
522979	39671	39690	AGTGCAAGAGTTACCTCCTC	67	4106
522980	39672	39691	CAGTGCAAGAGTTACCTCCT	67	4107
522981	39673	39692	GCAGTGCAAGAGTTACCTCC	60	4108
522982	39674	39693	AGCAGTGCAAGAGTTACCTC	63	4109
522983	39681	39700	ATCAGTTAGCAGTGCAAGAG	46	4110
522984	39682	39701	TATCAGTTAGCAGTGCAAGA	43	4111
522985	39683	39702	CTATCAGTTAGCAGTGCAAG	52	4112
522986	39684	39703	CCTATCAGTTAGCAGTGCAA	64	4113
522987	39686	39705	TTCCTATCAGTTAGCAGTGC	61	4114
522988	39687	39706	ATTCCTATCAGTTAGCAGTG	47	4115
522989	39688	39707	AATTCCTATCAGTTAGCAGT	16	4116
522990	39689	39708	TAATTCCTATCAGTTAGCAG	11	4117
522991	39814	39833	TCTATGCTGCAGTCATATTA	28	4118
522992	39815	39834	GTCTATGCTGCAGTCATATT	20	4119
522993	39816	39835	GGTCTATGCTGCAGTCATAT	45	4120
522994	39817	39836	AGGTCTATGCTGCAGTCATA	40	4121
522995	39819	39838	ACAGGTCTATGCTGCAGTCA	56	4122
522996	39820	39839	GACAGGTCTATGCTGCAGTC	70	4123
522997	39821	39840	TGACAGGTCTATGCTGCAGT	65	4124
522998	39822	39841	CTGACAGGTCTATGCTGCAG	54	4125
522999	39829	39848	CACTCTTCTGACAGGTCTAT	54	4126
523000	39830	39849	CCACTCTTCTGACAGGTCTA	70	4127
523001	39831	39850	TCCACTCTTCTGACAGGTCT	69	4128
523002	39832	39851	TTCCACTCTTCTGACAGGTC	84	4129
523003	39834	39853	TTTTCCACTCTTCTGACAGG	35	4130
523004	39835	39854	GTTTTCCACTCTTCTGACAG	25	4131
523005	39836	39855	TGTTTTCCACTCTTCTGACA	24	4132

523006	40329	40348	ATCTCTTCCATCTCCACTGC	30	4133
523007	40330	40349	CATCTCTTCCATCTCCACTG	32	4134
523008	40331	40350	ACATCTCTTCCATCTCCACT	39	4135
523009	40332	40351	CACATCTCTTCCATCTCCAC	40	4136
523010	40334	40353	TGCACATCTCTTCCATCTCC	50	4137
523011	40335	40354	ATGCACATCTCTTCCATCTC	35	4138
523012	40336	40355	CATGCACATCTCTTCCATCT	43	4139
523013	40337	40356	TCATGCACATCTCTTCCATC	28	4140
369255	41310	41329	CCAGGGCCTCCATGTACATG	33	103
411947	41315	41334	CTTCACCAGGGCCTCCATGT	22	123
366746	41337	41356	TGGTCTTGTGCTTGTCGAAG	46	151

Table 11

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NOs: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	82	32431	32450	425
472154	105	124	GACACCTGGAGCTGCGGCCG	51	9726	9745	573
472155	106	125	GGACACCTGGAGCTGCGGCC	79	9727	9746	574
472156	107	126	AGGACACCTGGAGCTGCGGC	79	9728	9747	575
472157	108	127	TAGGACACCTGGAGCTGCGG	56	9729	9748	576
472158	110	129	GCTAGGACACCTGGAGCTGC	76	9731	9750	577
472159	111	130	GGCTAGGACACCTGGAGCTG	63	9732	9751	578
472160	161	180	CAGGGCTTCGCGCAGAGCAC	46	9782	9801	579
472161	162	181	CCAGGGCTTCGCGCAGAGCA	42	9783	9802	580
472162	164	183	GGCCAGGGCTTCGCGCAGAG	6	9785	9804	581
472163	253	272	TGAGGGTCTTCATGGCTGAA	40	9874	9893	582
472164	255	274	TATGAGGGTCTTCATGGCTG	69	9876	9895	583
472165	256	275	CTATGAGGGTCTTCATGGCT	62	9877	9896	584
472166	257	276	GCTATGAGGGTCTTCATGGC	53	9878	9897	585
472167	259	278	CGGCTATGAGGGTCTTCATG	59	9880	9899	586
472168	260	279	GCGGCTATGAGGGTCTTCAT	54	9881	9900	587
472169	261	280	GGCGGCTATGAGGGTCTTCA	57	9882	9901	588
472170	262	281	AGGCGGCTATGAGGGTCTTC	69	9883	9902	589
472171	264	283	GTAGGCGGCTATGAGGGTCT	32	9885	9904	590
472172	265	284	AGTAGGCGGCTATGAGGGTC	23	9886	9905	591
472173	267	286	GGAGTAGGCGGCTATGAGGG	15	9888	9907	592
472174	268	287	CGGAGTAGGCGGCTATGAGG	48	9889	9908	593
472175	270	289	CCCGGAGTAGGCGGCTATGA	80	9891	9910	594
472176	271	290	CCCCGGAGTAGGCGGCTATG	75	9892	9911	595

472177	273	292	GACCCCGGAGTAGGCGGCTA	69	9894	9913	596
472178	274	293	GGACCCCGGAGTAGGCGGCT	76	9895	9914	597
334177	275	294	AGGACCCCGGAGTAGGCGGC	74	9896	9915	145
472179	305	324	CGGTCAGCCTCGGCCTGACG	30	9926	9945	598
472180	306	325	CCGGTCAGCCTCGGCCTGAC	5	9927	9946	599
472181	308	327	CTCCGGTCAGCCTCGGCCTG	43	9929	9948	600
472182	309	328	GCTCCGGTCAGCCTCGGCCT	61	9930	9949	601
472183	311	330	TGGCTCCGGTCAGCCTCGGC	48	9932	9951	602
472184	312	331	CTGGCTCCGGTCAGCCTCGG	28	9933	9952	603
472185	313	332	GCTGGCTCCGGTCAGCCTCG	35	9934	9953	604
472186	314	333	CGCTGGCTCCGGTCAGCCTC	44	9935	9954	605
472187	315	334	GCGCTGGCTCCGGTCAGCCT	43	9936	9955	606
472188	332	351	GCAGGTCCTCCGTGAGAGCG	63	9953	9972	607
472189	333	352	CGCAGGTCCTCCGTGAGAGC	68	9954	9973	608
472190	334	353	GCGCAGGTCCTCCGTGAGAG	40	9955	9974	609
472191	335	354	AGCGCAGGTCCTCCGTGAGA	39	9956	9975	610
472192	336	355	CAGCGCAGGTCCTCCGTGAG	54	9957	9976	611
472193	337	356	ACAGCGCAGGTCCTCCGTGA	36	9958	9977	612
472194	338	357	GACAGCGCAGGTCCTCCGTG	63	9959	9978	613
472195	340	359	GCGACAGCGCAGGTCCTCCG	62	9961	9980	614
472196	341	360	CGCGACAGCGCAGGTCCTCC	65	9962	9981	615
472197	342	361	GCGCGACAGCGCAGGTCCTC	57	9963	9982	616
472198	343	362	CGCGCGACAGCGCAGGTCCT	58	9964	9983	617
472199	344	363	TCGCGCGACAGCGCAGGTCC	53	9965	9984	618
472200	345	364	CTCGCGCGACAGCGCAGGTC	52	9966	9985	619
472201	346	365	CCTCGCGCGACAGCGCAGGT	26	9967	9986	620
472202	347	366	CCCTCGCGCGACAGCGCAGG	32	9968	9987	621
472203	349	368	ACCCCTCGCGCGACAGCGCA	67	9970	9989	622
472204	350	369	GACCCCTCGCGCGACAGCGC	72	9971	9990	623
472205	351	370	AGACCCCTCGCGCGACAGCG	74	9972	9991	624
472206	352	371	CAGACCCCTCGCGCGACAGC	67	9973	9992	625
472207	353	372	CCAGACCCCTCGCGCGACAG	53	9974	9993	626
472208	354	373	CCCAGACCCCTCGCGCGACA	70	9975	9994	627
472209	356	375	CTCCCAGACCCCTCGCGCGA	50	9977	9996	628
472210	357	376	TCTCCCAGACCCCTCGCGCG	31	9978	9997	629
472211	358	377	ATCTCCCAGACCCCTCGCGC	54	9979	9998	630
472212	359	378	CATCTCCCAGACCCCTCGCG	51	9980	9999	631
472213	360	379	CCATCTCCCAGACCCCTCGC	42	9981	10000	632
472214	362	381	CCCCATCTCCCAGACCCCTC	48	9983	10002	633
472215	363	382	GCCCCATCTCCCAGACCCCT	32	n/a	n/a	634
472216	364	383	TGCCCCATCTCCCAGACCCC	46	n/a	n/a	635
472217	365	384	GTGCCCCATCTCCCAGACCC	43	n/a	n/a	636

472218	366	385	AGTGCCCCATCTCCCAGACC	19	n/a	n/a	637
472219	368	387	CCAGTGCCCCATCTCCCAGA	9	n/a	n/a	638
472220	369	388	TCCAGTGCCCCATCTCCCAG	0	n/a	n/a	639
472221	371	390	GATCCAGTGCCCCATCTCCC	0	n/a	n/a	640
472222	372	391	GGATCCAGTGCCCCATCTCC	2	n/a	n/a	641
472223	374	393	CTGGATCCAGTGCCCCATCT	31	n/a	n/a	642
472224	375	394	GCTGGATCCAGTGCCCCATC	39	n/a	n/a	643
472225	377	396	ATGCTGGATCCAGTGCCCCA	36	n/a	n/a	644
472226	378	397	GATGCTGGATCCAGTGCCCC	18	n/a	n/a	645
472227	380	399	AGGATGCTGGATCCAGTGCC	41	25506	25525	646
472228	381	400	GAGGATGCTGGATCCAGTGC	17	25507	25526	647
472229	383	402	GAGAGGATGCTGGATCCAGT	6	25509	25528	648

Table 12

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NOs: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	75	32431	32450	425
472373	782	801	ACTTCTGTGGCCTCTGTGCT	31	37310	37329	649
472374	784	803	TCACTTCTGTGGCCTCTGTG	42	37312	37331	650
472375	785	804	CTCACTTCTGTGGCCTCTGT	53	37313	37332	651
472376	787	806	TGCTCACTTCTGTGGCCTCT	66	37315	37334	652
472377	788	807	TTGCTCACTTCTGTGGCCTC	78	37316	37335	653
472378	790	809	TCTTGCTCACTTCTGTGGCC	57	37318	37337	654
472379	791	810	TTCTTGCTCACTTCTGTGGC	43	37319	37338	655
472380	793	812	ACTTCTTGCTCACTTCTGTG	41	37321	37340	656
472381	794	813	AACTTCTTGCTCACTTCTGT	14	37322	37341	657
472382	796	815	GGAACTTCTTGCTCACTTCT	39	37324	37343	658
472383	797	816	GGGAACTTCTTGCTCACTTC	47	37325	37344	659
472384	799	818	CTGGGAACTTCTTGCTCACT	65	37327	37346	660
472385	800	819	CCTGGGAACTTCTTGCTCAC	0	37328	37347	661
472386	802	821	TGCCTGGGAACTTCTTGCTC	54	37330	37349	662
472387	803	822	ATGCCTGGGAACTTCTTGCT	24	37331	37350	663
472388	805	824	GTATGCCTGGGAACTTCTTG	26	37333	37352	664
472389	806	825	CGTATGCCTGGGAACTTCTT	46	37334	37353	665
472390	807	826	CCGTATGCCTGGGAACTTCT	41	37335	37354	666
472391	809	828	GGCCGTATGCCTGGGAACTT	47	37337	37356	667
472392	810	829	AGGCCGTATGCCTGGGAACT	45	37338	37357	668
472393	812	831	TAAGGCCGTATGCCTGGGAA	38	37340	37359	669
472394	813	832	GTAAGGCCGTATGCCTGGGA	53	37341	37360	670

472395	821	840	GTAGCCAGGTAAGGCCGTAT	53	37349	37368	671
472396	822	841	TGTAGCCAGGTAAGGCCGTA	41	37350	37369	672
472397	824	843	AGTGTAGCCAGGTAAGGCCG	36	37352	37371	673
472398	825	844	CAGTGTAGCCAGGTAAGGCC	63	37353	37372	674
472399	826	845	CCAGTGTAGCCAGGTAAGGC	45	37354	37373	675
472400	862	881	GGTACTCCCTCAACACAGGC	42	37390	37409	676
472401	863	882	AGGTACTCCCTCAACACAGG	11	37391	37410	677
472402	865	884	TCAGGTACTCCCTCAACACA	20	37393	37412	678
472403	866	885	ATCAGGTACTCCCTCAACAC	13	37394	37413	679
472404	868	887	ACATCAGGTACTCCCTCAAC	11	37396	37415	680
472405	869	888	GACATCAGGTACTCCCTCAA	27	37397	37416	681
472406	871	890	CAGACATCAGGTACTCCCTC	39	37399	37418	682
472407	872	891	CCAGACATCAGGTACTCCCT	46	37400	37419	683
472408	873	892	TCCAGACATCAGGTACTCCC	32	37401	37420	684
472409	874	893	CTCCAGACATCAGGTACTCC	29	37402	37421	685
472410	879	898	GATACCTCCAGACATCAGGT	33	n/a	n/a	686
472411	880	899	AGATACCTCCAGACATCAGG	17	n/a	n/a	687
472412	882	901	GCAGATACCTCCAGACATCA	9	n/a	n/a	688
472413	883	902	GGCAGATACCTCCAGACATC	44	n/a	n/a	689
472414	885	904	AGGGCAGATACCTCCAGACA	0	n/a	n/a	690
472415	886	905	CAGGGCAGATACCTCCAGAC	16	n/a	n/a	691
472416	888	907	GACAGGGCAGATACCTCCAG	1	n/a	n/a	692
472417	889	908	TGACAGGGCAGATACCTCCA	31	n/a	n/a	693
472418	911	930	AAATAGTCTATGGTGTCCCG	25	38064	38083	694
472419	912	931	CAAATAGTCTATGGTGTCCC	32	38065	38084	695
472420	914	933	AGCAAATAGTCTATGGTGTC	54	38067	38086	696
472421	915	934	AAGCAAATAGTCTATGGTGT	22	38068	38087	697
472422	917	936	GAAAGCAAATAGTCTATGGT	24	38070	38089	698
472423	918	937	TGAAAGCAAATAGTCTATGG	19	38071	38090	699
472424	920	939	TTTGAAAGCAAATAGTCTAT	17	38073	38092	700
472425	921	940	CTTTGAAAGCAAATAGTCTA	0	38074	38093	701
472426	923	942	TTCTTTGAAAGCAAATAGTC	24	38076	38095	702
472427	924	943	ATTCTTTGAAAGCAAATAGT	9	38077	38096	703
472428	926	945	CCATTCTTTGAAAGCAAATA	31	38079	38098	704
472429	927	946	CCCATTCTTTGAAAGCAAAT	48	38080	38099	705
380132	929	948	CTCCCATTCTTTGAAAGCAA	75	38082	38101	706
472430	930	949	ACTCCCATTCTTTGAAAGCA	35	38083	38102	707
472431	931	950	CACTCCCATTCTTTGAAAGC	35	38084	38103	708
472432	933	952	GCCACTCCCATTCTTTGAAA	69	38086	38105	709
472433	934	953	TGCCACTCCCATTCTTTGAA	73	38087	38106	710
217328	938	957	GCATTGCCACTCCCATTCTT	76	38091	38110	144
472434	944	963	ATGATAGCATTGCCACTCCC	65	38097	38116	711

472435	945	964	GATGATAGCATTGCCACTCC	50	38098	38117	712
472436	946	965	TGATGATAGCATTGCCACTC	56	38099	38118	713
380134	947	966	ATGATGATAGCATTGCCACT	34	38100	38119	714
472437	949	968	CGATGATGATAGCATTGCCA	56	38102	38121	715
472438	950	969	ACGATGATGATAGCATTGCC	51	38103	38122	716
472439	951	970	CACGATGATGATAGCATTGC	56	38104	38123	717
472440	952	971	CCACGATGATGATAGCATTG	63	38105	38124	718
472441	974	993	AGAGACTCAGCCGCACCCCC	63	38127	38146	719
472442	975	994	CAGAGACTCAGCCGCACCCC	66	38128	38147	720
366730	979	998	AGCTCAGAGACTCAGCCGCA	67	38132	38151	150
423442	980	999	GAGCTCAGAGACTCAGCCGC	52	38133	38152	489
423444	982	1001	TGGAGCTCAGAGACTCAGCC	63	38135	38154	153
472443	989	1008	CCAGGCATGGAGCTCAGAGA	47	38142	38161	721

Table 13

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	94	32431	32450	425
472230	384	403	GGAGAGGATGCTGGATCCAG	38	25510	25529	722
472231	386	405	GCGGAGAGGATGCTGGATCC	41	25512	25531	723
472232	387	406	GGCGGAGAGGATGCTGGATC	28	25513	25532	724
472233	389	408	AGGGCGGAGAGGATGCTGGA	0	25515	25534	725
472234	390	409	GAGGGCGGAGAGGATGCTGG	66	25516	25535	726
472235	391	410	GGAGGGCGGAGAGGATGCTG	28	25517	25536	727
472236	392	411	TGGAGGGCGGAGAGGATGCT	35	25518	25537	728
472237	394	413	CCTGGAGGGCGGAGAGGATG	9	25520	25539	729
472238	395	414	TCCTGGAGGGCGGAGAGGAT	0	25521	25540	730
472239	397	416	GGTCCTGGAGGGCGGAGAGG	0	25523	25542	731
472240	398	417	AGGTCCTGGAGGGCGGAGAG	32	25524	25543	732
472241	399	418	GAGGTCCTGGAGGGCGGAGA	33	25525	25544	733
472242	400	419	AGAGGTCCTGGAGGGCGGAG	0	25526	25545	734
472243	401	420	AAGAGGTCCTGGAGGGCGGA	35	25527	25546	735
472244	402	421	GAAGAGGTCCTGGAGGGCGG	16	25528	25547	736
472245	403	422	AGAAGAGGTCCTGGAGGGCG	53	25529	25548	737
366710	425	444	GACCTATTGAGCCAGGTGAC	62	25551	25570	146
472246	426	445	GGACCTATTGAGCCAGGTGA	63	25552	25571	738
472247	427	446	TGGACCTATTGAGCCAGGTG	58	25553	25572	739
472248	428	447	TTGGACCTATTGAGCCAGGT	71	25554	25573	740
472249	429	448	CTTGGACCTATTGAGCCAGG	63	25555	25574	741

472250	431	450	ACCTTGGACCTATTGAGCCA	80	25557	25576	742
472251	432	451	CACCTTGGACCTATTGAGCC	70	25558	25577	743
472252	433	452	CCACCTTGGACCTATTGAGC	74	25559	25578	744
472253	434	453	TCCACCTTGGACCTATTGAG	68	25560	25579	745
472254	436	455	TTTCCACCTTGGACCTATTG	41	25562	25581	746
472255	437	456	TTTTCCACCTTGGACCTATT	43	25563	25582	747
472256	438	457	CTTTTCCACCTTGGACCTAT	48	25564	25583	748
472257	439	458	GCTTTTCCACCTTGGACCTA	75	25565	25584	749
472258	441	460	CTGCTTTTCCACCTTGGACC	83	25567	25586	750
472259	442	461	GCTGCTTTTCCACCTTGGAC	83	25568	25587	751
472260	443	462	AGCTGCTTTTCCACCTTGGA	84	25569	25588	152
472261	444	463	TAGCTGCTTTTCCACCTTGG	76	25570	25589	752
366714	445	464	GTAGCTGCTTTTCCACCTTG	70	25571	25590	147
472262	446	465	TGTAGCTGCTTTTCCACCTT	39	25572	25591	753
472263	447	466	CTGTAGCTGCTTTTCCACCT	72	25573	25592	754
380086	449	468	ACCTGTAGCTGCTTTTCCAC	70	25575	25594	755
472264	450	469	GACCTGTAGCTGCTTTTCCA	77	25576	25595	756
472265	452	471	ATGACCTGTAGCTGCTTTTC	57	25578	25597	757
472266	453	472	GATGACCTGTAGCTGCTTTT	74	25579	25598	758
472267	454	473	AGATGACCTGTAGCTGCTTT	67	25580	25599	759
472268	456	475	TGAGATGACCTGTAGCTGCT	77	25582	25601	760
472269	457	476	CTGAGATGACCTGTAGCTGC	78	25583	25602	761
472270	459	478	CACTGAGATGACCTGTAGCT	80	25585	25604	762
472271	460	479	GCACTGAGATGACCTGTAGC	77	25586	25605	763
472272	462	481	GAGCACTGAGATGACCTGTA	71	25588	25607	764
472273	463	482	GGAGCACTGAGATGACCTGT	75	25589	25608	765
472274	465	484	CTGGAGCACTGAGATGACCT	72	25591	25610	766
472275	466	485	ACTGGAGCACTGAGATGACC	62	25592	25611	767
423453	474	493	CAGGACCCACTGGAGCACTG	92	25600	25619	457
472276	477	496	GGACAGGACCCACTGGAGCA	72	25603	25622	768
472277	478	497	AGGACAGGACCCACTGGAGC	74	25604	25623	769
472278	480	499	GAAGGACAGGACCCACTGGA	53	25606	25625	770
472279	481	500	GGAAGGACAGGACCCACTGG	48	25607	25626	771
472280	483	502	AAGGAAGGACAGGACCCACT	54	25609	25628	772
472281	484	503	CAAGGAAGGACAGGACCCAC	40	25610	25629	773
472282	485	504	ACAAGGAAGGACAGGACCCA	65	25611	25630	774
472283	487	506	GTACAAGGAAGGACAGGACC	55	25613	25632	775
472284	488	507	AGTACAAGGAAGGACAGGAC	35	25614	25633	776
472285	489	508	CAGTACAAGGAAGGACAGGA	40	25615	25634	777
472286	490	509	CCAGTACAAGGAAGGACAGG	32	25616	25635	778
472287	492	511	TCCCAGTACAAGGAAGGACA	58	n/a	n/a	779
472288	493	512	CTCCCAGTACAAGGAAGGAC	33	n/a	n/a	780

472289	495	514	CACTCCCAGTACAAGGAAGG	47	n/a	n/a	781
472290	496	515	CCACTCCCAGTACAAGGAAG	4	n/a	n/a	782
472291	498	517	GGCCACTCCCAGTACAAGGA	12	n/a	n/a	783
472292	499	518	AGGCCACTCCCAGTACAAGG	2	n/a	n/a	784
472293	501	520	GCAGGCCACTCCCAGTACAA	0	n/a	n/a	785
472294	502	521	TGCAGGCCACTCCCAGTACA	0	n/a	n/a	786
472295	504	523	ACTGCAGGCCACTCCCAGTA	43	n/a	n/a	787
472296	505	524	CACTGCAGGCCACTCCCAGT	14	n/a	n/a	788
472297	507	526	GGCACTGCAGGCCACTCCCA	73	n/a	n/a	789
472298	508	527	TGGCACTGCAGGCCACTCCC	25	n/a	n/a	790
472299	509	528	ATGGCACTGCAGGCCACTCC	46	31076	31095	791
472300	511	530	GGATGGCACTGCAGGCCACT	43	31078	31097	792
472301	512	531	AGGATGGCACTGCAGGCCAC	61	31079	31098	793
472302	513	532	GAGGATGGCACTGCAGGCCA	69	31080	31099	794

Table 14

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	90	32431	32450	425
472303	514	533	TGAGGATGGCACTGCAGGCC	45	31081	31100	795
472304	516	535	CATGAGGATGGCACTGCAGG	24	31083	31102	796
472305	517	536	ACATGAGGATGGCACTGCAG	19	31084	31103	797
472306	518	537	TACATGAGGATGGCACTGCA	59	31085	31104	798
472307	521	540	ATGTACATGAGGATGGCACT	32	31088	31107	799
472308	522	541	TATGTACATGAGGATGGCAC	22	31089	31108	800
472309	523	542	ATATGTACATGAGGATGGCA	39	31090	31109	801
472310	524	543	AATATGTACATGAGGATGGC	34	31091	31110	802
472311	526	545	AGAATATGTACATGAGGATG	1	31093	31112	803
472312	527	546	CAGAATATGTACATGAGGAT	48	31094	31113	804
472313	528	547	GCAGAATATGTACATGAGGA	44	31095	31114	805
472314	529	548	TGCAGAATATGTACATGAGG	43	31096	31115	806
366722	530	549	GTGCAGAATATGTACATGAG	65	31097	31116	148
472315	552	571	CACAGCGATGAGCCAGCAAT	65	31119	31138	807
472316	553	572	GCACAGCGATGAGCCAGCAA	84	31120	31139	808
472317	555	574	GAGCACAGCGATGAGCCAGC	87	31122	31141	809
472318	556	575	AGAGCACAGCGATGAGCCAG	83	31123	31142	810
472319	558	577	GTAGAGCACAGCGATGAGCC	73	31125	31144	811
472320	559	578	AGTAGAGCACAGCGATGAGC	68	31126	31145	812
472321	560	579	AAGTAGAGCACAGCGATGAG	48	31127	31146	813

472322	561	580	GAAGTAGAGCACAGCGATGA	22	31128	31147	814
472323	563	582	GTGAAGTAGAGCACAGCGAT	64	31130	31149	815
472324	564	583	AGTGAAGTAGAGCACAGCGA	51	31131	31150	816
472325	565	584	AAGTGAAGTAGAGCACAGCG	39	31132	31151	817
472326	566	585	CAAGTGAAGTAGAGCACAGC	26	31133	31152	818
472327	568	587	GCCAAGTGAAGTAGAGCACA	64	31135	31154	819
472328	569	588	AGCCAAGTGAAGTAGAGCAC	65	31136	31155	820
472329	571	590	CCAGCCAAGTGAAGTAGAGC	51	31138	31157	821
472330	572	591	ACCAGCCAAGTGAAGTAGAG	47	31139	31158	822
472331	574	593	ACACCAGCCAAGTGAAGTAG	35	31141	31160	823
472332	575	594	AACACCAGCCAAGTGAAGTA	34	31142	31161	824
472333	577	596	CAAACACCAGCCAAGTGAAG	33	31144	31163	825
472334	578	597	TCAAACACCAGCCAAGTGAA	34	31145	31164	826
472335	580	599	AGTCAAACACCAGCCAAGTG	39	31147	31166	827
472336	581	600	CAGTCAAACACCAGCCAAGT	37	31148	31167	828
472337	583	602	TCCAGTCAAACACCAGCCAA	53	31150	31169	829
472338	584	603	TTCCAGTCAAACACCAGCCA	52	31151	31170	830
472339	586	605	TGTTCCAGTCAAACACCAGC	38	31153	31172	831
472340	587	606	GTGTTCCAGTCAAACACCAG	43	31154	31173	832
472341	589	608	GTGTGTTCCAGTCAAACACC	26	31156	31175	833
472342	590	609	GGTGTGTTCCAGTCAAACAC	41	31157	31176	834
472343	592	611	TGGGTGTGTTCCAGTCAAAC	7	31159	31178	835
472344	593	612	TTGGGTGTGTTCCAGTCAAA	15	31160	31179	836
472345	595	614	TCTTGGGTGTGTTCCAGTCA	54	31162	31181	837
472346	596	615	TTCTTGGGTGTGTTCCAGTC	47	31163	31182	838
472347	616	635	ACTGTGACCTCCTGCCACCT	66	31548	31567	839
472348	617	636	CACTGTGACCTCCTGCCACC	55	31549	31568	840
472349	619	638	CCCACTGTGACCTCCTGCCA	79	31551	31570	841
472350	620	639	ACCCACTGTGACCTCCTGCC	77	31552	31571	842
472351	622	641	GGACCCACTGTGACCTCCTG	80	31554	31573	843
472352	623	642	CGGACCCACTGTGACCTCCT	63	31555	31574	844
472353	624	643	TCGGACCCACTGTGACCTCC	82	31556	31575	845
423459	631	650	CCCAGTTTCGGACCCACTGT	49	31563	31582	463
472354	633	652	AGCCCAGTTTCGGACCCACT	79	31565	31584	846
472355	634	653	CAGCCCAGTTTCGGACCCAC	48	31566	31585	847
472356	636	655	CACAGCCCAGTTTCGGACCC	72	31568	31587	848
472357	637	656	ACACAGCCCAGTTTCGGACC	63	31569	31588	849
472358	639	658	CCACACAGCCCAGTTTCGGA	75	31571	31590	850
472359	640	659	GCCACACAGCCCAGTTTCGG	74	31572	31591	851
472360	641	660	CGCCACACAGCCCAGTTTCG	77	31573	31592	852
472361	659	678	AAGTAGTCTCGAAAGTAGCG	7	31591	31610	853
472362	660	679	AAAGTAGTCTCGAAAGTAGC	0	31592	31611	854

472363	662	681	GGAAAGTAGTCTCGAAAGTA	15	31594	31613	855
472364	663	682	GGGAAAGTAGTCTCGAAAGT	0	31595	31614	856
472365	664	683	TGGGAAAGTAGTCTCGAAAG	57	31596	31615	857
472366	666	685	GATGGGAAAGTAGTCTCGAA	17	31598	31617	858
472367	667	686	GGATGGGAAAGTAGTCTCGA	21	31599	31618	859
411897	685	704	TGTGTGTCTTCACCAGCTGG	41	n/a	n/a	60
217317	693	712	CAGCAGGTTGTGTGTCTTCA	57	37221	37240	21
411901	695	714	GTCAGCAGGTTGTGTGTCTT	45	37223	37242	64
411902	697	716	TGGTCAGCAGGTTGTGTGTC	28	37225	37244	65
472368	724	743	GGTGGTATCCAAAGATATAG	50	37252	37271	860
472369	725	744	GGGTGGTATCCAAAGATATA	27	37253	37272	861
366728	757	776	TGCAGAAGGCACCCAGGCCC	63	37285	37304	149
472370	758	777	TTGCAGAAGGCACCCAGGCC	31	37286	37305	862
472371	759	778	GTTGCAGAAGGCACCCAGGC	46	37287	37306	863
472372	781	800	CTTCTGTGGCCTCTGTGCTG	33	37309	37328	864

Table 15

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	89	32431	32450	425
472521	1210	1229	TGTCGGAGGAGAAGAGGCCT	32	39257	39276	865
472522	1212	1231	GGTGTCGGAGGAGAAGAGGC	0	39259	39278	866
472523	1213	1232	AGGTGTCGGAGGAGAAGAGG	0	39260	39279	867
472524	1214	1233	CAGGTGTCGGAGGAGAAGAG	9	39261	39280	868
472525	1216	1235	CCCAGGTGTCGGAGGAGAAG	3	39263	39282	869
472526	1217	1236	CCCCAGGTGTCGGAGGAGAA	36	39264	39283	870
472527	1219	1238	GCCCCCAGGTGTCGGAGGAG	10	39266	39285	871
472528	1220	1239	AGCCCCCAGGTGTCGGAGGA	13	39267	39286	872
472529	1221	1240	CAGCCCCCAGGTGTCGGAGG	32	39268	39287	873
472530	1223	1242	ACCAGCCCCCAGGTGTCGGA	40	39270	39289	874
472531	1251	1270	AACAGTGGTGATGGGCTTGG	17	39298	39317	875
472532	1252	1271	CAACAGTGGTGATGGGCTTG	28	39299	39318	876
472533	1323	1342	CATGGTGTGGTACAGGTCGA	42	41294	41313	877
472534	1324	1343	ACATGGTGTGGTACAGGTCG	63	41295	41314	878
411878	1325	1344	TACATGGTGTGGTACAGGTC	63	41296	41315	879
472535	1326	1345	GTACATGGTGTGGTACAGGT	70	41297	41316	880
472536	1328	1347	ATGTACATGGTGTGGTACAG	56	41299	41318	881
472537	1329	1348	CATGTACATGGTGTGGTACA	50	41300	41319	882
472538	1331	1350	TCCATGTACATGGTGTGGTA	53	41302	41321	883

472539	1332	1351	CTCCATGTACATGGTGTGGT	68	41303	41322	884
472540	1333	1352	CCTCCATGTACATGGTGTGG	63	41304	41323	885
472541	1335	1354	GGCCTCCATGTACATGGTGT	48	41306	41325	886
472542	1336	1355	GGGCCTCCATGTACATGGTG	51	41307	41326	887
472543	1337	1356	AGGGCCTCCATGTACATGGT	56	41308	41327	888
369255	1339	1358	CCAGGGCCTCCATGTACATG	35	41310	41329	103
411944	1340	1359	ACCAGGGCCTCCATGTACAT	47	41311	41330	120
411947	1344	1363	CTTCACCAGGGCCTCCATGT	22	41315	41334	123
411948	1345	1364	GCTTCACCAGGGCCTCCATG	43	41316	41335	124
411950	1347	1366	GAGCTTCACCAGGGCCTCCA	47	41318	41337	126
411951	1349	1368	AAGAGCTTCACCAGGGCCTC	51	41320	41339	127
472544	1352	1371	TCGAAGAGCTTCACCAGGGC	60	41323	41342	889
472545	1353	1372	GTCGAAGAGCTTCACCAGGG	73	41324	41343	890
472546	1355	1374	TTGTCGAAGAGCTTCACCAG	45	41326	41345	891
472547	1356	1375	CTTGTCGAAGAGCTTCACCA	65	41327	41346	892
472548	1357	1376	GCTTGTCGAAGAGCTTCACC	86	41328	41347	893
472549	1358	1377	TGCTTGTCGAAGAGCTTCAC	68	41329	41348	894
472550	1360	1379	TGTGCTTGTCGAAGAGCTTC	70	41331	41350	895
472551	1361	1380	TTGTGCTTGTCGAAGAGCTT	40	41332	41351	896
472552	1362	1381	CTTGTGCTTGTCGAAGAGCT	77	41333	41352	897
366746	1366	1385	TGGTCTTGTGCTTGTCGAAG	37	41337	41356	151
472553	1368	1387	CTTGGTCTTGTGCTTGTCGA	58	41339	41358	898
472554	1369	1388	ACTTGGTCTTGTGCTTGTCG	60	41340	41359	899
472555	1370	1389	AACTTGGTCTTGTGCTTGTC	61	41341	41360	900
472556	1372	1391	CGAACTTGGTCTTGTGCTTG	55	41343	41362	901
472557	1373	1392	CCGAACTTGGTCTTGTGCTT	63	41344	41363	902
472558	1374	1393	GCCGAACTTGGTCTTGTGCT	59	41345	41364	903
472559	1375	1394	GGCCGAACTTGGTCTTGTGC	60	41346	41365	904
472560	1377	1396	GAGGCCGAACTTGGTCTTGT	53	41348	41367	905
472561	1378	1397	GGAGGCCGAACTTGGTCTTG	35	41349	41368	906
472562	1400	1419	ACCTCCAGGACCTCAGTCTC	66	41371	41390	907
472563	1401	1420	CACCTCCAGGACCTCAGTCT	19	41372	41391	908
472564	1402	1421	TCACCTCCAGGACCTCAGTC	40	41373	41392	909
472565	1404	1423	GTTCACCTCCAGGACCTCAG	60	41375	41394	910
472566	1405	1424	AGTTCACCTCCAGGACCTCA	23	41376	41395	911
472567	1406	1425	CAGTTCACCTCCAGGACCTC	13	41377	41396	912
472568	1408	1427	CTCAGTTCACCTCCAGGACC	67	41379	41398	913
472569	1409	1428	GCTCAGTTCACCTCCAGGAC	71	41380	41399	914
472570	1410	1429	GGCTCAGTTCACCTCCAGGA	84	41381	41400	915
472571	1411	1430	TGGCTCAGTTCACCTCCAGG	74	41382	41401	916
411955	1502	1521	AAATAACCCACAGACACCCA	81	41473	41492	131
411958	1506	1525	TTTTAAATAACCCACAGACA	68	41477	41496	134

472572	1538	1557	TTGTAATGGTTTAGCAAAAT	7	41509	41528	917
472573	1539	1558	ATTGTAATGGTTTAGCAAAA	47	41510	41529	918
472574	1540	1559	CATTGTAATGGTTTAGCAAA	18	41511	41530	919
472575	1541	1560	ACATTGTAATGGTTTAGCAA	40	41512	41531	920
472576	1543	1562	TAACATTGTAATGGTTTAGC	58	41514	41533	921
472577	1544	1563	CTAACATTGTAATGGTTTAG	49	41515	41534	922
472578	1545	1564	CCTAACATTGTAATGGTTTA	67	41516	41535	923
472579	1546	1565	ACCTAACATTGTAATGGTTT	27	41517	41536	924
472580	1548	1567	AGACCTAACATTGTAATGGT	54	41519	41538	925
472581	1549	1568	AAGACCTAACATTGTAATGG	46	41520	41539	926
472582	1550	1569	AAAGACCTAACATTGTAATG	34	41521	41540	927
472583	1551	1570	AAAAGACCTAACATTGTAAT	33	41522	41541	928
472584	1553	1572	AAAAAAGACCTAACATTGTA	53	41524	41543	929
472585	1554	1573	TAAAAAAGACCTAACATTGT	58	41525	41544	930
472586	1556	1575	CTTAAAAAAGACCTAACATT	25	41527	41546	931
472587	1557	1576	TCTTAAAAAAGACCTAACAT	23	41528	41547	932

Example 4: Antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Antisense oligonucleotides were designed targeting a DGAT2 nucleic acid and were tested for their effects on DGAT2 mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. ISIS 413433, which consistently demonstrated higher potency than any of the previously disclosed oligonucleotides in the studies above was included in this study as a benchmark oligonucleotide. Antisense oligonucleotides that demonstrated about the same or greater potency than ISIS 413433 were therefore considered for further experimentation.

The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 4,500 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. The potency of some oligonucleotides was measured with human primer probe set RTS2367 (forward sequence GGCCTCCCGGAGACTGA, designated herein as SEQ ID NO: 4; reverse sequence AAGTGATTTGCAGCTGGTTCCT, designated herein as SEQ ID NO: 5; probe sequence AGGTGAACTGAGCCAGCCTTCGGG, designated herein as SEQ ID NO: 6). DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. The results show several antisense oligonucleotides demonstrate greater potency than the benchmark oligonucleotides.

The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE gapmers or 3-10-4 MOE gapmers. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the

central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 3-10-4 MOE gapmers are 17 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising three and four nucleosides respectively. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to SEQ ID NO: 1, SEQ ID NO: 2, or both. 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity. In case the sequence alignment for a target gene in a particular table is not shown, it is understood that none of the oligonucleotides presented in that table align with 100% complementarity with that target gene.

Table 16

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	% inhibition	SEQ ID NO
483799	221	240	ACGGCCCCGCGGGAAGCCGC	9842	9861	8	569
483800	226	245	CAGTCACGGCCCCGCGGGAA	9847	9866	46	570
483801	231	250	CCGCCCAGTCACGGCCCCGC	9852	9871	0	571
483802	236	255	GAAGCCCGCCCAGTCACGGC	9857	9876	50	572
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	32431	32450	85	425
483803	n/a	n/a	ACCCCATCTCCCAGACCCCT	9984	10003	75	496
483804	n/a	n/a	CACTCACCCCATCTCCCAGA	9989	10008	46	497
483805	n/a	n/a	CAGGTCCATAACCCCTGCGC	10014	10033	51	498
483806	n/a	n/a	TCTCGCAGGTCCATAACCCC	10019	10038	6	499
483807	n/a	n/a	AATCTTCTCGCAGGTCCATA	10024	10043	50	500
483808	n/a	n/a	CAGAAAATCTTCTCGCAGGT	10029	10048	49	501
483809	n/a	n/a	CTTTCCAGAAAATCTTCTCG	10034	10053	37	502
483810	n/a	n/a	GGGCCCTTTCCAGAAAATCT	10039	10058	40	503
483811	n/a	n/a	CCACAGGGCCCTTTCCAGAA	10044	10063	85	504
483812	n/a	n/a	GCCTGCCACAGGGCCCTTTC	10049	10068	76	505
483813	n/a	n/a	CACCAGCCTGCCACAGGGCC	10054	10073	80	506
483814	n/a	n/a	CACGGATGAGGGAAACAAGC	10160	10179	73	507
483815	n/a	n/a	AATATCCCTAATAACTAAGA	10205	10224	35	508
483816	n/a	n/a	TCTCGAATATCCCTAATAAC	10210	10229	84	509
483817	n/a	n/a	GGAGTTCTCGAATATCCCTA	10215	10234	96	510

483818	n/a	n/a	AAACCCATACCATCCTGCCC	10327	10346	76	511
483819	n/a	n/a	TGGTGGCTGTCTCAGGAGAC	10351	10370	49	512
483820	n/a	n/a	CCGTCTGGTGGCTGTCTCAG	10356	10375	36	513
483821	n/a	n/a	GGCAGACACACCTGTTCCAG	10389	10408	64	514
483822	n/a	n/a	GACAGGGCAGACACACCTGT	10394	10413	64	515
483823	n/a	n/a	CAGAGGACAGGGCAGACACA	10399	10418	69	516
483824	n/a	n/a	CCAGAGCCTGGGCGAGAGGA	10430	10449	45	517
483825	n/a	n/a	CAGGGTCCTCTCCGCTGCCT	10490	10509	91	518
483826	n/a	n/a	CTGAGGACCTCAGTTCTACC	10522	10541	83	519
483827	n/a	n/a	ATTCACTGAGGACCTCAGTT	10527	10546	67	520
483828	n/a	n/a	GCGCGATTCACTGAGGACCT	10532	10551	88	521
483829	n/a	n/a	ACTCTGCGCGATTCACTGAG	10537	10556	73	522
483830	n/a	n/a	CTCCCACTTCAGTTTCTCCA	10645	10664	83	523
483831	n/a	n/a	GCTTCCTCCCACTTCAGTTT	10650	10669	86	524
483832	n/a	n/a	GGCATGCTTCCTCCCACTTC	10655	10674	89	525
483833	n/a	n/a	ACTTAGGCATGCTTCCTCCC	10660	10679	89	526
483834	n/a	n/a	GGAAAACTTAGGCATGCTTC	10665	10684	92	527
483835	n/a	n/a	GCTAAGGAAAACTTAGGCAT	10670	10689	85	528
483836	n/a	n/a	CATCAGCTAAGGAAAACTTA	10675	10694	53	529
483837	n/a	n/a	CAAGGCATCAGCTAAGGAAA	10680	10699	27	530
483838	n/a	n/a	ATTTGTACTTGAATCCAGGG	10702	10721	77	531
483839	n/a	n/a	GTGATGACTTCCCAGGGTCT	10727	10746	87	532
483840	n/a	n/a	CAGCTGTGATGACTTCCCAG	10732	10751	84	533
483841	n/a	n/a	CAGGACAGCTGTGATGACTT	10737	10756	80	534
483842	n/a	n/a	CAGACCAGGACAGCTGTGAT	10742	10761	72	535
483843	n/a	n/a	CACACGCAGACCAGGACAGC	10748	10767	54	536
483844	n/a	n/a	AGACACACACGCAGACCAGG	10753	10772	44	537
483845	n/a	n/a	ATGCAAGACACACACGCAGA	10758	10777	45	538
483846	n/a	n/a	GCTTCATGCAAGACACACAC	10763	10782	78	539
483847	n/a	n/a	ATGTCAGAGAGGCTCAGCAA	10814	10833	67	540
483848	n/a	n/a	AATCCATGTCAGAGAGGCTC	10819	10838	93	541
483849	n/a	n/a	AGAAAAATCCATGTCAGAGA	10824	10843	37	542
483850	n/a	n/a	ACTAAAGAAAAATCCATGTC	10829	10848	49	543
483851	n/a	n/a	TAGTTACTAAAGAAAAATCC	10834	10853	21	544
483852	n/a	n/a	GGATAGTCGATTTACCAGAA	10940	10959	88	545
483853	n/a	n/a	TCTTTGGATAGTCGATTTAC	10945	10964	66	546
483854	n/a	n/a	ACTAAAATGCTAATAGGAAG	10968	10987	2	547
483855	n/a	n/a	GATATACTAAAATGCTAATA	10973	10992	9	548
483856	n/a	n/a	CAAGAGATATACTAAAATGC	10978	10997	32	549
483857	n/a	n/a	ATGATCAAGAGATATACTAA	10983	11002	36	550
483858	n/a	n/a	AGAAAATGATCAAGAGATAT	10988	11007	6	551
483859	n/a	n/a	TATAAAGAAAATGATCAAGA	10993	11012	6	552

483860	n/a	n/a	ATGTGTATAAAGAAAATGAT	10998	11017	0	553
483861	n/a	n/a	ATGCAATGTGTATAAAGAAA	11003	11022	36	554
483862	n/a	n/a	TATCTATGCAATGTGTATAA	11008	11027	75	555
483863	n/a	n/a	ATTCATAACTATATCTACAG	11042	11061	52	556
483864	n/a	n/a	ACAAGATTCATAACTATATC	11047	11066	31	557
483865	n/a	n/a	AGAAAACAAGATTCATAACT	11052	11071	33	558
483866	n/a	n/a	CCTCGATGTTACATTAAGGG	11074	11093	90	559
483867	n/a	n/a	GGAAACCTCGATGTTACATT	11079	11098	59	560
483868	n/a	n/a	ATTGCAACCACTAGGACATT	11123	11142	60	561
483869	n/a	n/a	GGGTTATTGCAACCACTAGG	11128	11147	91	562
483870	n/a	n/a	CACAGTTAAAGTGTGGTACA	11158	11177	86	563
483871	n/a	n/a	TAGGTCACAGTTAAAGTGTG	11163	11182	60	564
483872	n/a	n/a	ATGCCTAGGTCACAGTTAAA	11168	11187	74	565
483873	n/a	n/a	TGCCAATGCCTAGGTCACAG	11173	11192	90	566
483874	n/a	n/a	AGCAATGCCAATGCCTAGGT	11178	11197	91	567
483875	n/a	n/a	CACAGCGATAATCACACAAG	11199	11218	87	568

Table 17

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	89	32431	32450	425
472665	1870	1889	CTCCAACTCCTCCCCTTGGC	56	41841	41860	933
472666	1871	1890	TCTCCAACTCCTCCCCTTGG	37	41842	41861	934
472667	1873	1892	GCTCTCCAACTCCTCCCCTT	63	41844	41863	935
472668	1874	1893	TGCTCTCCAACTCCTCCCCT	65	41845	41864	936
472669	1917	1936	CATTCCAGATGCCTACTACT	63	41888	41907	937
472670	1918	1937	GCATTCCAGATGCCTACTAC	68	41889	41908	938
472671	1919	1938	AGCATTCCAGATGCCTACTA	81	41890	41909	939
472672	1920	1939	GAGCATTCCAGATGCCTACT	77	41891	41910	940
472673	1993	2012	CCTGGAGGCCAGTCCAGGCT	33	41964	41983	941
472674	1994	2013	TCCTGGAGGCCAGTCCAGGC	22	41965	41984	942
472675	1996	2015	CATCCTGGAGGCCAGTCCAG	14	41967	41986	943
472676	1997	2016	TCATCCTGGAGGCCAGTCCA	47	41968	41987	944
472677	1999	2018	CCTCATCCTGGAGGCCAGTC	57	41970	41989	945
472678	2000	2019	TCCTCATCCTGGAGGCCAGT	37	41971	41990	946
472679	2001	2020	ATCCTCATCCTGGAGGCCAG	50	41972	41991	947
472680	2002	2021	CATCCTCATCCTGGAGGCCA	56	41973	41992	948
472681	2004	2023	CCCATCCTCATCCTGGAGGC	29	41975	41994	949
472682	2005	2024	CCCCATCCTCATCCTGGAGG	21	41976	41995	950

472683	2007	2026	ACCCCCATCCTCATCCTGGA	24	41978	41997	951
472684	2008	2027	CACCCCCATCCTCATCCTGG	8	41979	41998	952
472685	2009	2028	CCACCCCCATCCTCATCCTG	39	41980	41999	953
472686	2011	2030	TGCCACCCCCATCCTCATCC	46	41982	42001	954
472687	2012	2031	TTGCCACCCCCATCCTCATC	48	41983	42002	955
472688	2013	2032	ATTGCCACCCCCATCCTCAT	57	41984	42003	956
472689	2015	2034	TCATTGCCACCCCCATCCTC	43	41986	42005	957
472690	2016	2035	GTCATTGCCACCCCCATCCT	29	41987	42006	958
472691	2017	2036	TGTCATTGCCACCCCCATCC	51	41988	42007	959
472692	2019	2038	GGTGTCATTGCCACCCCCAT	74	41990	42009	960
472693	2079	2098	GCTCATGGTGGCGGCATCCT	77	42050	42069	961
472694	2080	2099	AGCTCATGGTGGCGGCATCC	66	42051	42070	962
472695	2082	2101	CTAGCTCATGGTGGCGGCAT	65	42053	42072	963
472696	2083	2102	CCTAGCTCATGGTGGCGGCA	68	42054	42073	964
472697	2085	2104	CACCTAGCTCATGGTGGCGG	49	42056	42075	965
472698	2086	2105	CCACCTAGCTCATGGTGGCG	44	42057	42076	966
472699	2088	2107	CTCCACCTAGCTCATGGTGG	18	42059	42078	967
472700	2089	2108	ACTCCACCTAGCTCATGGTG	61	42060	42079	968
472701	2090	2109	TACTCCACCTAGCTCATGGT	46	42061	42080	969
472702	2092	2111	GTTACTCCACCTAGCTCATG	51	42063	42082	970
472703	2093	2112	AGTTACTCCACCTAGCTCAT	58	42064	42083	971
472704	2094	2113	CAGTTACTCCACCTAGCTCA	66	42065	42084	972
472705	2095	2114	CCAGTTACTCCACCTAGCTC	80	42066	42085	973
472706	2097	2116	AACCAGTTACTCCACCTAGC	71	42068	42087	974
472707	2098	2117	AAACCAGTTACTCCACCTAG	68	42069	42088	975
472708	2100	2119	AAAAACCAGTTACTCCACCT	67	42071	42090	976
472709	2101	2120	GAAAAACCAGTTACTCCACC	68	42072	42091	977
472710	2103	2122	AAGAAAAACCAGTTACTCCA	53	42074	42093	978
472711	2104	2123	CAAGAAAAACCAGTTACTCC	61	42075	42094	979
472712	2106	2125	CCCAAGAAAAACCAGTTACT	67	42077	42096	980
472713	2107	2126	ACCCAAGAAAAACCAGTTAC	71	42078	42097	981
472714	2108	2127	CACCCAAGAAAAACCAGTTA	56	42079	42098	982
472715	2109	2128	CCACCCAAGAAAAACCAGTT	61	42080	42099	983
472716	2111	2130	AGCCACCCAAGAAAAACCAG	62	42082	42101	984
472717	2112	2131	CAGCCACCCAAGAAAAACCA	69	42083	42102	985
472718	2114	2133	ATCAGCCACCCAAGAAAAAC	58	42085	42104	986
472719	2115	2134	CATCAGCCACCCAAGAAAAA	46	42086	42105	987
472720	2116	2135	TCATCAGCCACCCAAGAAAA	64	42087	42106	988
472721	2118	2137	TGTCATCAGCCACCCAAGAA	48	42089	42108	989
472722	2119	2138	ATGTCATCAGCCACCCAAGA	50	42090	42109	990
472723	2121	2140	CCATGTCATCAGCCACCCAA	79	42092	42111	991
472724	2122	2141	TCCATGTCATCAGCCACCCA	79	42093	42112	992

472725	2123	2142	ATCCATGTCATCAGCCACCC	83	42094	42113	993
472726	2124	2143	CATCCATGTCATCAGCCACC	80	42095	42114	994
472727	2126	2145	TGCATCCATGTCATCAGCCA	81	42097	42116	995
472728	2127	2146	CTGCATCCATGTCATCAGCC	78	42098	42117	996
413319	2128	2147	GCTGCATCCATGTCATCAGC	74	42099	42118	154
472729	2129	2148	TGCTGCATCCATGTCATCAG	80	42100	42119	997
472730	2130	2149	GTGCTGCATCCATGTCATCA	68	42101	42120	998
472731	2132	2151	CTGTGCTGCATCCATGTCAT	64	42103	42122	999
472732	2133	2152	TCTGTGCTGCATCCATGTCA	80	42104	42123	1000
472733	2134	2153	GTCTGTGCTGCATCCATGTC	83	42105	42124	1001
472734	2135	2154	AGTCTGTGCTGCATCCATGT	68	42106	42125	1002
472735	2137	2156	TGAGTCTGTGCTGCATCCAT	71	42108	42127	1003
472736	2138	2157	CTGAGTCTGTGCTGCATCCA	78	42109	42128	1004
472737	2139	2158	GCTGAGTCTGTGCTGCATCC	80	42110	42129	1005
472738	2140	2159	GGCTGAGTCTGTGCTGCATC	84	42111	42130	1006
472739	2141	2160	AGGCTGAGTCTGTGCTGCAT	76	42112	42131	1007
472740	2142	2161	AAGGCTGAGTCTGTGCTGCA	81	42113	42132	1008

Table 18

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	89	32431	32450	425
411901	695	714	GTCAGCAGGTTGTGTGTCTT	64	37223	37242	64
472741	2144	2163	CCAAGGCTGAGTCTGTGCTG	60	42115	42134	1009
472742	2145	2164	GCCAAGGCTGAGTCTGTGCT	63	42116	42135	1010
472743	2147	2166	AGGCCAAGGCTGAGTCTGTG	55	42118	42137	1011
472744	2148	2167	CAGGCCAAGGCTGAGTCTGT	39	42119	42138	1012
472745	2150	2169	TCCAGGCCAAGGCTGAGTCT	56	42121	42140	1013
472746	2151	2170	CTCCAGGCCAAGGCTGAGTC	62	42122	42141	1014
472747	2152	2171	GCTCCAGGCCAAGGCTGAGT	77	42123	42142	1015
472748	2153	2172	TGCTCCAGGCCAAGGCTGAG	43	42124	42143	1016
472749	2155	2174	TGTGCTCCAGGCCAAGGCTG	63	42126	42145	1017
472750	2156	2175	ATGTGCTCCAGGCCAAGGCT	69	42127	42146	1018
472751	2181	2200	AGGTAAACTGAGGCCACCAG	35	42152	42171	1019
472752	2183	2202	GAAGGTAAACTGAGGCCACC	72	42154	42173	1020
472753	2184	2203	GGAAGGTAAACTGAGGCCAC	45	42155	42174	1021
472754	2214	2233	TCTTCCTCACATCCAGAATC	49	42185	42204	1022
472755	2215	2234	CTCTTCCTCACATCCAGAAT	62	42186	42205	1023
472756	2237	2256	CAGGCCCCTTCTGAAGAGGG	73	42208	42227	1024

472757	2238	2257	CCAGGCCCCTTCTGAAGAGG	68	42209	42228	1025
472758	2240	2259	GGCCAGGCCCCTTCTGAAGA	41	42211	42230	1026
472759	2241	2260	AGGCCAGGCCCCTTCTGAAG	51	42212	42231	1027
472760	2243	2262	GAAGGCCAGGCCCCTTCTGA	32	42214	42233	1028
472761	2244	2263	AGAAGGCCAGGCCCCTTCTG	28	42215	42234	1029
472762	2245	2264	CAGAAGGCCAGGCCCCTTCT	24	42216	42235	1030
472763	2247	2266	CTCAGAAGGCCAGGCCCCTT	54	42218	42237	1031
472764	2248	2267	GCTCAGAAGGCCAGGCCCCT	72	42219	42238	1032
472765	2250	2269	CTGCTCAGAAGGCCAGGCCC	60	42221	42240	1033
472766	2251	2270	GCTGCTCAGAAGGCCAGGCC	81	42222	42241	1034
472767	2253	2272	CTGCTGCTCAGAAGGCCAGG	51	42224	42243	1035
472768	2254	2273	TCTGCTGCTCAGAAGGCCAG	79	42225	42244	1036
472769	2255	2274	ATCTGCTGCTCAGAAGGCCA	63	42226	42245	1037
472770	2256	2275	AATCTGCTGCTCAGAAGGCC	69	42227	42246	1038
472771	2258	2277	CTAATCTGCTGCTCAGAAGG	57	42229	42248	1039
472772	2259	2278	ACTAATCTGCTGCTCAGAAG	63	42230	42249	1040
472773	2260	2279	AACTAATCTGCTGCTCAGAA	52	42231	42250	1041
472774	2261	2280	GAACTAATCTGCTGCTCAGA	45	42232	42251	1042
472775	2262	2281	GGAACTAATCTGCTGCTCAG	70	42233	42252	1043
472776	2263	2282	TGGAACTAATCTGCTGCTCA	73	42234	42253	1044
472777	2264	2283	TTGGAACTAATCTGCTGCTC	70	42235	42254	1045
472778	2266	2285	CTTTGGAACTAATCTGCTGC	69	42237	42256	1046
472779	2267	2286	GCTTTGGAACTAATCTGCTG	70	42238	42257	1047
472780	2268	2287	TGCTTTGGAACTAATCTGCT	76	42239	42258	1048
472781	2269	2288	CTGCTTTGGAACTAATCTGC	71	42240	42259	1049
472782	2270	2289	CCTGCTTTGGAACTAATCTG	55	42241	42260	1050
472783	2272	2291	CACCTGCTTTGGAACTAATC	65	42243	42262	1051
472784	2273	2292	CCACCTGCTTTGGAACTAAT	78	42244	42263	1052
472785	2275	2294	GGCCACCTGCTTTGGAACTA	66	42246	42265	1053
472786	2276	2295	GGGCCACCTGCTTTGGAACT	67	42247	42266	1054
472787	2296	2315	AAAGTGAGGCTTGGGTTCGG	58	42267	42286	1055
472788	2297	2316	AAAAGTGAGGCTTGGGTTCG	54	42268	42287	1056
472789	2299	2318	AGAAAAGTGAGGCTTGGGTT	65	42270	42289	1057
472790	2300	2319	CAGAAAAGTGAGGCTTGGGT	61	42271	42290	1058
472791	2302	2321	CACAGAAAAGTGAGGCTTGG	70	42273	42292	1059
472792	2303	2322	GCACAGAAAAGTGAGGCTTG	81	42274	42293	1060
472793	2305	2324	AGGCACAGAAAAGTGAGGCT	82	42276	42295	1061
472794	2306	2325	AAGGCACAGAAAAGTGAGGC	58	42277	42296	1062
472795	2308	2327	GGAAGGCACAGAAAAGTGAG	29	42279	42298	1063
472796	2309	2328	AGGAAGGCACAGAAAAGTGA	24	42280	42299	1064
472797	2311	2330	TCAGGAAGGCACAGAAAAGT	67	42282	42301	1065
472798	2312	2331	CTCAGGAAGGCACAGAAAAG	32	42283	42302	1066

472799	2314	2333	CCCTCAGGAAGGCACAGAAA	48	42285	42304	1067
472800	2315	2334	CCCCTCAGGAAGGCACAGAA	55	42286	42305	1068
472801	2316	2335	CCCCCTCAGGAAGGCACAGA	57	42287	42306	1069
472802	2318	2337	AACCCCCTCAGGAAGGCACA	57	42289	42308	1070
472803	2319	2338	CAACCCCCTCAGGAAGGCAC	63	42290	42309	1071
472804	2320	2339	CCAACCCCCTCAGGAAGGCA	66	42291	42310	1072
472805	2321	2340	CCCAACCCCCTCAGGAAGGC	67	42292	42311	1073
472806	2322	2341	GCCCAACCCCCTCAGGAAGG	1	42293	42312	1074
472807	2372	2391	CTCATCAAGAGATAACAGAA	47	42343	42362	1075
472808	2374	2393	ATCTCATCAAGAGATAACAG	56	42345	42364	1076
472809	2375	2394	GATCTCATCAAGAGATAACA	48	42346	42365	1077
472810	2377	2396	ATGATCTCATCAAGAGATAA	69	42348	42367	1078
472811	2398	2417	ACAAAAGTCTGACATGGTGC	82	42369	42388	1079
472812	2400	2419	ATACAAAAGTCTGACATGGT	74	42371	42390	1080
472813	2401	2420	TATACAAAAGTCTGACATGG	52	42372	42391	1081
472814	2403	2422	CATATACAAAAGTCTGACAT	45	42374	42393	1082
472815	2404	2423	GCATATACAAAAGTCTGACA	78	42375	42394	1083
472816	2405	2424	GGCATATACAAAAGTCTGAC	81	42376	42395	1084

Table 19

Inhibition of DGAT2 mRNA by 3-10-4 MOE gapmers targeting SEQ ID NOs: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
496047	1000	1016	CATTCTTGCCAGGCATG	42	38153	38169	1102
496048	1003	1019	CTGCATTCTTGCCAGGC	61	38156	38172	1103
496049	1004	1020	ACTGCATTCTTGCCAGG	43	38157	38173	1104
496050	1005	1021	GACTGCATTCTTGCCAG	31	38158	38174	1105
496051	1015	1031	TCCGCAGGGTGACTGCA	59	38168	38184	1106
496052	1016	1032	TTCCGCAGGGTGACTGC	60	38169	38185	1107
496053	1017	1033	GTTCCGCAGGGTGACTG	64	38170	38186	1108
496054	1096	1112	ACACTTCATTCTCTCCA	39	39143	39159	1109
496055	1097	1113	TACACTTCATTCTCTCC	39	39144	39160	1110
496056	1098	1114	GTACACTTCATTCTCTC	44	39145	39161	1111
496057	1099	1115	TGTACACTTCATTCTCT	36	39146	39162	1112
496058	1100	1116	TTGTACACTTCATTCTC	28	39147	39163	1113
496059	1101	1117	CTTGTACACTTCATTCT	35	39148	39164	1114
496060	1102	1118	GCTTGTACACTTCATTC	48	39149	39165	1115
496061	1103	1119	TGCTTGTACACTTCATT	40	39150	39166	1116
496062	1104	1120	CTGCTTGTACACTTCAT	63	39151	39167	1117
496063	1105	1121	CCTGCTTGTACACTTCA	62	39152	39168	1118

496064	1106	1122	ACCTGCTTGTACACTTC	47	39153	39169	1119
496065	1107	1123	CACCTGCTTGTACACTT	39	39154	39170	1120
496066	1108	1124	TCACCTGCTTGTACACT	43	39155	39171	1121
496067	1109	1125	ATCACCTGCTTGTACAC	23	39156	39172	1122
496068	1119	1135	CTCCTCGAAGATCACCT	9	39166	39182	1123
496069	1120	1136	CCTCCTCGAAGATCACC	26	39167	39183	1124
496070	1121	1137	CCCTCCTCGAAGATCAC	25	39168	39184	1125
496071	1357	1373	TGTCGAAGAGCTTCACC	36	41328	41344	1126
496072	1358	1374	TTGTCGAAGAGCTTCAC	7	41329	41345	1127
496073	1359	1375	CTTGTCGAAGAGCTTCA	22	41330	41346	1128
496074	1362	1378	GTGCTTGTCGAAGAGCT	44	41333	41349	1129
496075	1363	1379	TGTGCTTGTCGAAGAGC	33	41334	41350	1130
496076	1364	1380	TTGTGCTTGTCGAAGAG	10	41335	41351	1131
496077	1410	1426	TCAGTTCACCTCCAGGA	11	41381	41397	1132
496078	1411	1427	CTCAGTTCACCTCCAGG	11	41382	41398	1133
496079	1412	1428	GCTCAGTTCACCTCCAG	25	41383	41399	1134
496080	1413	1429	GGCTCAGTTCACCTCCA	56	41384	41400	1135
496081	1502	1518	TAACCCACAGACACCCA	61	41473	41489	1136
496082	1503	1519	ATAACCCACAGACACCC	55	41474	41490	1137
496083	1504	1520	AATAACCCACAGACACC	59	41475	41491	1138
496084	1627	1643	AGATTTAGCCACCACCT	17	41598	41614	1139
496085	1628	1644	CAGATTTAGCCACCACC	58	41599	41615	1140
496086	1629	1645	CCAGATTTAGCCACCAC	60	41600	41616	1141
496087	1630	1646	CCCAGATTTAGCCACCA	62	41601	41617	1142
496088	1631	1647	GCCCAGATTTAGCCACC	28	41602	41618	1143
496089	1853	1869	AGAGAAACTGGTCCTGC	0	41824	41840	1144
496090	1854	1870	CAGAGAAACTGGTCCTG	0	41825	41841	1145
496091	1855	1871	GCAGAGAAACTGGTCCT	42	41826	41842	1146
496092	2123	2139	CATGTCATCAGCCACCC	52	42094	42110	1147
496093	2124	2140	CCATGTCATCAGCCACC	62	42095	42111	1148
496094	2125	2141	TCCATGTCATCAGCCAC	60	42096	42112	1149
496095	2134	2150	TGTGCTGCATCCATGTC	53	42105	42121	1150
496096	2135	2151	CTGTGCTGCATCCATGT	21	42106	42122	1151
496097	2136	2152	TCTGTGCTGCATCCATG	33	42107	42123	1152
496098	2140	2156	TGAGTCTGTGCTGCATC	60	42111	42127	1153
496099	2141	2157	CTGAGTCTGTGCTGCAT	58	42112	42128	1154
496100	2142	2158	GCTGAGTCTGTGCTGCA	72	42113	42129	1155
496101	2305	2321	CACAGAAAAGTGAGGCT	53	42276	42292	1156
496102	2306	2322	GCACAGAAAAGTGAGGC	49	42277	42293	1157
496103	2307	2323	GGCACAGAAAAGTGAGG	28	42278	42294	1158
496104	2398	2414	AAAGTCTGACATGGTGC	65	42369	42385	1159
496105	2399	2415	AAAAGTCTGACATGGTG	54	42370	42386	1160

496106	2400	2416	CAAAAGTCTGACATGGT	39	42371	42387	1161
496036	474	490	GACCCACTGGAGCACTG	49	25600	25616	1091
496037	475	491	GGACCCACTGGAGCACT	76	25601	25617	1092
496038	476	492	AGGACCCACTGGAGCAC	72	25602	25618	1093
496039	553	569	CAGCGATGAGCCAGCAA	67	31120	31136	1094
496040	554	570	ACAGCGATGAGCCAGCA	67	31121	31137	1095
496041	555	571	CACAGCGATGAGCCAGC	78	31122	31138	1096
496042	556	572	GCACAGCGATGAGCCAG	61	31123	31139	1097
496043	557	573	AGCACAGCGATGAGCCA	70	31124	31140	1098
496044	558	574	GAGCACAGCGATGAGCC	48	31125	31141	1099
496045	998	1014	TTCTTGCCAGGCATGGA	39	38151	38167	1100
496046	999	1015	ATTCTTGCCAGGCATGG	31	38152	38168	1101
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	68	32431	32450	425
496107	n/a	n/a	CAGGGCCCTTTCCAGAA	34	10044	10060	1085
496108	n/a	n/a	ACAGGGCCCTTTCCAGA	39	10045	10061	1086
496109	n/a	n/a	CACAGGGCCCTTTCCAG	39	10046	10062	1087
496110	n/a	n/a	CGAATATCCCTAATAAC	14	10210	10226	1088
496111	n/a	n/a	TCGAATATCCCTAATAA	9	10211	10227	1089
496112	n/a	n/a	CTCGAATATCCCTAATA	17	10212	10228	1090

Table 20

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
483876	14332	14351	GTGAGATCCCCAGAGAGGAA	26	1162
483877	14337	14356	AAGGAGTGAGATCCCCAGAG	34	1163
483878	14360	14379	TTCTGACCCTATTTTCCAGA	52	1164
483879	14385	14404	CCCTCCATCCTTGAGAATCT	76	1165
483880	14427	14446	ATGTCACAAGTTCACAAACA	49	1166
483881	14432	14451	CATGAATGTCACAAGTTCAC	38	1167
483882	14437	14456	ACTAACATGAATGTCACAAG	35	1168
483883	14442	14461	CAAGGACTAACATGAATGTC	0	1169
483884	14447	14466	AATGACAAGGACTAACATGA	24	1170
483885	14452	14471	GGACAAATGACAAGGACTAA	12	1171
483886	14457	14476	ACACAGGACAAATGACAAGG	62	1172
483887	14462	14481	GTGTAACACAGGACAAATGA	82	1173
483888	14467	14486	TGAATGTGTAACACAGGACA	75	1174
483889	14503	14522	CAGGGTCTGCCACTCTCTAC	88	1175
483890	14508	14527	TAGAGCAGGGTCTGCCACTC	85	1176
483891	14532	14551	TCAGTGAAGCCTTCCTGGAT	31	1177
483892	14537	14556	CTTCCTCAGTGAAGCCTTCC	72	1178

483893	14542	14561	AGTCCCTTCCTCAGTGAAGC	59	1179
483894	14547	14566	CCCCAAGTCCCTTCCTCAGT	51	1180
483895	14648	14667	CACAGTCATCTTGTGTACAT	93	1181
483896	14653	14672	CTCTGCACAGTCATCTTGTG	59	1182
483897	14658	14677	GATCACTCTGCACAGTCATC	83	1183
483898	14663	14682	GCTCAGATCACTCTGCACAG	94	1184
483899	14668	14687	TCATTGCTCAGATCACTCTG	71	1185
483900	14673	14692	TCCTGTCATTGCTCAGATCA	81	1186
483901	14678	14697	GTCTTTCCTGTCATTGCTCA	86	1187
483902	14715	14734	TCAGGGTGATCAAGCTCCCC	70	1188
483903	14720	14739	TGACCTCAGGGTGATCAAGC	75	1189
483904	14725	14744	TTCCCTGACCTCAGGGTGAT	49	1190
483905	14730	14749	AAGACTTCCCTGACCTCAGG	46	1191
483906	14735	14754	CCAGGAAGACTTCCCTGACC	65	1192
483907	14740	14759	CTCTTCCAGGAAGACTTCCC	68	1193
483908	14745	14764	GTCACCTCTTCCAGGAAGAC	94	1194
483909	14750	14769	TGAATGTCACCTCTTCCAGG	84	1195
483910	14755	14774	CGGACTGAATGTCACCTCTT	95	1196
483911	14760	14779	AGATCCGGACTGAATGTCAC	79	1197
483912	14765	14784	TTTCCAGATCCGGACTGAAT	79	1198
483913	14770	14789	TCATCTTTCCAGATCCGGAC	95	1199
483914	14775	14794	TCTATTCATCTTTCCAGATC	55	1200
483915	14802	14821	TGAATGTTCTTGCCTGTCTT	48	1201
483916	14807	14826	GTACCTGAATGTTCTTGCCT	85	1202
483917	14812	14831	TTCCTGTACCTGAATGTTCT	71	1203
483918	14852	14871	TGCCTCTCCCATCCAAATCT	75	1204
483919	14882	14901	GTTGGTCACTCAGAGGCCCT	86	1205
483920	14953	14972	ACAGGCCTGGATCCAGCATC	77	1206
483921	14986	15005	TCTTCCTCCTGCTGCAGACA	86	1207
483922	14991	15010	TCAAGTCTTCCTCCTGCTGC	68	1208
483923	14996	15015	AGCTCTCAAGTCTTCCTCCT	87	1209
483924	15001	15020	CCATGAGCTCTCAAGTCTTC	82	1210
483925	15006	15025	CTTTCCCATGAGCTCTCAAG	68	1211
483926	15011	15030	GGCTCCTTTCCCATGAGCTC	77	1212
483927	15016	15035	CACCAGGCTCCTTTCCCATG	84	1213
483928	15021	15040	AACTGCACCAGGCTCCTTTC	70	1214
483929	15026	15045	AAACTAACTGCACCAGGCTC	65	1215
483930	15031	15050	CCAATAAACTAACTGCACCA	36	1216
483931	15036	15055	GGAGGCCAATAAACTAACTG	37	1217
483932	15041	15060	GTGCTGGAGGCCAATAAACT	60	1218
483933	15046	15065	TCAAAGTGCTGGAGGCCAAT	66	1219
483934	15073	15092	AGCCAGCAGCTCCATACCAG	70	1220

483935	15078	15097	AAATCAGCCAGCAGCTCCAT	56	1221
483936	15083	15102	CCCTCAAATCAGCCAGCAGC	62	1222
483937	15088	15107	TGAGGCCCTCAAATCAGCCA	52	1223
483938	15093	15112	GCCCATGAGGCCCTCAAATC	44	1224
483939	15098	15117	GCCCTGCCCATGAGGCCCTC	44	1225
483940	15103	15122	CCTGGGCCCTGCCCATGAGG	28	1226
483941	15144	15163	GCCAAGCAGGAGCTGGACAG	35	1227
483942	15178	15197	TAGTGGCTTGCTGAGGCTGC	67	1228
483943	15183	15202	AAGGGTAGTGGCTTGCTGAG	31	1229
483944	15188	15207	TAAGGAAGGGTAGTGGCTTG	5	1230
483945	15199	15218	GAGACTGAGGGTAAGGAAGG	31	1231
483946	15204	15223	ATGAGGAGACTGAGGGTAAG	41	1232
483947	15209	15228	CATAGATGAGGAGACTGAGG	42	1233
483948	15214	15233	CATTTCATAGATGAGGAGAC	71	1234
483949	15219	15238	TTGCTCATTTCATAGATGAG	78	1235
483950	15224	15243	CACTTTTGCTCATTTCATAG	74	1236
483951	15247	15266	ATAATCTGCACAGGTTCTTA	47	1237
483952	15252	15271	GCACCATAATCTGCACAGGT	92	1238
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	87	425

Table 21

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
483953	17938	17957	GGGTCTAGGTGAGTGAGAAA	42	1239
483954	17960	17979	ATCTGGACCTAATGTCTGCC	71	1240
483955	17965	17984	GGCCCATCTGGACCTAATGT	41	1241
483956	17970	17989	ACCTGGGCCCATCTGGACCT	61	1242
483957	18042	18061	CTCTTGGGCTCCTTGAGGCA	33	1243
483958	18047	18066	ACAGCCTCTTGGGCTCCTTG	33	1244
483959	18052	18071	TGTGAACAGCCTCTTGGGCT	49	1245
483960	18057	18076	AGAGGTGTGAACAGCCTCTT	0	1246
483961	18078	18097	GCCAGAAAGATGCCAGCTAA	67	1247
483962	18083	18102	AGAGAGCCAGAAAGATGCCA	57	1248
483963	18113	18132	AAAAGGGCCAGAATGTCTGG	24	1249
483964	18136	18155	TAAGGAATCTAAATAACTTA	21	1250
483965	18141	18160	TGTCATAAGGAATCTAAATA	16	1251
483966	18146	18165	AGGATTGTCATAAGGAATCT	54	1252
483967	18151	18170	AATCCAGGATTGTCATAAGG	59	1253
483968	18156	18175	GCTTTAATCCAGGATTGTCA	80	1254

483969	18161	18180	CCTTAGCTTTAATCCAGGAT	86	1255
483970	18166	18185	GTCCTCCTTAGCTTTAATCC	80	1256
483971	18171	18190	TCAGTGTCCTCCTTAGCTTT	65	1257
483972	18176	18195	GGGACTCAGTGTCCTCCTTA	81	1258
483973	18181	18200	TCCCTGGGACTCAGTGTCCT	77	1259
483974	18220	18239	GATTCTTACCTGCAATGAGA	36	1260
483975	18225	18244	GCTCTGATTCTTACCTGCAA	70	1261
483976	18230	18249	CCCTGGCTCTGATTCTTACC	60	1262
483977	18235	18254	TCAAACCCTGGCTCTGATTC	70	1263
483978	18240	18259	AGGATTCAAACCCTGGCTCT	72	1264
483979	18286	18305	ATGCCTGCCCTGCCTAGGAA	75	1265
483980	18291	18310	AAATAATGCCTGCCCTGCCT	37	1266
483981	18296	18315	GGGTAAAATAATGCCTGCCC	65	1267
483982	18301	18320	TTGATGGGTAAAATAATGCC	9	1268
483983	18306	18325	CCTGTTTGATGGGTAAAATA	60	1269
483984	18311	18330	CCTCTCCTGTTTGATGGGTA	89	1270
483985	18316	18335	GGTGTCCTCTCCTGTTTGAT	78	1271
483986	18321	18340	GCCTCGGTGTCCTCTCCTGT	84	1272
483987	18326	18345	AGTAAGCCTCGGTGTCCTCT	87	1273
483988	18331	18350	TACCAAGTAAGCCTCGGTGT	87	1274
483989	18336	18355	TTAATTACCAAGTAAGCCTC	74	1275
483990	18369	18388	TTCATAAAAAGTAAAGATCT	51	1276
483991	18374	18393	AGAGCTTCATAAAAAGTAAA	0	1277
483992	18379	18398	AGCCAAGAGCTTCATAAAAA	87	1278
483993	18417	18436	TCACCAGATTGTTGTGGGAA	84	1279
483994	18422	18441	CTACCTCACCAGATTGTTGT	75	1280
483995	18427	18446	AATACCTACCTCACCAGATT	63	1281
483996	18432	18451	GGGCTAATACCTACCTCACC	81	1282
483997	18450	18469	TTCCTCATCTATACAGTGGG	85	1283
483998	18455	18474	TCAGCTTCCTCATCTATACA	52	1284
483999	18460	18479	AAGCTTCAGCTTCCTCATCT	35	1285
484000	18465	18484	TATACAAGCTTCAGCTTCCT	44	1286
484001	18470	18489	CTTCCTATACAAGCTTCAGC	77	1287
484002	18475	18494	AGTCACTTCCTATACAAGCT	64	1288
484003	18513	18532	AGAACCTGGCCTCTAACTCG	42	1289
484004	18581	18600	CATACTGGCATCTGGCAGGG	84	1290
484005	18586	18605	ACCTCCATACTGGCATCTGG	66	1291
484006	18591	18610	ACCTCACCTCCATACTGGCA	79	1292
484007	18747	18766	ATGAAGAAAAATAATTTGGG	0	1293
484008	18821	18840	TTAACTTCTGCTGAGGGAGA	63	1294
484009	18826	18845	GATGCTTAACTTCTGCTGAG	68	1295
484010	18831	18850	GTTAGGATGCTTAACTTCTG	78	1296

484011	18836	18855	GTTAAGTTAGGATGCTTAAC	65	1297
484012	18869	18888	ATAGGCCTGGATGCCCAAGT	78	1298
	20779	20798			
484013	18880	18899	CAGAGGCAGCTATAGGCCTG	69	1299
	20790	20809			
484014	18885	18904	TGCCTCAGAGGCAGCTATAG	30	1300
484015	18890	18909	TGTCCTGCCTCAGAGGCAGC	65	1301
484016	18895	18914	GATGATGTCCTGCCTCAGAG	61	1302
484017	18900	18919	CAGCAGATGATGTCCTGCCT	85	1303
484018	18982	19001	GGGACAGAGCTAAGACCCAA	58	1304
484019	19013	19032	GTCAAAGGTGGCTTCCTGGG	74	1305
484020	19018	19037	GAGTAGTCAAAGGTGGCTTC	78	1306
484021	19023	19042	GGAATGAGTAGTCAAAGGTG	27	1307
484022	19028	19047	AAGTTGGAATGAGTAGTCAA	14	1308
484023	19041	19060	GCTGAGAATAAAGAAGTTGG	55	1309
484024	19046	19065	TAGAAGCTGAGAATAAAGAA	36	1310
484025	19051	19070	TGAAATAGAAGCTGAGAATA	20	1311
484026	19112	19131	GGAGTTCTAATGAGGCAGAC	50	1312
484027	19117	19136	TGCAGGGAGTTCTAATGAGG	53	1313
484028	19122	19141	AGCCTTGCAGGGAGTTCTAA	62	1314
484029	19127	19146	AACAAAGCCTTGCAGGGAGT	30	1315
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	76	425

Table 22

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
484030	22439	22458	ATGGCAAGTGCTTCCGTGGG	79	1316
484031	22444	22463	ACCAAATGGCAAGTGCTTCC	82	1317
484032	22449	22468	CAAATACCAAATGGCAAGTG	34	1318
484033	22474	22493	CTGCAAGGTGGTGAGCTCTA	28	1319
484034	22513	22532	CCTCACTTCCCATCTGCCTG	24	1320
484035	22518	22537	TGAACCCTCACTTCCCATCT	14	1321
484036	22523	22542	CCAAGTGAACCCTCACTTCC	12	1322
484037	22528	22547	GTCTACCAAGTGAACCCTCA	20	1323
484038	22533	22552	ATGCAGTCTACCAAGTGAAC	39	1324
484039	22538	22557	GGGAAATGCAGTCTACCAAG	55	1325
484040	22543	22562	CAAGTGGGAAATGCAGTCTA	53	1326
484041	22548	22567	GCCAACAAGTGGGAAATGCA	85	1327
484042	22573	22592	CCAACTACCGCCCACAGCTC	43	1328
484043	22578	22597	CAGCCCCAACTACCGCCCAC	29	1329

484044	22583	22602	TTATCCAGCCCCAACTACCG	10	1330
484045	22588	22607	CTGCCTTATCCAGCCCCAAC	43	1331
484046	22593	22612	TCACCCTGCCTTATCCAGCC	51	1332
484047	22713	22732	TCTTGTTCAACCCTCACCCC	45	1333
484048	22766	22785	CTTATTAGGTGTCTTAAAAT	43	1334
484049	22771	22790	CTAAGCTTATTAGGTGTCTT	85	1335
484050	22776	22795	CTCTGCTAAGCTTATTAGGT	69	1336
484051	22820	22839	ACTGAGAAGACCTAAAAATT	0	1337
484052	22825	22844	AAACAACTGAGAAGACCTAA	45	1338
484053	22830	22849	AACTGAAACAACTGAGAAGA	32	1339
484054	22835	22854	TCCCCAACTGAAACAACTGA	65	1340
484055	22841	22860	GACATATCCCCAACTGAAAC	67	1341
484056	22846	22865	CTGATGACATATCCCCAACT	71	1342
484057	22851	22870	TTTCACTGATGACATATCCC	69	1343
484058	22856	22875	AGAAATTTCACTGATGACAT	56	1344
484059	22861	22880	AGTATAGAAATTTCACTGAT	18	1345
484060	22866	22885	GGAGGAGTATAGAAATTTCA	53	1346
484061	22871	22890	TTGGAGGAGGAGTATAGAAA	48	1347
484062	22876	22895	GCAGCTTGGAGGAGGAGTAT	32	1348
484063	22881	22900	CCCATGCAGCTTGGAGGAGG	68	1349
484064	22886	22905	CAGCCCCCATGCAGCTTGGA	84	1350
484065	22891	22910	AGGGCCAGCCCCCATGCAGC	67	1351
484066	22916	22935	TTATCTAGCTCCCTACCTTG	57	1352
484067	22968	22987	TGAAGCCAGTGGTTTGAGGG	30	1353
484068	22992	23011	TGCTTCCCGTTGCAGACAGG	34	1354
484069	23095	23114	GTCCAAACACTCAGGTAGGG	72	1355
484070	23100	23119	CTTCAGTCCAAACACTCAGG	85	1356
484071	23128	23147	TTAAGTCTGAGAAACACCAC	77	1357
484072	23133	23152	GGTGATTAAGTCTGAGAAAC	64	1358
484073	23138	23157	CCCCAGGTGATTAAGTCTGA	73	1359
484074	23143	23162	AAGATCCCCAGGTGATTAAG	26	1360
484075	23148	23167	TTAACAAGATCCCCAGGTGA	22	1361
484076	23154	23173	TGCATTTTAACAAGATCCCC	0	1362
484077	23159	23178	AAATCTGCATTTTAACAAGA	20	1363
484078	23164	23183	AATCAAAATCTGCATTTTAA	40	1364
484079	23169	23188	TACTGAATCAAAATCTGCAT	53	1365
484080	23174	23193	GGATTTACTGAATCAAAATC	31	1366
484081	23179	23198	AGACTGGATTTACTGAATCA	65	1367
484082	23184	23203	GCTCCAGACTGGATTTACTG	72	1368
484083	23232	23251	AGCAGCATCAGCATCACCTG	79	1369
484084	23237	23256	GGAACAGCAGCATCAGCATC	39	1370
484085	23242	23261	GTCTGGGAACAGCAGCATCA	90	1371

484086	23271	23290	TACTCTAGCACTTTCCTACT	53	1372
484087	23276	23295	AAATGTACTCTAGCACTTTC	41	1373
484088	23281	23300	AGACAAAATGTACTCTAGCA	58	1374
484089	23305	23324	GGCTGGATGCCCTGGCTAGA	79	1375
484090	23310	23329	AGGCAGGCTGGATGCCCTGG	55	1376
484091	23315	23334	ATCTGAGGCAGGCTGGATGC	59	1377
484092	23417	23436	ATCTTCCAGCAGCTGGCTCT	28	1378
484093	23422	23441	AAGTCATCTTCCAGCAGCTG	41	1379
484094	23427	23446	TGGACAAGTCATCTTCCAGC	85	1380
484095	23470	23489	AAGTCCAAGCACAGGCTTGA	44	1381
484096	23475	23494	AAGTGAAGTCCAAGCACAGG	39	1382
484097	23480	23499	GAGGGAAGTGAAGTCCAAGC	63	1383
484098	23547	23566	TCCTTGAGGGTCTCATAACC	66	1384
484099	23552	23571	GCTTATCCTTGAGGGTCTCA	84	1385
484100	23557	23576	CACATGCTTATCCTTGAGGG	82	1386
484101	23562	23581	TTCATCACATGCTTATCCTT	75	1387
484102	23567	23586	ATGAGTTCATCACATGCTTA	78	1388
484103	23597	23616	TCAACCTGCCCAGCAGTGGG	62	1389
484104	23641	23660	CTCTGTACACAGGACACAGT	70	1390
484105	23646	23665	AAAGGCTCTGTACACAGGAC	79	1391
484106	23651	23670	AGTGCAAAGGCTCTGTACAC	66	1392
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	86	425

Table 23

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	84	425
484107	26390	26409	GGCAACCTAAGGAGTGAGGG	71	1393
484108	26395	26414	TGGATGGCAACCTAAGGAGT	40	1394
484109	26400	26419	TGGCCTGGATGGCAACCTAA	57	1395
484110	26479	26498	GCTATGCTGAGAGCACAGGG	79	1396
484111	26484	26503	TACCTGCTATGCTGAGAGCA	71	1397
484112	26489	26508	GAAGCTACCTGCTATGCTGA	46	1398
484113	26494	26513	CTGAGGAAGCTACCTGCTAT	36	1399
484114	26516	26535	CAGGTTCATCTGCCTTGACG	70	1400
484115	26521	26540	TGGAGCAGGTTCATCTGCCT	83	1401
484116	26526	26545	TGCTCTGGAGCAGGTTCATC	81	1402
484117	26531	26550	TGTGATGCTCTGGAGCAGGT	80	1403
484118	26536	26555	CACTCTGTGATGCTCTGGAG	74	1404
484119	26541	26560	GAATGCACTCTGTGATGCTC	68	1405

484120	26566	26585	CAGAGGGACTGGCTCACAGG	21	1406
484121	26590	26609	TACAGTCCCGAAGAGTGGGT	38	1407
484122	26595	26614	GCCTATACAGTCCCGAAGAG	51	1408
484123	26600	26619	TACCAGCCTATACAGTCCCG	60	1409
484124	26605	26624	TCCCCTACCAGCCTATACAG	59	1410
484125	26610	26629	GATGATCCCCTACCAGCCTA	68	1411
484126	26615	26634	GTCCTGATGATCCCCTACCA	80	1412
484127	26620	26639	GGTAAGTCCTGATGATCCCC	86	1413
484128	26625	26644	GACATGGTAAGTCCTGATGA	54	1414
484129	26630	26649	GCACTGACATGGTAAGTCCT	87	1415
484130	26635	26654	GCTCAGCACTGACATGGTAA	85	1416
484131	26640	26659	CAGCTGCTCAGCACTGACAT	80	1417
484132	26645	26664	AAGGACAGCTGCTCAGCACT	60	1418
484133	26711	26730	GTGAAGTTCTATCCCTTGGC	89	1419
484134	26716	26735	CACCTGTGAAGTTCTATCCC	69	1420
484135	26721	26740	TTTCTCACCTGTGAAGTTCT	79	1421
484136	26755	26774	AGCAGGTAGTTGATGAACCT	70	1422
484137	26778	26797	TGCCATTTAATGAGCTTCAC	86	1423
484138	26783	26802	AACTCTGCCATTTAATGAGC	55	1424
484139	26788	26807	ATCCCAACTCTGCCATTTAA	81	1425
484140	26811	26830	GAATGCACTGAGTTTCTGCT	89	1426
484141	26849	26868	CACTAATTCTGGGCTTCCAG	87	1427
484142	26854	26873	CAGTTCACTAATTCTGGGCT	79	1428
484143	26859	26878	AGCCCCAGTTCACTAATTCT	52	1429
484144	26864	26883	GTTTCAGCCCCAGTTCACTA	54	1430
484145	26869	26888	TGGCTGTTTCAGCCCCAGTT	70	1431
484146	26874	26893	AAGACTGGCTGTTTCAGCCC	79	1432
484147	26879	26898	AGGTGAAGACTGGCTGTTTC	76	1433
484148	26884	26903	CCTAAAGGTGAAGACTGGCT	91	1434
484149	26889	26908	TTGGGCCTAAAGGTGAAGAC	64	1435
484150	26894	26913	CGTTCTTGGGCCTAAAGGTG	57	1436
484151	26899	26918	AAGCCCGTTCTTGGGCCTAA	23	1437
484152	26926	26945	TTAAGGGTTCATGGATCCCC	66	1438
484153	26931	26950	TAATTTTAAGGGTTCATGGA	29	1439
484154	27005	27024	CTGTAAGACTTTGAGGACAG	60	1440
484155	27010	27029	TGTCCCTGTAAGACTTTGAG	43	1441
484156	27046	27065	GTTCTTCCAACCAGTGTTTG	84	1442
484157	27051	27070	GCTCAGTTCTTCCAACCAGT	94	1443
484158	27056	27075	AGTTTGCTCAGTTCTTCCAA	85	1444
484159	27061	27080	TGTTTAGTTTGCTCAGTTCT	68	1445
484160	27101	27120	AAATGCAAGCCATGTTAGGG	54	1446
484161	27106	27125	TGGCCAAATGCAAGCCATGT	72	1447

484162	27111	27130	GTAAGTGGCCAAATGCAAGC	67	1448
484163	27116	27135	TTCTAGTAAGTGGCCAAATG	57	1449
484164	27174	27193	CAGGCCTCCACTTCCTTTTT	66	1450
484165	27211	27230	TCTTCTCATGTGACCCCAAG	69	1451
484166	27216	27235	TACTTTCTTCTCATGTGACC	59	1452
484167	27221	27240	CCCAGTACTTTCTTCTCATG	85	1453
484168	27226	27245	CTGGTCCCAGTACTTTCTTC	63	1454
484169	27231	27250	TTGTCCTGGTCCCAGTACTT	86	1455
484170	27236	27255	GGTTCTTGTCCTGGTCCCAG	90	1456
484171	27241	27260	CCCTGGGTTCTTGTCCTGGT	82	1457
484172	27246	27265	GGAGTCCCTGGGTTCTTGTC	74	1458
484173	27251	27270	AGGCTGGAGTCCCTGGGTTC	53	1459
484174	27256	27275	CTGGGAGGCTGGAGTCCCTG	55	1460
484175	27352	27371	ACCAGCCAGGCCCAGACCCA	34	1461
484176	27357	27376	TCCCTACCAGCCAGGCCCAG	17	1462
484177	27362	27381	TCAGCTCCCTACCAGCCAGG	47	1463
484178	27367	27386	GCTGCTCAGCTCCCTACCAG	74	1464
484179	27372	27391	TACAAGCTGCTCAGCTCCCT	67	1465
484180	27377	27396	TGTTCTACAAGCTGCTCAGC	73	1466
484181	27382	27401	GCTGGTGTTCTACAAGCTGC	92	1467
484182	27387	27406	CGTGAGCTGGTGTTCTACAA	80	1468
484183	27437	27456	TCTGATCAATTATTAACCTA	21	1469

Table 24

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
484184	29480	29499	TGGATGTAGACTCTCCATGA	61	1470
484185	29485	29504	AAGGCTGGATGTAGACTCTC	72	1471
484186	29490	29509	AAGATAAGGCTGGATGTAGA	28	1472
484187	29495	29514	GGGAGAAGATAAGGCTGGAT	50	1473
484188	29500	29519	CCCATGGGAGAAGATAAGGC	62	1474
484189	29505	29524	GGTTTCCCATGGGAGAAGAT	50	1475
484190	29538	29557	CATGCTCTCTTCTCACCATG	71	1476
484191	29543	29562	GATGTCATGCTCTCTTCTCA	66	1477
484192	29548	29567	CTCTGGATGTCATGCTCTCT	82	1478
484193	29570	29589	CCAGGTGCTGTAGGCTGCCT	84	1479
484194	29575	29594	TGGTCCCAGGTGCTGTAGGC	75	1480
484195	29580	29599	CCTGGTGGTCCCAGGTGCTG	62	1481
484196	29607	29626	AGGCCAACCCTTGCTGTGTG	63	1482
484197	29612	29631	AAGGGAGGCCAACCCTTGCT	60	1483

484198	29635	29654	TAGGACTTTTTCCACTGCCC	72	1484
484199	29640	29659	CCTTCTAGGACTTTTTCCAC	41	1485
484200	29663	29682	GTTTGGTGGGAGAAGCATGG	25	1486
484201	29668	29687	CTCATGTTTGGTGGGAGAAG	45	1487
484202	29673	29692	AGGTACTCATGTTTGGTGGG	77	1488
484203	29678	29697	GCAGCAGGTACTCATGTTTG	86	1489
484204	29683	29702	CAAGGGCAGCAGGTACTCAT	81	1490
484205	29762	29781	ACATATCATCTCTTGCCTGT	59	1491
484206	29767	29786	TATCTACATATCATCTCTTG	31	1492
484207	29772	29791	CATACTATCTACATATCATC	10	1493
484208	29777	29796	AATATCATACTATCTACATA	21	1494
484209	29782	29801	TCCCCAATATCATACTATCT	84	1495
484210	29804	29823	ACCTCAGCTCTTCAAGAAGT	61	1496
484211	29809	29828	CTCAGACCTCAGCTCTTCAA	76	1497
484212	29814	29833	CCTATCTCAGACCTCAGCTC	58	1498
484213	29819	29838	TAAGGCCTATCTCAGACCTC	66	1499
484214	29824	29843	ACCTTTAAGGCCTATCTCAG	4	1500
484215	29829	29848	ACCCAACCTTTAAGGCCTAT	86	1501
484216	29834	29853	TTTTTACCCAACCTTTAAGG	53	1502
484217	29839	29858	TCCATTTTTTACCCAACCTT	87	1503
484218	29844	29863	CTCTTTCCATTTTTTACCCA	80	1504
484219	29849	29868	CTTCTCTCTTTCCATTTTTT	75	1505
484220	29854	29873	CAGGGCTTCTCTCTTTCCAT	83	1506
484221	29859	29878	CTCAGCAGGGCTTCTCTCTT	66	1507
484222	29864	29883	CTGCCCTCAGCAGGGCTTCT	0	1508
484223	29869	29888	ACTAGCTGCCCTCAGCAGGG	28	1509
484224	29902	29921	TTGTGCCATGCCTGCTTTAT	39	1510
484225	30358	30377	GCAGAGCCCATCAGCCTCCC	44	1511
484226	30363	30382	AAAGCGCAGAGCCCATCAGC	48	1512
484227	30407	30426	CTGGCTCCCTTCCAACATAA	64	1513
484228	30412	30431	GAGGGCTGGCTCCCTTCCAA	41	1514
484229	30417	30436	AGGAGGAGGGCTGGCTCCCT	12	1515
484230	30422	30441	TGCCCAGGAGGAGGGCTGGC	4	1516
484231	30483	30502	TAGGCTTTAGAAATTCACCA	91	1517
484232	30514	30533	CAGGTCTGACTCTACAGTCC	78	1518
484233	30519	30538	AAACACAGGTCTGACTCTAC	55	1519
484234	30524	30543	GATTCAAACACAGGTCTGAC	62	1520
484235	30529	30548	GCCAGGATTCAAACACAGGT	82	1521
484236	30534	30553	GCAGAGCCAGGATTCAAACA	55	1522
484237	30539	30558	CAGTGGCAGAGCCAGGATTC	66	1523
484238	30544	30563	CAGGACAGTGGCAGAGCCAG	27	1524
484239	30549	30568	CCCAGCAGGACAGTGGCAGA	39	1525

484240	30554	30573	GGTCACCCAGCAGGACAGTG	65	1526
484241	30559	30578	CCCAAGGTCACCCAGCAGGA	76	1527
484242	30564	30583	ACTTGCCCAAGGTCACCCAG	68	1528
484243	30569	30588	AGATAACTTGCCCAAGGTCA	62	1529
484244	30610	30629	TTGCCCCATTTTAGAGATAA	26	1530
484245	30615	30634	TGACTTTGCCCCATTTTAGA	0	1531
484246	30621	30640	GCAGGGTGACTTTGCCCCAT	35	1532
484247	30644	30663	TGAGCCACTGTCTCAAGTGT	42	1533
484248	30669	30688	TGCCTCTGCATCTCAAGACT	75	1534
484249	30674	30693	CCCAGTGCCTCTGCATCTCA	83	1535
484250	30712	30731	CCAGCCCAGACACTGTGGAT	60	1536
484251	30717	30736	AGCACCCAGCCCAGACACTG	59	1537
484252	30749	30768	TACTGTCCCCTCCTTGTGTG	16	1538
484253	30773	30792	TTCAGCTTCTTGTGAAGCTG	0	1539
484254	30778	30797	TAGGCTTCAGCTTCTTGTGA	25	1540
484255	30783	30802	GGAGATAGGCTTCAGCTTCT	58	1541
484256	30788	30807	CCAAAGGAGATAGGCTTCAG	49	1542
484257	30887	30906	AGCAGATTCCTGGGACAAGA	62	1543
484258	30922	30941	GAGAAATAGCTACAGGAATG	36	1544
484259	30927	30946	ACCCTGAGAAATAGCTACAG	22	1545
484260	30932	30951	CACAAACCCTGAGAAATAGC	0	1546
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	88	425

Table 25

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
484261	32253	32272	AAGACTGGGCTTAGGCTAAG	50	1547
484262	32303	32322	TCAGGAAAAGGAGAAGGAAC	36	1548
484263	32336	32355	AGCTTCAAATTTTCTGCAGT	72	1549
484264	32399	32418	AGTTTCTTTACCTCCAAAAT	48	1550
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	87	425
423463	32432	32451	AGCCTGGACAAGTCCTGCCC	90	467
423464	32433	32452	CAGCCTGGACAAGTCCTGCC	86	468
423465	32434	32453	GCAGCCTGGACAAGTCCTGC	74	469
484265	32436	32455	ATGCAGCCTGGACAAGTCCT	74	1551
484266	32441	32460	AGACTATGCAGCCTGGACAA	63	1552
484267	32446	32465	ATACTAGACTATGCAGCCTG	82	1553
484268	32451	32470	CCATCATACTAGACTATGCA	87	1554
484269	32456	32475	TGTTGCCATCATACTAGACT	83	1555
484270	32461	32480	TGCAATGTTGCCATCATACT	89	1556

484271	32466	32485	GTGGTTGCAATGTTGCCATC	90	1557
484272	32471	32490	GGATGGTGGTTGCAATGTTG	55	1558
484273	32476	32495	AGCCTGGATGGTGGTTGCAA	86	1559
484274	32481	32500	CAATAAGCCTGGATGGTGGT	79	1560
484275	32486	32505	GAATTCAATAAGCCTGGATG	66	1561
484276	32510	32529	TCAGTGGAAAAGAACCTGGG	71	1562
484277	32515	32534	GGAAATCAGTGGAAAAGAAC	55	1563
484278	32520	32539	CAGTAGGAAATCAGTGGAAA	54	1564
484279	32525	32544	ACAGGCAGTAGGAAATCAGT	51	1565
484280	32530	32549	GAGAAACAGGCAGTAGGAAA	56	1566
484281	32586	32605	GACCCAGGAAGCTGGAATCA	66	1567
484282	32591	32610	AGGGAGACCCAGGAAGCTGG	60	1568
484283	32619	32638	ACTGAGATCTCCAGCAGCAA	90	1569
484284	32645	32664	AATGGAGTGACAGGGCAGGA	82	1570
484285	32670	32689	AGGGAGCAATGGTGGCAGGT	71	1571
484286	32675	32694	TGGACAGGGAGCAATGGTGG	46	1572
484287	32680	32699	TGCACTGGACAGGGAGCAAT	36	1573
484288	32685	32704	AGCCCTGCACTGGACAGGGA	41	1574
484289	32706	32725	TTGTGTCCCCATGCCCAGCA	58	1575
484290	32711	32730	CTGACTTGTGTCCCCATGCC	78	1576
484291	32716	32735	CAGGGCTGACTTGTGTCCCC	52	1577
484292	32752	32771	ACAAAGTCTATCAGGATGCA	83	1578
484293	32757	32776	AAGTGACAAAGTCTATCAGG	83	1579
484294	32781	32800	GTCTGCCCATGGCCCCATGG	31	1580
484295	32786	32805	AGAAAGTCTGCCCATGGCCC	45	1581
484296	32791	32810	GCTTGAGAAAGTCTGCCCAT	35	1582
484297	32796	32815	AGCAGGCTTGAGAAAGTCTG	18	1583
484298	32801	32820	GGCTCAGCAGGCTTGAGAAA	60	1584
484299	32806	32825	GATGAGGCTCAGCAGGCTTG	68	1585
484300	32811	32830	TTGCAGATGAGGCTCAGCAG	48	1586
484301	32816	32835	CCATTTTGCAGATGAGGCTC	80	1587
484302	32821	32840	CAGCTCCATTTTGCAGATGA	77	1588
484303	32878	32897	AGAACAGTCTATCATCACTC	34	1589
484304	32899	32918	GAGGTGAGAGAGAAAGCAGA	11	1590
484305	32904	32923	CCCCTGAGGTGAGAGAGAAA	46	1591
484306	32909	32928	CCTGGCCCCTGAGGTGAGAG	38	1592
484307	32914	32933	TGGAGCCTGGCCCCTGAGGT	12	1593
484308	32919	32938	AACACTGGAGCCTGGCCCCT	18	1594
484309	32924	32943	CAGAGAACACTGGAGCCTGG	35	1595
484310	32929	32948	GGCAACAGAGAACACTGGAG	62	1596
484311	32934	32953	ACAGTGGCAACAGAGAACAC	0	1597
484312	32940	32959	CAGGCCACAGTGGCAACAGA	3	1598

484313	32945	32964	AGGACCAGGCCACAGTGGCA	31	1599
484314	32950	32969	TCCAGAGGACCAGGCCACAG	22	1600
484315	32973	32992	GGGCTACTGGCCTCCTGGAG	47	1601
484316	33038	33057	CAAAGGACACCTGCCTGTCC	46	1602
484317	33043	33062	GATAGCAAAGGACACCTGCC	48	1603
484318	33065	33084	TCTTTTGGAAGGGTGGAGAT	16	1604
484319	33070	33089	TTGGTTCTTTTGGAAGGGTG	62	1605
484320	33096	33115	GATGTGAGAAGGACACAGGG	79	1606
484321	33101	33120	ACAGAGATGTGAGAAGGACA	77	1607
484322	33106	33125	TTGGAACAGAGATGTGAGAA	71	1608
484323	33111	33130	ACTTCTTGGAACAGAGATGT	69	1609
484324	33161	33180	GCCCTCACAGGGCCAGGTTG	77	1610
484325	33170	33189	CCCCAGGGAGCCCTCACAGG	68	1611
484326	33175	33194	TAGTGCCCCAGGGAGCCCTC	51	1612
484327	33180	33199	TGTCCTAGTGCCCCAGGGAG	86	1613
484328	33217	33236	TCAACACCCCAGCCTGCCTC	56	1614
484329	33222	33241	GAGGCTCAACACCCCAGCCT	47	1615
484330	33360	33379	AGGAGGGTCACACACACCCC	56	1616
484331	33388	33407	GCAAGAGGCCAGGAAAAGGG	53	1617
484332	33393	33412	TACTGGCAAGAGGCCAGGAA	53	1618
484333	33398	33417	ATGATTACTGGCAAGAGGCC	45	1619
484334	33403	33422	ATTACATGATTACTGGCAAG	30	1620

Table 26

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	94	425
484335	35661	35680	AAAATATACATGCTCTTTTT	52	1621
484336	35666	35685	ACTCAAAAATATACATGCTC	88	1622
484337	35671	35690	TTTCTACTCAAAAATATACA	28	1623
484338	35676	35695	TCCTTTTTCTACTCAAAAAT	64	1624
484339	36215	36234	TTCTGATTAGAAAAATAATA	15	1625
484340	36220	36239	TTTTATTCTGATTAGAAAAA	33	1626
484341	36243	36262	TATTCTGCTCATAAAAACAT	44	1627
484342	36248	36267	AAGGGTATTCTGCTCATAAA	78	1628
484343	36253	36272	TGAGTAAGGGTATTCTGCTC	89	1629
484344	36258	36277	GACAATGAGTAAGGGTATTC	88	1630
484345	36263	36282	AGAGAGACAATGAGTAAGGG	46	1631
484346	36268	36287	GGCTGAGAGAGACAATGAGT	72	1632
484347	36318	36337	AGCCTGTGACACCTACCCTG	68	1633

484348	36354	36373	ATGCAGTGTCCCTAAACCCT	82	1634
484349	36359	36378	GGGTGATGCAGTGTCCCTAA	73	1635
484350	36409	36428	TGGCTTCCTCAGGGCCCACC	90	1636
484351	36454	36473	CCTGACCTGTGGTACTAAGG	68	1637
484352	36512	36531	AGCCCTGTGCCAGCCAGCCT	74	1638
484353	36517	36536	GCGACAGCCCTGTGCCAGCC	92	1639
484354	36522	36541	GACAAGCGACAGCCCTGTGC	60	1640
484355	36573	36592	CCACAGTCAGCTGGGCTCAG	72	1641
484356	36578	36597	CTTTCCCACAGTCAGCTGGG	70	1642
484357	36583	36602	GGAAACTTTCCCACAGTCAG	89	1643
484358	36588	36607	CAAATGGAAACTTTCCCACA	56	1644
484359	36617	36636	GGCCTGGAAAAGGGACACTG	71	1645
484360	36622	36641	CCCCTGGCCTGGAAAAGGGA	48	1646
484361	36627	36646	CTACTCCCCTGGCCTGGAAA	21	1647
484362	36632	36651	ACCTCCTACTCCCCTGGCCT	67	1648
484363	36637	36656	AGCCCACCTCCTACTCCCCT	68	1649
484364	36642	36661	CAGGCAGCCCACCTCCTACT	66	1650
484365	36647	36666	TGAGACAGGCAGCCCACCTC	66	1651
484366	36652	36671	CAGAATGAGACAGGCAGCCC	56	1652
484367	36676	36695	CTCTGTGGGCTCCTCCACAG	45	1653
484368	36681	36700	CTGTGCTCTGTGGGCTCCTC	81	1654
484369	36686	36705	TGGCCCTGTGCTCTGTGGGC	42	1655
484370	36691	36710	TTACTTGGCCCTGTGCTCTG	75	1656
484371	36733	36752	ACTGTCAGTCTCTCCAAACT	73	1657
484372	36738	36757	CCCCCACTGTCAGTCTCTCC	78	1658
484373	36743	36762	CTCTGCCCCCACTGTCAGTC	72	1659
484374	36748	36767	GCAAGCTCTGCCCCCACTGT	71	1660
484375	36753	36772	TGGCTGCAAGCTCTGCCCCC	70	1661
484376	36758	36777	GGCCTTGGCTGCAAGCTCTG	76	1662
484377	36841	36860	AATCCAACCCTTGTCACTCT	88	1663
484378	36846	36865	ACTCAAATCCAACCCTTGTC	81	1664
484379	36855	36874	TATTCTAAAACTCAAATCCA	61	1665
484380	36860	36879	GTGATTATTCTAAAACTCAA	65	1666
484381	36865	36884	CCAGAGTGATTATTCTAAAA	73	1667
484382	36896	36915	CCTCCCTCTGGGCCCATCCT	74	1668
484383	36923	36942	TTTGCACTCTGCCAGCCTCC	78	1669
484384	36928	36947	TCTTCTTTGCACTCTGCCAG	69	1670
484385	36969	36988	TGCCCTTGTTCCTCTCAGTC	68	1671
484386	36974	36993	ATGTTTGCCCTTGTTCCTCT	62	1672
484387	37022	37041	GTTGGGCAGTCACCATTTGC	63	1673
484388	37027	37046	CTGGTGTTGGGCAGTCACCA	30	1674
484389	37032	37051	CAGTGCTGGTGTTGGGCAGT	30	1675

484390	37054	37073	CAGACTCTCATCCCCAGGGC	72	1676
484391	37119	37138	GGATGTGTCATTTCCCCTGG	86	1677
484392	37174	37193	AGGAAACTGGCTGGGAGAGG	20	1678
484393	37179	37198	GTCAGAGGAAACTGGCTGGG	48	1679
484394	37184	37203	CTTGGGTCAGAGGAAACTGG	37	1680
484395	37189	37208	ATGACCTTGGGTCAGAGGAA	38	1681
484396	37194	37213	CAAGGATGACCTTGGGTCAG	36	1682
484397	37199	37218	AGCTGCAAGGATGACCTTGG	48	1683
484398	37204	37223	TCACCAGCTGCAAGGATGAC	24	1684
484399	37440	37459	AACAGTGCCCAGCAGGAGCA	14	1685
484400	37445	37464	TTGACAACAGTGCCCAGCAG	19	1686
484401	37450	37469	AGGCCTTGACAACAGTGCCC	36	1687
484402	37455	37474	GGCTCAGGCCTTGACAACAG	57	1688
484403	37460	37479	GGAGAGGCTCAGGCCTTGAC	53	1689
484404	37485	37504	GGCTCCCTGTGTCACCCTGC	61	1690
484405	37490	37509	GTGTTGGCTCCCTGTGTCAC	39	1691
484406	37495	37514	ATGGTGTGTTGGCTCCCTGT	36	1692
484407	37500	37519	AAGGAATGGTGTGTTGGCTC	48	1693
484408	37505	37524	GCACCAAGGAATGGTGTGTT	30	1694
484409	37510	37529	GCCCAGCACCAAGGAATGGT	48	1695
484410	37515	37534	TGCAGGCCCAGCACCAAGGA	55	1696
484411	37520	37539	CCCAATGCAGGCCCAGCACC	67	1697

Table 27

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
495425	10040	10059	AGGGCCCTTTCCAGAAAATC	84	1698
495426	10041	10060	CAGGGCCCTTTCCAGAAAAT	29	1699
495427	10042	10061	ACAGGGCCCTTTCCAGAAAA	14	1700
495428	10043	10062	CACAGGGCCCTTTCCAGAAA	64	1701
495429	10045	10064	GCCACAGGGCCCTTTCCAGA	86	1702
495430	10046	10065	TGCCACAGGGCCCTTTCCAG	77	1703
495431	10047	10066	CTGCCACAGGGCCCTTTCCA	50	1704
495432	10048	10067	CCTGCCACAGGGCCCTTTCC	44	1705
495433	10206	10225	GAATATCCCTAATAACTAAG	18	1706
495434	10207	10226	CGAATATCCCTAATAACTAA	8	1707
495435	10208	10227	TCGAATATCCCTAATAACTA	18	1708
495436	10209	10228	CTCGAATATCCCTAATAACT	66	1709
495437	10211	10230	TTCTCGAATATCCCTAATAA	31	1710
495438	10212	10231	GTTCTCGAATATCCCTAATA	69	1711

495439	10213	10232	AGTTCTCGAATATCCCTAAT	36	1712
495440	10214	10233	GAGTTCTCGAATATCCCTAA	84	1713
495441	10216	10235	AGGAGTTCTCGAATATCCCT	79	1714
495442	10217	10236	GAGGAGTTCTCGAATATCCC	83	1715
495443	10218	10237	GGAGGAGTTCTCGAATATCC	78	1716
495444	10219	10238	GGGAGGAGTTCTCGAATATC	64	1717
495445	10491	10510	GCAGGGTCCTCTCCGCTGCC	70	1718
495446	10492	10511	TGCAGGGTCCTCTCCGCTGC	80	1719
495447	10528	10547	GATTCACTGAGGACCTCAGT	71	1720
495448	10529	10548	CGATTCACTGAGGACCTCAG	78	1721
495449	10530	10549	GCGATTCACTGAGGACCTCA	94	1722
495450	10531	10550	CGCGATTCACTGAGGACCTC	90	1723
495451	10533	10552	TGCGCGATTCACTGAGGACC	82	1724
495452	10534	10553	CTGCGCGATTCACTGAGGAC	77	1725
495453	10535	10554	TCTGCGCGATTCACTGAGGA	81	1726
495454	10536	10555	CTCTGCGCGATTCACTGAGG	85	1727
495455	10646	10665	CCTCCCACTTCAGTTTCTCC	64	1728
495456	10647	10666	TCCTCCCACTTCAGTTTCTC	71	1729
495457	10648	10667	TTCCTCCCACTTCAGTTTCT	63	1730
495458	10649	10668	CTTCCTCCCACTTCAGTTTC	70	1731
495459	10651	10670	TGCTTCCTCCCACTTCAGTT	63	1732
495460	10652	10671	ATGCTTCCTCCCACTTCAGT	55	1733
495461	10653	10672	CATGCTTCCTCCCACTTCAG	70	1734
495462	10654	10673	GCATGCTTCCTCCCACTTCA	78	1735
495463	10656	10675	AGGCATGCTTCCTCCCACTT	81	1736
495464	10657	10676	TAGGCATGCTTCCTCCCACT	85	1737
495465	10658	10677	TTAGGCATGCTTCCTCCCAC	78	1738
495466	10659	10678	CTTAGGCATGCTTCCTCCCA	83	1739
495467	10661	10680	AACTTAGGCATGCTTCCTCC	82	1740
495468	10662	10681	AAACTTAGGCATGCTTCCTC	76	1741
495469	10663	10682	AAAACTTAGGCATGCTTCCT	83	1742
495470	10664	10683	GAAAACTTAGGCATGCTTCC	87	1743
495471	10666	10685	AGGAAAACTTAGGCATGCTT	83	1744
495472	10667	10686	AAGGAAAACTTAGGCATGCT	85	1745
495473	10668	10687	TAAGGAAAACTTAGGCATGC	76	1746
495474	10669	10688	CTAAGGAAAACTTAGGCATG	59	1747
495475	10671	10690	AGCTAAGGAAAACTTAGGCA	65	1748
495476	10672	10691	CAGCTAAGGAAAACTTAGGC	70	1749
495477	10673	10692	TCAGCTAAGGAAAACTTAGG	40	1750
495478	10674	10693	ATCAGCTAAGGAAAACTTAG	25	1751
495479	10728	10747	TGTGATGACTTCCCAGGGTC	75	1752
495480	10729	10748	CTGTGATGACTTCCCAGGGT	72	1753

495481	10730	10749	GCTGTGATGACTTCCCAGGG	87	1754
495482	10731	10750	AGCTGTGATGACTTCCCAGG	80	1755
495483	10733	10752	ACAGCTGTGATGACTTCCCA	79	1756
495484	10734	10753	GACAGCTGTGATGACTTCCC	86	1757
495485	10735	10754	GGACAGCTGTGATGACTTCC	80	1758
495486	10736	10755	AGGACAGCTGTGATGACTTC	62	1759
495487	10815	10834	CATGTCAGAGAGGCTCAGCA	72	1760
495488	10816	10835	CCATGTCAGAGAGGCTCAGC	87	1761
495489	10817	10836	TCCATGTCAGAGAGGCTCAG	86	1762
495490	10818	10837	ATCCATGTCAGAGAGGCTCA	88	1763
495491	10820	10839	AAATCCATGTCAGAGAGGCT	85	1764
495492	10821	10840	AAAATCCATGTCAGAGAGGC	86	1765
495493	10822	10841	AAAAATCCATGTCAGAGAGG	57	1766
495494	10823	10842	GAAAAATCCATGTCAGAGAG	52	1767
495495	10941	10960	TGGATAGTCGATTTACCAGA	92	1768
495496	10942	10961	TTGGATAGTCGATTTACCAG	89	1769
495497	10944	10963	CTTTGGATAGTCGATTTACC	89	1770
495498	11075	11094	ACCTCGATGTTACATTAAGG	90	1771
495499	11076	11095	AACCTCGATGTTACATTAAG	72	1772
495500	11077	11096	AAACCTCGATGTTACATTAA	64	1773
495501	11078	11097	GAAACCTCGATGTTACATTA	71	1774
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	74	425

Table 28

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
495502	11124	11143	TATTGCAACCACTAGGACAT	78	1775
495503	11125	11144	TTATTGCAACCACTAGGACA	72	1776
495504	11126	11145	GTTATTGCAACCACTAGGAC	79	1777
495505	11127	11146	GGTTATTGCAACCACTAGGA	91	1778
495506	11129	11148	TGGGTTATTGCAACCACTAG	91	1779
495507	11130	11149	GTGGGTTATTGCAACCACTA	86	1780
495508	11131	11150	GGTGGGTTATTGCAACCACT	85	1781
495509	11159	11178	TCACAGTTAAAGTGTGGTAC	82	1782
495510	11160	11179	GTCACAGTTAAAGTGTGGTA	84	1783
495511	11161	11180	GGTCACAGTTAAAGTGTGGT	78	1784
495512	11162	11181	AGGTCACAGTTAAAGTGTGG	7	1785
495513	11169	11188	AATGCCTAGGTCACAGTTAA	46	1786
495514	11170	11189	CAATGCCTAGGTCACAGTTA	80	1787
495515	11171	11190	CCAATGCCTAGGTCACAGTT	88	1788

495516	11172	11191	GCCAATGCCTAGGTCACAGT	94	1789
495517	11174	11193	ATGCCAATGCCTAGGTCACA	92	1790
495518	11175	11194	AATGCCAATGCCTAGGTCAC	93	1791
495519	11176	11195	CAATGCCAATGCCTAGGTCA	92	1792
495520	11177	11196	GCAATGCCAATGCCTAGGTC	92	1793
495521	11200	11219	CCACAGCGATAATCACACAA	84	1794
495522	11201	11220	ACCACAGCGATAATCACACA	92	1795
495523	11202	11221	AACCACAGCGATAATCACAC	94	1796
495524	11203	11222	TAACCACAGCGATAATCACA	91	1797
495525	14504	14523	GCAGGGTCTGCCACTCTCTA	86	1798
495526	14505	14524	AGCAGGGTCTGCCACTCTCT	92	1799
495527	14506	14525	GAGCAGGGTCTGCCACTCTC	91	1800
495528	14507	14526	AGAGCAGGGTCTGCCACTCT	82	1801
495529	14649	14668	GCACAGTCATCTTGTGTACA	86	1802
495530	14650	14669	TGCACAGTCATCTTGTGTAC	81	1803
495531	14651	14670	CTGCACAGTCATCTTGTGTA	80	1804
495532	14652	14671	TCTGCACAGTCATCTTGTGT	64	1805
495533	14659	14678	AGATCACTCTGCACAGTCAT	81	1806
495534	14660	14679	CAGATCACTCTGCACAGTCA	87	1807
495535	14661	14680	TCAGATCACTCTGCACAGTC	90	1808
495536	14662	14681	CTCAGATCACTCTGCACAGT	86	1809
495537	14664	14683	TGCTCAGATCACTCTGCACA	87	1810
495538	14665	14684	TTGCTCAGATCACTCTGCAC	78	1811
495539	14666	14685	ATTGCTCAGATCACTCTGCA	84	1812
495540	14667	14686	CATTGCTCAGATCACTCTGC	88	1813
495541	14741	14760	CCTCTTCCAGGAAGACTTCC	80	1814
495542	14742	14761	ACCTCTTCCAGGAAGACTTC	72	1815
495543	14743	14762	CACCTCTTCCAGGAAGACTT	88	1816
495544	14744	14763	TCACCTCTTCCAGGAAGACT	86	1817
495545	14746	14765	TGTCACCTCTTCCAGGAAGA	82	1818
495546	14747	14766	ATGTCACCTCTTCCAGGAAG	42	1819
495547	14748	14767	AATGTCACCTCTTCCAGGAA	50	1820
495548	14749	14768	GAATGTCACCTCTTCCAGGA	74	1821
495549	14751	14770	CTGAATGTCACCTCTTCCAG	75	1822
495550	14752	14771	ACTGAATGTCACCTCTTCCA	81	1823
495551	14753	14772	GACTGAATGTCACCTCTTCC	81	1824
495552	14754	14773	GGACTGAATGTCACCTCTTC	88	1825
495553	14756	14775	CCGGACTGAATGTCACCTCT	90	1826
495554	14757	14776	TCCGGACTGAATGTCACCTC	91	1827
495555	14758	14777	ATCCGGACTGAATGTCACCT	91	1828
495556	14759	14778	GATCCGGACTGAATGTCACC	85	1829
495557	14766	14785	CTTTCCAGATCCGGACTGAA	67	1830

495558	14767	14786	TCTTTCCAGATCCGGACTGA	77	1831
495559	14768	14787	ATCTTTCCAGATCCGGACTG	69	1832
495560	14769	14788	CATCTTTCCAGATCCGGACT	88	1833
495561	14771	14790	TTCATCTTTCCAGATCCGGA	89	1834
495562	14772	14791	ATTCATCTTTCCAGATCCGG	94	1835
495563	14773	14792	TATTCATCTTTCCAGATCCG	92	1836
495564	14774	14793	CTATTCATCTTTCCAGATCC	84	1837
495565	14992	15011	CTCAAGTCTTCCTCCTGCTG	79	1838
495566	14993	15012	TCTCAAGTCTTCCTCCTGCT	83	1839
495567	14994	15013	CTCTCAAGTCTTCCTCCTGC	63	1840
495568	14995	15014	GCTCTCAAGTCTTCCTCCTG	86	1841
495569	14997	15016	GAGCTCTCAAGTCTTCCTCC	84	1842
495570	14998	15017	TGAGCTCTCAAGTCTTCCTC	90	1843
495571	14999	15018	ATGAGCTCTCAAGTCTTCCT	91	1844
495572	15000	15019	CATGAGCTCTCAAGTCTTCC	85	1845
495573	15248	15267	CATAATCTGCACAGGTTCTT	84	1846
495574	15249	15268	CCATAATCTGCACAGGTTCT	87	1847
495575	15250	15269	ACCATAATCTGCACAGGTTC	91	1848
495576	15251	15270	CACCATAATCTGCACAGGTT	94	1849
495577	15253	15272	TGCACCATAATCTGCACAGG	90	1850
495578	15254	15273	CTGCACCATAATCTGCACAG	86	1851
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	92	425

Table 29

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
495579	15255	15274	TCTGCACCATAATCTGCACA	78	1852
495580	15256	15275	ATCTGCACCATAATCTGCAC	73	1853
495581	18152	18171	TAATCCAGGATTGTCATAAG	53	1854
495582	18153	18172	TTAATCCAGGATTGTCATAA	54	1855
495583	18154	18173	TTTAATCCAGGATTGTCATA	40	1856
495584	18155	18174	CTTTAATCCAGGATTGTCAT	70	1857
495585	18157	18176	AGCTTTAATCCAGGATTGTC	81	1858
495586	18158	18177	TAGCTTTAATCCAGGATTGT	37	1859
495587	18159	18178	TTAGCTTTAATCCAGGATTG	60	1860
495588	18160	18179	CTTAGCTTTAATCCAGGATT	75	1861
495589	18162	18181	TCCTTAGCTTTAATCCAGGA	78	1862
495590	18163	18182	CTCCTTAGCTTTAATCCAGG	77	1863
495591	18164	18183	CCTCCTTAGCTTTAATCCAG	82	1864
495592	18165	18184	TCCTCCTTAGCTTTAATCCA	73	1865

495593	18167	18186	TGTCCTCCTTAGCTTTAATC	69	1866
495594	18168	18187	GTGTCCTCCTTAGCTTTAAT	61	1867
495595	18169	18188	AGTGTCCTCCTTAGCTTTAA	51	1868
495596	18170	18189	CAGTGTCCTCCTTAGCTTTA	61	1869
495597	18172	18191	CTCAGTGTCCTCCTTAGCTT	76	1870
495598	18173	18192	ACTCAGTGTCCTCCTTAGCT	81	1871
495599	18174	18193	GACTCAGTGTCCTCCTTAGC	83	1872
495600	18175	18194	GGACTCAGTGTCCTCCTTAG	80	1873
495601	18177	18196	TGGGACTCAGTGTCCTCCTT	64	1874
495602	18178	18197	CTGGGACTCAGTGTCCTCCT	72	1875
495603	18179	18198	CCTGGGACTCAGTGTCCTCC	77	1876
495604	18180	18199	CCCTGGGACTCAGTGTCCTC	88	1877
495605	18307	18326	TCCTGTTTGATGGGTAAAAT	77	1878
495606	18308	18327	CTCCTGTTTGATGGGTAAAA	83	1879
495607	18309	18328	TCTCCTGTTTGATGGGTAAA	78	1880
495608	18310	18329	CTCTCCTGTTTGATGGGTAA	81	1881
495609	18312	18331	TCCTCTCCTGTTTGATGGGT	83	1882
495610	18313	18332	GTCCTCTCCTGTTTGATGGG	77	1883
495611	18314	18333	TGTCCTCTCCTGTTTGATGG	69	1884
495612	18315	18334	GTGTCCTCTCCTGTTTGATG	76	1885
495613	18317	18336	CGGTGTCCTCTCCTGTTTGA	77	1886
495614	18318	18337	TCGGTGTCCTCTCCTGTTTG	72	1887
495615	18319	18338	CTCGGTGTCCTCTCCTGTTT	69	1888
495616	18320	18339	CCTCGGTGTCCTCTCCTGTT	77	1889
495617	18322	18341	AGCCTCGGTGTCCTCTCCTG	72	1890
495618	18323	18342	AAGCCTCGGTGTCCTCTCCT	84	1891
495619	18324	18343	TAAGCCTCGGTGTCCTCTCC	88	1892
495620	18325	18344	GTAAGCCTCGGTGTCCTCTC	91	1893
495621	18327	18346	AAGTAAGCCTCGGTGTCCTC	86	1894
495622	18328	18347	CAAGTAAGCCTCGGTGTCCT	81	1895
495623	18330	18349	ACCAAGTAAGCCTCGGTGTC	79	1896
495624	18418	18437	CTCACCAGATTGTTGTGGGA	79	1897
495625	18419	18438	CCTCACCAGATTGTTGTGGG	77	1898
495626	18420	18439	ACCTCACCAGATTGTTGTGG	79	1899
495627	18421	18440	TACCTCACCAGATTGTTGTG	47	1900
495628	18428	18447	TAATACCTACCTCACCAGAT	56	1901
495629	18429	18448	CTAATACCTACCTCACCAGA	49	1902
495630	18430	18449	GCTAATACCTACCTCACCAG	60	1903
495631	18431	18450	GGCTAATACCTACCTCACCA	70	1904
495632	18451	18470	CTTCCTCATCTATACAGTGG	72	1905
495633	18452	18471	GCTTCCTCATCTATACAGTG	72	1906
495634	18453	18472	AGCTTCCTCATCTATACAGT	63	1907

495635	18454	18473	CAGCTTCCTCATCTATACAG	66	1908
495636	18582	18601	CCATACTGGCATCTGGCAGG	78	1909
495637	18583	18602	TCCATACTGGCATCTGGCAG	73	1910
495638	18584	18603	CTCCATACTGGCATCTGGCA	78	1911
495639	18585	18604	CCTCCATACTGGCATCTGGC	82	1912
495640	18587	18606	CACCTCCATACTGGCATCTG	51	1913
495641	18588	18607	TCACCTCCATACTGGCATCT	71	1914
495642	18589	18608	CTCACCTCCATACTGGCATC	72	1915
495643	18590	18609	CCTCACCTCCATACTGGCAT	70	1916
495644	18592	18611	CACCTCACCTCCATACTGGC	68	1917
495645	18593	18612	CCACCTCACCTCCATACTGG	54	1918
495646	18594	18613	CCCACCTCACCTCCATACTG	45	1919
495647	18595	18614	ACCCACCTCACCTCCATACT	37	1920
495648	18827	18846	GGATGCTTAACTTCTGCTGA	67	1921
495649	18828	18847	AGGATGCTTAACTTCTGCTG	83	1922
495650	18829	18848	TAGGATGCTTAACTTCTGCT	84	1923
495651	18830	18849	TTAGGATGCTTAACTTCTGC	68	1924
495652	18832	18851	AGTTAGGATGCTTAACTTCT	50	1925
495653	18833	18852	AAGTTAGGATGCTTAACTTC	49	1926
495654	18834	18853	TAAGTTAGGATGCTTAACTT	49	1927
495655	18835	18854	TTAAGTTAGGATGCTTAACT	42	1928
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	82	425

Table 30

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
423461	32429	32448	CTGGACAAGTCCTGCCCATC	73	465
423462	32430	32449	CCTGGACAAGTCCTGCCCAT	70	466
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	87	425
495656	18870	18889	TATAGGCCTGGATGCCCAAG	70	1929
	20780	20799			
495657	18871	18890	CTATAGGCCTGGATGCCCAA	72	1930
	20781	20800			
495658	18896	18915	AGATGATGTCCTGCCTCAGA	30	1931
495659	18897	18916	CAGATGATGTCCTGCCTCAG	37	1932
495660	18898	18917	GCAGATGATGTCCTGCCTCA	65	1933
495661	18899	18918	AGCAGATGATGTCCTGCCTC	72	1934
495662	19014	19033	AGTCAAAGGTGGCTTCCTGG	67	1935
495663	19015	19034	TAGTCAAAGGTGGCTTCCTG	57	1936
495664	19016	19035	GTAGTCAAAGGTGGCTTCCT	75	1937

495665	19017	19036	AGTAGTCAAAGGTGGCTTCC	66	1938
495666	19020	19039	ATGAGTAGTCAAAGGTGGCT	73	1939
495667	19021	19040	AATGAGTAGTCAAAGGTGGC	64	1940
495668	19022	19041	GAATGAGTAGTCAAAGGTGG	31	1941
495669	20775	20794	GCCTGGATGCCCAAGTTAGA	72	1942
495670	20776	20795	GGCCTGGATGCCCAAGTTAG	73	1943
495671	20777	20796	AGGCCTGGATGCCCAAGTTA	77	1944
495672	20778	20797	TAGGCCTGGATGCCCAAGTT	57	1945
495673	22544	22563	ACAAGTGGGAAATGCAGTCT	48	1946
495674	22545	22564	AACAAGTGGGAAATGCAGTC	42	1947
495675	22546	22565	CAACAAGTGGGAAATGCAGT	35	1948
495676	22547	22566	CCAACAAGTGGGAAATGCAG	62	1949
495677	22549	22568	TGCCAACAAGTGGGAAATGC	70	1950
495678	22550	22569	CTGCCAACAAGTGGGAAATG	52	1951
495679	22551	22570	TCTGCCAACAAGTGGGAAAT	39	1952
495680	22552	22571	CTCTGCCAACAAGTGGGAAA	34	1953
495681	22767	22786	GCTTATTAGGTGTCTTAAAA	51	1954
495682	22768	22787	AGCTTATTAGGTGTCTTAAA	56	1955
495683	22769	22788	AAGCTTATTAGGTGTCTTAA	59	1956
495684	22770	22789	TAAGCTTATTAGGTGTCTTA	63	1957
495685	22772	22791	GCTAAGCTTATTAGGTGTCT	86	1958
495686	22773	22792	TGCTAAGCTTATTAGGTGTC	80	1959
495687	22774	22793	CTGCTAAGCTTATTAGGTGT	68	1960
495688	22775	22794	TCTGCTAAGCTTATTAGGTG	64	1961
495689	22882	22901	CCCCATGCAGCTTGGAGGAG	60	1962
495690	22883	22902	CCCCCATGCAGCTTGGAGGA	53	1963
495691	22884	22903	GCCCCCATGCAGCTTGGAGG	43	1964
495692	22885	22904	AGCCCCCATGCAGCTTGGAG	61	1965
495693	22887	22906	CCAGCCCCCATGCAGCTTGG	66	1966
495694	22888	22907	GCCAGCCCCCATGCAGCTTG	78	1967
495695	22889	22908	GGCCAGCCCCCATGCAGCTT	71	1968
495696	22890	22909	GGGCCAGCCCCCATGCAGCT	63	1969
495697	23096	23115	AGTCCAAACACTCAGGTAGG	82	1970
495698	23097	23116	CAGTCCAAACACTCAGGTAG	68	1971
495699	23098	23117	TCAGTCCAAACACTCAGGTA	74	1972
495700	23099	23118	TTCAGTCCAAACACTCAGGT	72	1973
495701	23238	23257	GGGAACAGCAGCATCAGCAT	77	1974
495702	23239	23258	TGGGAACAGCAGCATCAGCA	83	1975
495703	23240	23259	CTGGGAACAGCAGCATCAGC	68	1976
495704	23241	23260	TCTGGGAACAGCAGCATCAG	65	1977
495705	23243	23262	GGTCTGGGAACAGCAGCATC	84	1978
495706	23244	23263	TGGTCTGGGAACAGCAGCAT	81	1979

495707	23245	23264	GTGGTCTGGGAACAGCAGCA	84	1980
495708	23423	23442	CAAGTCATCTTCCAGCAGCT	57	1981
495709	23424	23443	ACAAGTCATCTTCCAGCAGC	36	1982
495710	23425	23444	GACAAGTCATCTTCCAGCAG	38	1983
495711	23426	23445	GGACAAGTCATCTTCCAGCA	77	1984
495712	23428	23447	CTGGACAAGTCATCTTCCAG	53	1985
495713	23429	23448	GCTGGACAAGTCATCTTCCA	66	1986
495714	23430	23449	GGCTGGACAAGTCATCTTCC	76	1987
495715	23431	23450	GGGCTGGACAAGTCATCTTC	45	1988
495716	23548	23567	ATCCTTGAGGGTCTCATAAC	58	1989
495717	23549	23568	TATCCTTGAGGGTCTCATAA	61	1990
495718	23551	23570	CTTATCCTTGAGGGTCTCAT	83	1991
495719	23553	23572	TGCTTATCCTTGAGGGTCTC	79	1992
495720	23554	23573	ATGCTTATCCTTGAGGGTCT	73	1993
495721	23555	23574	CATGCTTATCCTTGAGGGTC	64	1994
495722	23556	23575	ACATGCTTATCCTTGAGGGT	60	1995
495723	26396	26415	CTGGATGGCAACCTAAGGAG	61	1996
495724	26397	26416	CCTGGATGGCAACCTAAGGA	74	1997
495725	26398	26417	GCCTGGATGGCAACCTAAGG	61	1998
495726	26399	26418	GGCCTGGATGGCAACCTAAG	60	1999
495727	26401	26420	CTGGCCTGGATGGCAACCTA	69	2000
495728	26480	26499	TGCTATGCTGAGAGCACAGG	69	2001
495729	26481	26500	CTGCTATGCTGAGAGCACAG	64	2002
495730	26482	26501	CCTGCTATGCTGAGAGCACA	81	2003

Table 31

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
495731	26483	26502	ACCTGCTATGCTGAGAGCAC	75	2004
495732	26485	26504	CTACCTGCTATGCTGAGAGC	69	2005
495733	26486	26505	GCTACCTGCTATGCTGAGAG	54	2006
495734	26487	26506	AGCTACCTGCTATGCTGAGA	67	2007
495735	26488	26507	AAGCTACCTGCTATGCTGAG	44	2008
495736	26517	26536	GCAGGTTCATCTGCCTTGAC	88	2009
495737	26518	26537	AGCAGGTTCATCTGCCTTGA	75	2010
495738	26519	26538	GAGCAGGTTCATCTGCCTTG	84	2011
495739	26520	26539	GGAGCAGGTTCATCTGCCTT	80	2012
495740	26532	26551	CTGTGATGCTCTGGAGCAGG	56	2013
495741	26533	26552	TCTGTGATGCTCTGGAGCAG	49	2014
495742	26534	26553	CTCTGTGATGCTCTGGAGCA	66	2015

495743	26535	26554	ACTCTGTGATGCTCTGGAGC	74	2016
495744	26537	26556	GCACTCTGTGATGCTCTGGA	85	2017
495745	26538	26557	TGCACTCTGTGATGCTCTGG	80	2018
495746	26539	26558	ATGCACTCTGTGATGCTCTG	70	2019
495747	26540	26559	AATGCACTCTGTGATGCTCT	60	2020
495748	26626	26645	TGACATGGTAAGTCCTGATG	79	2021
495749	26627	26646	CTGACATGGTAAGTCCTGAT	86	2022
495750	26628	26647	ACTGACATGGTAAGTCCTGA	79	2023
495751	26629	26648	CACTGACATGGTAAGTCCTG	84	2024
495752	26631	26650	AGCACTGACATGGTAAGTCC	90	2025
495753	26632	26651	CAGCACTGACATGGTAAGTC	86	2026
495754	26633	26652	TCAGCACTGACATGGTAAGT	73	2027
495755	26634	26653	CTCAGCACTGACATGGTAAG	63	2028
495756	26779	26798	CTGCCATTTAATGAGCTTCA	86	2029
495757	26780	26799	TCTGCCATTTAATGAGCTTC	77	2030
495758	26781	26800	CTCTGCCATTTAATGAGCTT	50	2031
495759	26782	26801	ACTCTGCCATTTAATGAGCT	43	2032
495760	26784	26803	CAACTCTGCCATTTAATGAG	34	2033
495761	26785	26804	CCAACTCTGCCATTTAATGA	39	2034
495762	26786	26805	CCCAACTCTGCCATTTAATG	74	2035
495763	26787	26806	TCCCAACTCTGCCATTTAAT	76	2036
495764	26789	26808	AATCCCAACTCTGCCATTTA	62	2037
495765	26790	26809	AAATCCCAACTCTGCCATTT	61	2038
495766	26927	26946	TTTAAGGGTTCATGGATCCC	70	2039
495767	26928	26947	TTTTAAGGGTTCATGGATCC	48	2040
495768	26929	26948	ATTTTAAGGGTTCATGGATC	23	2041
495769	26930	26949	AATTTTAAGGGTTCATGGAT	9	2042
495770	27247	27266	TGGAGTCCCTGGGTTCTTGT	51	2043
495771	27248	27267	CTGGAGTCCCTGGGTTCTTG	52	2044
495772	27249	27268	GCTGGAGTCCCTGGGTTCTT	72	2045
495773	27250	27269	GGCTGGAGTCCCTGGGTTCT	64	2046
495774	27252	27271	GAGGCTGGAGTCCCTGGGTT	64	2047
495775	27253	27272	GGAGGCTGGAGTCCCTGGGT	45	2048
495776	27255	27274	TGGGAGGCTGGAGTCCCTGG	24	2049
495777	27353	27372	TACCAGCCAGGCCCAGACCC	8	2050
495778	27354	27373	CTACCAGCCAGGCCCAGACC	7	2051
495779	27355	27374	CCTACCAGCCAGGCCCAGAC	6	2052
495780	27356	27375	CCCTACCAGCCAGGCCCAGA	9	2053
495781	27378	27397	GTGTTCTACAAGCTGCTCAG	64	2054
495782	27379	27398	GGTGTTCTACAAGCTGCTCA	77	2055
495783	27380	27399	TGGTGTTCTACAAGCTGCTC	68	2056
495784	27381	27400	CTGGTGTTCTACAAGCTGCT	74	2057

495785	27383	27402	AGCTGGTGTTCTACAAGCTG	80	2058
495786	27384	27403	GAGCTGGTGTTCTACAAGCT	61	2059
495787	27385	27404	TGAGCTGGTGTTCTACAAGC	58	2060
495788	27386	27405	GTGAGCTGGTGTTCTACAAG	62	2061
495789	27438	27457	GTCTGATCAATTATTAACCT	71	2062
495790	27439	27458	GGTCTGATCAATTATTAACC	57	2063
495791	27440	27459	GGGTCTGATCAATTATTAAC	60	2064
495792	27441	27460	TGGGTCTGATCAATTATTAA	40	2065
495793	29674	29693	CAGGTACTCATGTTTGGTGG	63	2066
495794	29675	29694	GCAGGTACTCATGTTTGGTG	75	2067
495795	29676	29695	AGCAGGTACTCATGTTTGGT	73	2068
495796	29677	29696	CAGCAGGTACTCATGTTTGG	66	2069
495797	29679	29698	GGCAGCAGGTACTCATGTTT	60	2070
495798	29680	29699	GGGCAGCAGGTACTCATGTT	58	2071
495799	29681	29700	AGGGCAGCAGGTACTCATGT	63	2072
495800	29682	29701	AAGGGCAGCAGGTACTCATG	75	2073
495801	29778	29797	CAATATCATACTATCTACAT	11	2074
495802	29779	29798	CCAATATCATACTATCTACA	13	2075
495803	29780	29799	CCCAATATCATACTATCTAC	51	2076
495804	29781	29800	CCCCAATATCATACTATCTA	71	2077
495805	29783	29802	TTCCCCAATATCATACTATC	50	2078
495806	29825	29844	AACCTTTAAGGCCTATCTCA	32	2079
495807	29826	29845	CAACCTTTAAGGCCTATCTC	25	2080
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	84	425

Table 32

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
495808	29827	29846	CCAACCTTTAAGGCCTATCT	82	2081
495809	29828	29847	CCCAACCTTTAAGGCCTATC	90	2082
495810	29830	29849	TACCCAACCTTTAAGGCCTA	82	2083
495811	29831	29850	TTACCCAACCTTTAAGGCCT	75	2084
495812	29832	29851	TTTACCCAACCTTTAAGGCC	73	2085
495813	29833	29852	TTTTACCCAACCTTTAAGGC	70	2086
495814	29835	29854	TTTTTTACCCAACCTTTAAG	32	2087
495815	29836	29855	ATTTTTTACCCAACCTTTAA	27	2088
495816	29837	29856	CATTTTTTACCCAACCTTTA	54	2089
495817	29838	29857	CCATTTTTTACCCAACCTTT	81	2090
495818	29840	29859	TTCCATTTTTTACCCAACCT	89	2091
495819	29841	29860	TTTCCATTTTTTACCCAACC	88	2092

495820	29842	29861	CTTTCCATTTTTTACCCAAC	85	2093
495821	29843	29862	TCTTTCCATTTTTTACCCAA	74	2094
495822	30484	30503	TTAGGCTTTAGAAATTCACC	85	2095
495823	30485	30504	ATTAGGCTTTAGAAATTCAC	69	2096
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	89	425
495824	32437	32456	TATGCAGCCTGGACAAGTCC	65	2097
495825	32447	32466	CATACTAGACTATGCAGCCT	91	2098
495826	32448	32467	TCATACTAGACTATGCAGCC	88	2099
495827	32449	32468	ATCATACTAGACTATGCAGC	86	2100
495828	32450	32469	CATCATACTAGACTATGCAG	82	2101
495829	32452	32471	GCCATCATACTAGACTATGC	92	2102
495830	32453	32472	TGCCATCATACTAGACTATG	81	2103
495831	32454	32473	TTGCCATCATACTAGACTAT	82	2104
495832	32455	32474	GTTGCCATCATACTAGACTA	88	2105
495833	32457	32476	ATGTTGCCATCATACTAGAC	78	2106
495834	32458	32477	AATGTTGCCATCATACTAGA	68	2107
495835	32459	32478	CAATGTTGCCATCATACTAG	85	2108
495836	32460	32479	GCAATGTTGCCATCATACTA	91	2109
495837	32462	32481	TTGCAATGTTGCCATCATAC	95	2110
495838	32463	32482	GTTGCAATGTTGCCATCATA	86	2111
495839	32464	32483	GGTTGCAATGTTGCCATCAT	94	2112
495840	32465	32484	TGGTTGCAATGTTGCCATCA	94	2113
495841	32467	32486	GGTGGTTGCAATGTTGCCAT	91	2114
495842	32468	32487	TGGTGGTTGCAATGTTGCCA	92	2115
495843	32469	32488	ATGGTGGTTGCAATGTTGCC	84	2116
495844	32470	32489	GATGGTGGTTGCAATGTTGC	82	2117
495845	32472	32491	TGGATGGTGGTTGCAATGTT	51	2118
495846	32473	32492	CTGGATGGTGGTTGCAATGT	48	2119
495847	32474	32493	CCTGGATGGTGGTTGCAATG	64	2120
495848	32475	32494	GCCTGGATGGTGGTTGCAAT	76	2121
495849	32477	32496	AAGCCTGGATGGTGGTTGCA	89	2122
495850	32478	32497	TAAGCCTGGATGGTGGTTGC	71	2123
495851	32479	32498	ATAAGCCTGGATGGTGGTTG	69	2124
495852	32480	32499	AATAAGCCTGGATGGTGGTT	85	2125
495853	32620	32639	AACTGAGATCTCCAGCAGCA	93	2126
495854	32621	32640	AAACTGAGATCTCCAGCAGC	82	2127
495855	32622	32641	TAAACTGAGATCTCCAGCAG	79	2128
495856	32623	32642	TTAAACTGAGATCTCCAGCA	81	2129
495857	32753	32772	GACAAAGTCTATCAGGATGC	90	2130
495858	32754	32773	TGACAAAGTCTATCAGGATG	67	2131
495859	32755	32774	GTGACAAAGTCTATCAGGAT	73	2132
495860	32756	32775	AGTGACAAAGTCTATCAGGA	72	2133

495861	32758	32777	AAAGTGACAAAGTCTATCAG	58	2134
495862	32759	32778	GAAAGTGACAAAGTCTATCA	67	2135
495863	32760	32779	AGAAAGTGACAAAGTCTATC	63	2136
495864	33176	33195	CTAGTGCCCCAGGGAGCCCT	63	2137
495865	33177	33196	CCTAGTGCCCCAGGGAGCCC	67	2138
495866	33178	33197	TCCTAGTGCCCCAGGGAGCC	60	2139
495867	33179	33198	GTCCTAGTGCCCCAGGGAGC	83	2140
495868	33181	33200	TTGTCCTAGTGCCCCAGGGA	87	2141
495869	33182	33201	TTTGTCCTAGTGCCCCAGGG	82	2142
495870	33183	33202	TTTTGTCCTAGTGCCCCAGG	66	2143
495871	36244	36263	GTATTCTGCTCATAAAAACA	42	2144
495872	36245	36264	GGTATTCTGCTCATAAAAAC	56	2145
495873	36246	36265	GGGTATTCTGCTCATAAAAA	72	2146
495874	36247	36266	AGGGTATTCTGCTCATAAAA	82	2147
495875	36249	36268	TAAGGGTATTCTGCTCATAA	89	2148
495876	36250	36269	GTAAGGGTATTCTGCTCATA	90	2149
495877	36251	36270	AGTAAGGGTATTCTGCTCAT	85	2150
495878	36252	36271	GAGTAAGGGTATTCTGCTCA	94	2151
495879	36259	36278	AGACAATGAGTAAGGGTATT	67	2152
495880	36260	36279	GAGACAATGAGTAAGGGTAT	47	2153
495881	36261	36280	AGAGACAATGAGTAAGGGTA	60	2154
495882	36262	36281	GAGAGACAATGAGTAAGGGT	77	2155
495883	36264	36283	GAGAGAGACAATGAGTAAGG	64	2156
495884	36265	36284	TGAGAGAGACAATGAGTAAG	31	2157

Table 33

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	87	425
495885	36266	36285	CTGAGAGAGACAATGAGTAA	51	2158
495886	36518	36537	AGCGACAGCCCTGTGCCAGC	67	2159
495887	36519	36538	AAGCGACAGCCCTGTGCCAG	43	2160
495888	36520	36539	CAAGCGACAGCCCTGTGCCA	15	2161
495889	36521	36540	ACAAGCGACAGCCCTGTGCC	25	2162
495890	36523	36542	GGACAAGCGACAGCCCTGTG	44	2163
495891	36524	36543	AGGACAAGCGACAGCCCTGT	42	2164
495892	36648	36667	ATGAGACAGGCAGCCCACCT	53	2165
495893	36649	36668	AATGAGACAGGCAGCCCACC	56	2166
495894	36650	36669	GAATGAGACAGGCAGCCCAC	46	2167
495895	36651	36670	AGAATGAGACAGGCAGCCCA	56	2168

495896	36653	36672	ACAGAATGAGACAGGCAGCC	42	2169
495897	36654	36673	CACAGAATGAGACAGGCAGC	47	2170
495898	36655	36674	TCACAGAATGAGACAGGCAG	24	2171
495899	36677	36696	GCTCTGTGGGCTCCTCCACA	72	2172
495900	36678	36697	TGCTCTGTGGGCTCCTCCAC	70	2173
495901	36679	36698	GTGCTCTGTGGGCTCCTCCA	76	2174
495902	36680	36699	TGTGCTCTGTGGGCTCCTCC	81	2175
495903	36682	36701	CCTGTGCTCTGTGGGCTCCT	65	2176
495904	36683	36702	CCCTGTGCTCTGTGGGCTCC	70	2177
495905	36684	36703	GCCCTGTGCTCTGTGGGCTC	31	2178
495906	36685	36704	GGCCCTGTGCTCTGTGGGCT	32	2179
495907	36687	36706	TTGGCCCTGTGCTCTGTGGG	46	2180
495908	36688	36707	CTTGGCCCTGTGCTCTGTGG	41	2181
495909	36689	36708	ACTTGGCCCTGTGCTCTGTG	66	2182
495910	36690	36709	TACTTGGCCCTGTGCTCTGT	52	2183
495911	36734	36753	CACTGTCAGTCTCTCCAAAC	75	2184
495912	36735	36754	CCACTGTCAGTCTCTCCAAA	75	2185
495913	36736	36755	CCCACTGTCAGTCTCTCCAA	60	2186
495914	36737	36756	CCCCACTGTCAGTCTCTCCA	63	2187
495915	36739	36758	GCCCCCACTGTCAGTCTCTC	48	2188
495916	36740	36759	TGCCCCCACTGTCAGTCTCT	46	2189
495917	36741	36760	CTGCCCCCACTGTCAGTCTC	55	2190
495918	36742	36761	TCTGCCCCCACTGTCAGTCT	68	2191
495919	36754	36773	TTGGCTGCAAGCTCTGCCCC	59	2192
495920	36755	36774	CTTGGCTGCAAGCTCTGCCC	63	2193
495921	36756	36775	CCTTGGCTGCAAGCTCTGCC	65	2194
495922	36757	36776	GCCTTGGCTGCAAGCTCTGC	65	2195
495923	36759	36778	GGGCCTTGGCTGCAAGCTCT	65	2196
495924	36856	36875	TTATTCTAAAACTCAAATCC	8	2197
495925	36857	36876	ATTATTCTAAAACTCAAATC	11	2198
495926	36859	36878	TGATTATTCTAAAACTCAAA	2	2199
495927	36861	36880	AGTGATTATTCTAAAACTCA	55	2200
495928	36862	36881	GAGTGATTATTCTAAAACTC	36	2201
495929	36863	36882	AGAGTGATTATTCTAAAACT	0	2202
495930	36864	36883	CAGAGTGATTATTCTAAAAC	28	2203
495931	37023	37042	TGTTGGGCAGTCACCATTTG	1	2204
495932	37024	37043	GTGTTGGGCAGTCACCATTT	17	2205
495933	37025	37044	GGTGTTGGGCAGTCACCATT	20	2206
495934	37026	37045	TGGTGTTGGGCAGTCACCAT	2	2207
495935	37185	37204	CCTTGGGTCAGAGGAAACTG	5	2208
495936	37186	37205	ACCTTGGGTCAGAGGAAACT	12	2209
495937	37187	37206	GACCTTGGGTCAGAGGAAAC	15	2210

495938	37188	37207	TGACCTTGGGTCAGAGGAAA	2	2211
495939	37190	37209	GATGACCTTGGGTCAGAGGA	18	2212
495940	37191	37210	GGATGACCTTGGGTCAGAGG	16	2213
495941	37192	37211	AGGATGACCTTGGGTCAGAG	13	2214
495942	37193	37212	AAGGATGACCTTGGGTCAGA	8	2215
495943	37195	37214	GCAAGGATGACCTTGGGTCA	26	2216
495944	37196	37215	TGCAAGGATGACCTTGGGTC	24	2217
495945	37197	37216	CTGCAAGGATGACCTTGGGT	32	2218
495946	37198	37217	GCTGCAAGGATGACCTTGGG	16	2219
495947	37200	37219	CAGCTGCAAGGATGACCTTG	7	2220
495948	37201	37220	CCAGCTGCAAGGATGACCTT	0	2221
495949	37203	37222	CACCAGCTGCAAGGATGACC	27	2222
495950	37491	37510	TGTGTTGGCTCCCTGTGTCA	38	2223
495951	37492	37511	GTGTGTTGGCTCCCTGTGTC	11	2224
495952	37493	37512	GGTGTGTTGGCTCCCTGTGT	40	2225
495953	37494	37513	TGGTGTGTTGGCTCCCTGTG	29	2226
495954	37496	37515	AATGGTGTGTTGGCTCCCTG	49	2227
495955	37497	37516	GAATGGTGTGTTGGCTCCCT	76	2228
495956	37498	37517	GGAATGGTGTGTTGGCTCCC	44	2229
495957	37499	37518	AGGAATGGTGTGTTGGCTCC	72	2230
495958	37501	37520	CAAGGAATGGTGTGTTGGCT	74	2231
495959	37502	37521	CCAAGGAATGGTGTGTTGGC	8	2232
495960	37503	37522	ACCAAGGAATGGTGTGTTGG	21	2233
495961	37504	37523	CACCAAGGAATGGTGTGTTG	18	2234

Table 34

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
423460	32428	32447	TGGACAAGTCCTGCCCATCT	65	464
423461	32429	32448	CTGGACAAGTCCTGCCCATC	70	465
423462	32430	32449	CCTGGACAAGTCCTGCCCAT	54	466
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	80	425
495962	37506	37525	AGCACCAAGGAATGGTGTGT	6	2235
495963	37507	37526	CAGCACCAAGGAATGGTGTG	19	2236
495964	37508	37527	CCAGCACCAAGGAATGGTGT	13	2237
495965	37509	37528	CCCAGCACCAAGGAATGGTG	26	2238
495966	37511	37530	GGCCCAGCACCAAGGAATGG	14	2239
495967	37512	37531	AGGCCCAGCACCAAGGAATG	4	2240
495968	37513	37532	CAGGCCCAGCACCAAGGAAT	8	2241
495969	37514	37533	GCAGGCCCAGCACCAAGGAA	33	2242

495970	37516	37535	ATGCAGGCCCAGCACCAAGG	33	2243
495971	37517	37536	AATGCAGGCCCAGCACCAAG	14	2244
495972	37518	37537	CAATGCAGGCCCAGCACCAA	16	2245
495973	37519	37538	CCAATGCAGGCCCAGCACCA	45	2246
495974	40192	40211	CTGAACTTCCCCTCCCAAAC	16	2247
495975	40197	40216	CAAATCTGAACTTCCCCTCC	0	2248
495976	40202	40221	AAATGCAAATCTGAACTTCC	30	2249
495977	40223	40242	GCAGCTCCAAGGATCATTTT	44	2250
495978	40228	40247	ATCCAGCAGCTCCAAGGATC	45	2251
495979	40233	40252	CTTCCATCCAGCAGCTCCAA	51	2252
495980	40238	40257	CCCATCTTCCATCCAGCAGC	49	2253
495981	40243	40262	TCTAACCCATCTTCCATCCA	28	2254
495982	40248	40267	ATTTTTCTAACCCATCTTCC	21	2255
495983	40253	40272	CTTCCATTTTTCTAACCCAT	64	2256
495984	40293	40312	GCCACTGGCTACCAAAACAG	37	2257
495985	40298	40317	TCCAAGCCACTGGCTACCAA	41	2258
495986	40303	40322	CTTGGTCCAAGCCACTGGCT	43	2259
495987	40308	40327	ACTCCCTTGGTCCAAGCCAC	44	2260
495988	40313	40332	CTGCTACTCCCTTGGTCCAA	40	2261
495989	40318	40337	CTCCACTGCTACTCCCTTGG	11	2262
495990	40323	40342	TCCATCTCCACTGCTACTCC	39	2263
495991	40328	40347	TCTCTTCCATCTCCACTGCT	36	2264
495992	40333	40352	GCACATCTCTTCCATCTCCA	82	2265
495993	40338	40357	ATCATGCACATCTCTTCCAT	39	2266
495994	40359	40378	TATTTCTGAAATTTTTCCCA	17	2267
495995	40364	40383	AATGCTATTTCTGAAATTTT	10	2268
495996	40386	40405	CAATCCATTCCTATGTCCTG	24	2269
495997	40391	40410	ATACCCAATCCATTCCTATG	13	2270
495998	40396	40415	TCTCCATACCCAATCCATTC	45	2271
495999	40401	40420	CTGCATCTCCATACCCAATC	59	2272
496000	40406	40425	TCCTGCTGCATCTCCATACC	38	2273
496001	40411	40430	TCTTATCCTGCTGCATCTCC	15	2274
496002	40416	40435	TATTTTCTTATCCTGCTGCA	46	2275
496003	40421	40440	TGCTTTATTTTCTTATCCTG	47	2276
496004	40444	40463	ACCAGCATTTATGATCTGTG	67	2277
496005	40807	40826	GACATGCTTTAAAAAGTGTA	25	2278
496006	40812	40831	AATGTGACATGCTTTAAAAA	23	2279
496007	40899	40918	AGCCATTCCTGCCTCTCTGA	12	2280
496008	40904	40923	GGGCAAGCCATTCCTGCCTC	5	2281
496009	40909	40928	GCTCTGGGCAAGCCATTCCT	60	2282
496010	40914	40933	GCTCTGCTCTGGGCAAGCCA	66	2283
496011	40919	40938	CTTTTGCTCTGCTCTGGGCA	50	2284

496012	40924	40943	CTTTGCTTTTGCTCTGCTCT	67	2285
496013	40929	40948	AACATCTTTGCTTTTGCTCT	59	2286
496014	40934	40953	AAGTAAACATCTTTGCTTTT	15	2287
496015	40939	40958	GGATCAAGTAAACATCTTTG	42	2288
496016	40967	40986	TCTGCTAGGAGGGTCTATGA	20	2289
496017	40972	40991	TGCATTCTGCTAGGAGGGTC	39	2290
496018	40977	40996	CCCACTGCATTCTGCTAGGA	27	2291
496019	40982	41001	TTGAACCCACTGCATTCTGC	6	2292
496020	40987	41006	ACTGGTTGAACCCACTGCAT	0	2293
496021	40992	41011	TCAAGACTGGTTGAACCCAC	8	2294
496022	40997	41016	TGGGATCAAGACTGGTTGAA	0	2295
496023	41002	41021	GCAGATGGGATCAAGACTGG	0	2296
496024	41007	41026	AAGCTGCAGATGGGATCAAG	0	2297
496025	41012	41031	GTGCTAAGCTGCAGATGGGA	39	2298
496026	41043	41062	GCATGTGAAGGGACCCACCC	14	2299
496027	41064	41083	TGAAAAGACTGAGGCCCAGG	1	2300
496028	41069	41088	ACAGATGAAAAGACTGAGGC	21	2301
496029	41074	41093	CTATTACAGATGAAAAGACT	0	2302
496030	41079	41098	GTCCCCTATTACAGATGAAA	34	2303
496031	41084	41103	TGGTTGTCCCCTATTACAGA	39	2304
496032	41089	41108	ATCTCTGGTTGTCCCCTATT	21	2305
496033	41094	41113	GCTGCATCTCTGGTTGTCCC	65	2306
496034	41099	41118	TATGTGCTGCATCTCTGGTT	51	2307
496035	42398	42417	TCTCACTTTCATTTATTTTC	70	2308

Table 35

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
501381	24794	24813	GCTTCAGGCAGCCTGAAGGA	46	2309
501382	24799	24818	AGTGAGCTTCAGGCAGCCTG	75	2310
501383	24823	24842	GCTTCCCCAAAGGGCCCAGT	70	2311
501384	24828	24847	CCTTTGCTTCCCCAAAGGGC	71	2312
501385	24878	24897	CCTCATCTCAGTGCCCAAAG	90	2313
501386	25018	25037	AGCATCCCCAATCCCTGCTC	65	2314
501387	25023	25042	CTTTGAGCATCCCCAATCCC	91	2315
501388	25028	25047	GTGTACTTTGAGCATCCCCA	82	2316
501389	25033	25052	TCCAAGTGTACTTTGAGCAT	85	2317
501390	25069	25088	AGAGGTTCAACATCCAATTT	81	2318
501391	25075	25094	AAGGACAGAGGTTCAACATC	88	2319

501392	25080	25099	AGGCCAAGGACAGAGGTTCA	82	2320
501393	25085	25104	CTGTGAGGCCAAGGACAGAG	88	2321
501394	25090	25109	TCTGTCTGTGAGGCCAAGGA	77	2322
501395	25095	25114	TGCTATCTGTCTGTGAGGCC	77	2323
501396	25183	25202	GTCTCTCATAATTGCCAGTT	82	2324
501397	25188	25207	GGGAAGTCTCTCATAATTGC	67	2325
501398	25193	25212	GCCTTGGGAAGTCTCTCATA	85	2326
501399	25198	25217	GCTAGGCCTTGGGAAGTCTC	76	2327
501400	25226	25245	TGAAGTATCTAAAGAGGCTA	71	2328
501401	25231	25250	CCACATGAAGTATCTAAAGA	74	2329
501402	25236	25255	GGAGACCACATGAAGTATCT	75	2330
501403	25241	25260	ATTTTGGAGACCACATGAAG	68	2331
501404	25246	25265	GGGTCATTTTGGAGACCACA	91	2332
501405	25267	25286	ATGGGAATGGTATCGCACTC	85	2333
501406	25272	25291	ACACAATGGGAATGGTATCG	80	2334
501407	25297	25316	CCCCTGTGCCCTGGTTTCTA	49	2335
501408	25302	25321	ATGCTCCCCTGTGCCCTGGT	44	2336
501409	25307	25326	TCTGCATGCTCCCCTGTGCC	44	2337
501410	25312	25331	GGCTGTCTGCATGCTCCCCT	76	2338
501411	25375	25394	CTATAGAATCAGACAGACCT	83	2339
501412	25380	25399	ATCAGCTATAGAATCAGACA	90	2340
501413	25424	25443	CAAACCTCACCTCCCACAGG	33	2341
501414	25429	25448	CAGTACAAACCTCACCTCCC	70	2342
501415	25468	25487	TCAGTCCACTGTCACCCTTC	33	2343
501416	25473	25492	AGATGTCAGTCCACTGTCAC	13	2344
501417	25478	25497	AGGGAAGATGTCAGTCCACT	0	2345
501418	25483	25502	AGCAGAGGGAAGATGTCAGT	0	2346
501419	25489	25508	GCCTACAGCAGAGGGAAGAT	29	2347
501420	25494	25513	CCAGTGCCTACAGCAGAGGG	38	2348
501421	25499	25518	TGGATCCAGTGCCTACAGCA	41	2349
501422	25505	25524	GGATGCTGGATCCAGTGCCT	74	2350
501423	25618	25637	ACCCAGTACAAGGAAGGACA	78	2351
501424	25623	25642	AGCTTACCCAGTACAAGGAA	31	2352
501425	25628	25647	GGCCCAGCTTACCCAGTACA	48	2353
501426	25717	25736	CTCTTATTCCCTCACCCCTG	77	2354
501427	25782	25801	CACTTGATCTGGGACCCAAA	96	2355
501428	25787	25806	TAGAGCACTTGATCTGGGAC	80	2356
501429	25841	25860	ACTATCACACCACCTCCCAC	85	2357
501430	25846	25865	TGGGAACTATCACACCACCT	95	2358
501431	25851	25870	GTAAATGGGAACTATCACAC	64	2359
501432	25856	25875	CATCTGTAAATGGGAACTAT	49	2360
501433	25861	25880	TTTCCCATCTGTAAATGGGA	0	2361

501434	25866	25885	TGAGGTTTCCCATCTGTAAA	61	2362
501435	25900	25919	GACCTTGGGCAAGTTACCTA	88	2363
501436	25905	25924	TGTGTGACCTTGGGCAAGTT	82	2364
501437	25910	25929	AAATCTGTGTGACCTTGGGC	67	2365
501438	25915	25934	GATTCAAATCTGTGTGACCT	89	2366
501439	25920	25939	ACAGGGATTCAAATCTGTGT	73	2367
501440	25950	25969	GGAAAGGCACAGGCTTTGGG	88	2368
501441	25981	26000	AATGTCTGTTGGTGGGCAGG	77	2369
501442	26005	26024	GGCAAAGTAACATACCTGCT	94	2370
501443	26010	26029	CTTAAGGCAAAGTAACATAC	91	2371
501444	26069	26088	TGTAAGGTCACAGAGCTTGT	54	2372
501445	26102	26121	GGAAACTAACACTCAGAGAG	70	2373
501446	26107	26126	AATGAGGAAACTAACACTCA	62	2374
501447	26165	26184	TTTCTTATCTTCAATCCTCA	95	2375
501448	26170	26189	TCTCATTTCTTATCTTCAAT	92	2376
501449	26175	26194	GGTGCTCTCATTTCTTATCT	81	2377
501450	26200	26219	CCCATCATGACCAGGCCCTG	91	2378
501451	26300	26319	AGGCCTCGGGAAGCACCTGG	89	2379
501452	26305	26324	GGAGCAGGCCTCGGGAAGCA	90	2380
501453	26331	26350	ATGTGGGCTGTGCTGAGAGA	64	2381
501454	26353	26372	AGAAAAAGCAACCAAAGCAC	89	2382
501455	26358	26377	CCTGCAGAAAAAGCAACCAA	81	2383
501456	26363	26382	CCAGACCTGCAGAAAAAGCA	76	2384
501457	26385	26404	CCTAAGGAGTGAGGGTATCT	79	2385
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	48	425

Table 36

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
501303	23656	23675	CTCTGAGTGCAAAGGCTCTG	40	2386
501304	23661	23680	AGCAGCTCTGAGTGCAAAGG	48	2387
501305	23666	23685	CCCAGAGCAGCTCTGAGTGC	45	2388
501306	23671	23690	CTTTCCCCAGAGCAGCTCTG	25	2389
501307	23694	23713	TGACCCTGCTTAGAGGACCT	29	2390
501308	23699	23718	ATTCCTGACCCTGCTTAGAG	5	2391
501309	23704	23723	CCAGCATTCCTGACCCTGCT	14	2392
501310	23709	23728	GAAACCCAGCATTCCTGACC	18	2393
501311	23714	23733	GGACTGAAACCCAGCATTCC	11	2394
501312	23719	23738	AGCCAGGACTGAAACCCAGC	34	2395
501313	23724	23743	GGCAGAGCCAGGACTGAAAC	47	2396

501314	23729	23748	TAGGCGGCAGAGCCAGGACT	43	2397
501315	23734	23753	GGCAGTAGGCGGCAGAGCCA	28	2398
501316	23770	23789	ACCAGAGACAGGCACTGACT	59	2399
501317	23792	23811	TGGACAGCCAGGGAGACTGG	36	2400
501318	23797	23816	CTAATTGGACAGCCAGGGAG	20	2401
501319	23802	23821	ATAGCCTAATTGGACAGCCA	63	2402
501320	23807	23826	CCAGTATAGCCTAATTGGAC	40	2403
501321	23813	23832	GGTCATCCAGTATAGCCTAA	53	2404
501322	23855	23874	GACTTGCCCAGCAACCCATC	65	2405
501323	23860	23879	CTCCAGACTTGCCCAGCAAC	28	2406
501324	23865	23884	CCCACCTCCAGACTTGCCCA	26	2407
501325	23870	23889	ACTTTCCCACCTCCAGACTT	18	2408
501326	23875	23894	ATAGGACTTTCCCACCTCCA	61	2409
501327	23880	23899	CCTTCATAGGACTTTCCCAC	56	2410
501328	23885	23904	TCCTACCTTCATAGGACTTT	40	2411
501329	23890	23909	AAAAATCCTACCTTCATAGG	0	2412
501330	23921	23940	TGCCTCATAATTGCTCCTTC	49	2413
501331	23926	23945	AGGTCTGCCTCATAATTGCT	8	2414
501332	23931	23950	TCCAGAGGTCTGCCTCATAA	64	2415
501333	23957	23976	ATAAAGAGGCTGGGCCATAG	8	2416
501334	23981	24000	CAGGATGTGAACTCACAAAA	59	2417
501335	24024	24043	GTAGCATCTAATAACACCAC	61	2418
501336	24029	24048	GTTCAGTAGCATCTAATAAC	59	2419
501337	24034	24053	TGGGTGTTCAGTAGCATCTA	50	2420
501338	24089	24108	TATGTGACCCCAGGCAAGCT	32	2421
501339	24094	24113	CTCACTATGTGACCCCAGGC	59	2422
501340	24099	24118	TTCTACTCACTATGTGACCC	56	2423
501341	24104	24123	TTTGGTTCTACTCACTATGT	57	2424
501342	24109	24128	CAGACTTTGGTTCTACTCAC	63	2425
501343	24114	24133	AGGTTCAGACTTTGGTTCTA	58	2426
501344	24119	24138	AACCTAGGTTCAGACTTTGG	59	2427
501345	24124	24143	AGTCAAACCTAGGTTCAGAC	68	2428
501346	24129	24148	AGAAGAGTCAAACCTAGGTT	56	2429
501347	24134	24153	TTAGCAGAAGAGTCAAACCT	38	2430
501348	24139	24158	TTAGTTTAGCAGAAGAGTCA	36	2431
501349	24164	24183	GTGTGATGCATCAGAGGGAA	40	2432
501350	24169	24188	CCCTGGTGTGATGCATCAGA	50	2433
501351	24174	24193	CCTTTCCCTGGTGTGATGCA	53	2434
501352	24197	24216	AAATGCTAGGCCTCAAGATG	17	2435
501353	24202	24221	GAAGGAAATGCTAGGCCTCA	64	2436
501354	24207	24226	GGAAGGAAGGAAATGCTAGG	31	2437
501355	24212	24231	TAGGAGGAAGGAAGGAAATG	11	2438

501356	24217	24236	ACTTTTAGGAGGAAGGAAGG	0	2439
501357	24222	24241	CTTTGACTTTTAGGAGGAAG	60	2440
501358	24227	24246	AACTGCTTTGACTTTTAGGA	39	2441
501359	24232	24251	TTAACAACTGCTTTGACTTT	30	2442
501360	24237	24256	GAAAGTTAACAACTGCTTTG	37	2443
501361	24447	24466	TACCATCTGCTCTGTGAAAG	21	2444
501362	24452	24471	CTTCATACCATCTGCTCTGT	29	2445
501363	24483	24502	CAAGCACCTACTGTGTGCCC	13	2446
501364	24488	24507	TTCACCAAGCACCTACTGTG	21	2447
501365	24493	24512	ACATCTTCACCAAGCACCTA	0	2448
501366	24516	24535	CCACTACATGCCCTTTGCTC	51	2449
501367	24557	24576	CTGAAGAAGTGGGCCACCTC	52	2450
501368	24582	24601	ACCCATACCCCATTCCTTCC	22	2451
501369	24587	24606	TCCTCACCCATACCCCATTC	9	2452
501370	24636	24655	AGCCTGGTGACTGCAGGAGA	61	2453
501371	24641	24660	CAGGAAGCCTGGTGACTGCA	45	2454
501372	24666	24685	TCCAGCAGCTGATGGGCAGT	43	2455
501373	24671	24690	TGGACTCCAGCAGCTGATGG	19	2456
501374	24695	24714	CTTGGTGCCCCTAGGATGAC	33	2457
501375	24700	24719	ATTGGCTTGGTGCCCCTAGG	8	2458
501376	24705	24724	ACTTAATTGGCTTGGTGCCC	36	2459
501377	24774	24793	CACTGAGGGCTGTAATTATG	21	2460
501378	24779	24798	AAGGACACTGAGGGCTGTAA	24	2461
501379	24784	24803	GCCTGAAGGACACTGAGGGC	2	2462
501380	24789	24808	AGGCAGCCTGAAGGACACTG	14	2463
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	81	425

Table 37

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
501226	21041	21060	TGTTCCTGACTCCTGGGTGG	26	2464
501227	21046	21065	CTGACTGTTCCTGACTCCTG	61	2465
501228	21091	21110	TGCTGCAATCAGATGCCACC	65	2466
501229	21096	21115	GCCGATGCTGCAATCAGATG	68	2467
501230	21101	21120	GGGATGCCGATGCTGCAATC	69	2468
501231	21119	21138	GTCCAGCAGAAGCTGGTGGG	19	2469
501232	21124	21143	GAGGAGTCCAGCAGAAGCTG	15	2470
501233	21129	21148	GCTGGGAGGAGTCCAGCAGA	12	2471
501234	21134	21153	CTGTGGCTGGGAGGAGTCCA	14	2472
501235	21139	21158	CCCAGCTGTGGCTGGGAGGA	0	2473

501236	21144	21163	TCTGCCCCAGCTGTGGCTGG	0	2474
501237	21149	21168	CTTCCTCTGCCCCAGCTGTG	41	2475
501238	21154	21173	CAGTACTTCCTCTGCCCCAG	40	2476
501239	21159	21178	GCTGTCAGTACTTCCTCTGC	50	2477
501240	21164	21183	ACCTGGCTGTCAGTACTTCC	70	2478
501241	21169	21188	TTGCCACCTGGCTGTCAGTA	68	2479
501242	21174	21193	AGTCCTTGCCACCTGGCTGT	50	2480
501243	21179	21198	CTGCCAGTCCTTGCCACCTG	53	2481
501244	21184	21203	AAACACTGCCAGTCCTTGCC	63	2482
501245	21213	21232	GGAAGTGAGGGTTCAGTTGG	30	2483
501246	21369	21388	CTCTCTGGGCTTCAGTTTCC	45	2484
501247	21374	21393	CTCACCTCTCTGGGCTTCAG	61	2485
501248	21379	21398	GTCTCCTCACCTCTCTGGGC	61	2486
501249	21384	21403	GCTAAGTCTCCTCACCTCTC	71	2487
501250	21490	21509	ATCTGTTTTCCTTCAGAGGG	55	2488
501251	21565	21584	TTCCTTCTCTCTGCTCCCCA	55	2489
501252	21570	21589	CCAAGTTCCTTCTCTCTGCT	15	2490
501253	21575	21594	TGTCCCCAAGTTCCTTCTCT	32	2491
501254	21659	21678	GGTCAAGGTCACTCAGCCAG	62	2492
501255	21681	21700	CCCTATTTTGATGGTGATAC	57	2493
501256	21708	21727	TGGACTCCTGTGAGTTTGGC	67	2494
501257	21713	21732	GCACTTGGACTCCTGTGAGT	25	2495
501258	21718	21737	CACAGGCACTTGGACTCCTG	27	2496
501259	21723	21742	CCTTGCACAGGCACTTGGAC	18	2497
501260	21728	21747	CATGCCCTTGCACAGGCACT	14	2498
501261	21733	21752	CCCTCCATGCCCTTGCACAG	29	2499
501262	21755	21774	AGGCCCATAAAGCTTTGGGA	49	2500
501263	21760	21779	ACAAGAGGCCCATAAAGCTT	26	2501
501264	21765	21784	GATGCACAAGAGGCCCATAA	65	2502
501265	21770	21789	GGTATGATGCACAAGAGGCC	58	2503
501266	21821	21840	CTGGCCACTCTTCAGGCCCC	32	2504
501267	21826	21845	GTGCTCTGGCCACTCTTCAG	0	2505
501268	21873	21892	GATCCATATCTGGATCCCCA	2	2506
501269	21878	21897	GGTCTGATCCATATCTGGAT	20	2507
501270	21933	21952	GCTGATTACAAGCTGATTCT	77	2508
501271	21938	21957	TAACTGCTGATTACAAGCTG	39	2509
501272	21996	22015	ACAATGGAGAAACAAAAGAG	6	2510
501273	22019	22038	TTTGAAGATAAAGTCAGACC	35	2511
501274	22075	22094	GTCTATGCAGGCCTGGAATT	54	2512
501275	22080	22099	CTAAGGTCTATGCAGGCCTG	53	2513
501276	22085	22104	AAACACTAAGGTCTATGCAG	32	2514
501277	22090	22109	ATGATAAACACTAAGGTCTA	43	2515

501278	22095	22114	CTGGGATGATAAACACTAAG	53	2516
501279	22100	22119	CTTCTCTGGGATGATAAACA	0	2517
501280	22105	22124	CTTTCCTTCTCTGGGATGAT	0	2518
501281	22126	22145	AAGCCTTTGGAAAGAGAAGG	31	2519
501282	22131	22150	CCAGGAAGCCTTTGGAAAGA	31	2520
501283	22136	22155	GTCTTCCAGGAAGCCTTTGG	51	2521
501284	22141	22160	CAGCAGTCTTCCAGGAAGCC	54	2522
501285	22146	22165	TAAGGCAGCAGTCTTCCAGG	59	2523
501286	22151	22170	GGTGATAAGGCAGCAGTCTT	56	2524
501287	22156	22175	GAGATGGTGATAAGGCAGCA	78	2525
501288	22162	22181	AACCCAGAGATGGTGATAAG	23	2526
501289	22167	22186	TTCAAAACCCAGAGATGGTG	64	2527
501290	22172	22191	CATCCTTCAAAACCCAGAGA	62	2528
501291	22194	22213	CTGATAATGAGATAAAGCAA	3	2529
501292	22231	22250	CAGAGGCCCTTCCCTGCTTT	42	2530
501293	22266	22285	TGGGAGCCCCCAGTCCACCT	48	2531
501294	22271	22290	GCCAGTGGGAGCCCCCAGTC	0	2532
501295	22311	22330	TGGCCTGGGAGCTGGCCTGG	13	2533
501296	22349	22368	CTCTCAGGCAATCCCAACCT	27	2534
501297	22354	22373	AGGCCCTCTCAGGCAATCCC	62	2535
501298	22359	22378	GGCCCAGGCCCTCTCAGGCA	34	2536
501299	22364	22383	TCTCAGGCCCAGGCCCTCTC	27	2537
501300	22403	22422	CTCCTGGAGAGGGAAGCTGG	31	2538
501301	22408	22427	GGAGGCTCCTGGAGAGGGAA	0	2539
501302	22413	22432	AGTTGGGAGGCTCCTGGAGA	0	2540
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	80	425

Table 38

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
484013	18880	18899	CAGAGGCAGCTATAGGCCTG	43	1299
	20790	20809			
495657	18871	18890	CTATAGGCCTGGATGCCCAA	72	1930
	20781	20800			
501152	19132	19151	GCTGGAACAAAGCCTTGCAG	52	2541
501153	19261	19280	AAGAAGAGGTCGCAGAGTGA	17	2542
501154	19360	19379	GCTACTGGCATTGCTCCTCC	75	2543
501155	19392	19411	ACATGTGGCATTTGTTAGGT	66	2544
501156	19421	19440	GGAACATTAAATTTTAAAAC	20	2545
501157	19775	19794	TAGGATGAGGGTGATAATCC	37	2546

501158	19804	19823	CCTAACTCTAGCTTTGGTTT	63	2547
501159	19809	19828	AGTCACCTAACTCTAGCTTT	20	2548
501160	19854	19873	GCCCTGGGCCAGCTCTGCCC	15	2549
501161	19867	19886	TCTGAGAAAGAGGGCCCTGG	26	2550
501162	19872	19891	CTAAATCTGAGAAAGAGGGC	0	2551
501163	19903	19922	CTGAGGGCAGCAGTGTCTGA	35	2552
501164	19908	19927	CATGCCTGAGGGCAGCAGTG	54	2553
501165	19913	19932	TCTCACATGCCTGAGGGCAG	74	2554
501166	19963	19982	CAGGAAGGCCACACCTCGGG	23	2555
501167	19968	19987	GTGACCAGGAAGGCCACACC	12	2556
501168	19973	19992	TCAAAGTGACCAGGAAGGCC	33	2557
501169	19978	19997	TGATATCAAAGTGACCAGGA	22	2558
501170	19983	20002	ATATCTGATATCAAAGTGAC	3	2559
501171	19988	20007	GCCCAATATCTGATATCAAA	74	2560
501172	20044	20063	GACCCAGGGCCCAGCCCAGG	18	2561
501173	20049	20068	TCTCAGACCCAGGGCCCAGC	55	2562
501174	20093	20112	TGAGACTGGATTCCACCCCC	24	2563
501175	20227	20246	TACAATGCTACGCTGTTGAG	36	2564
501176	20232	20251	ATCTCTACAATGCTACGCTG	73	2565
501177	20237	20256	TCATCATCTCTACAATGCTA	65	2566
501178	20242	20261	GTCCCTCATCATCTCTACAA	22	2567
501179	20247	20266	TCCCAGTCCCTCATCATCTC	49	2568
501180	20252	20271	CAGGCTCCCAGTCCCTCATC	16	2569
501181	20257	20276	GTATTCAGGCTCCCAGTCCC	7	2570
501182	20296	20315	TGCTTGAGGTCAGGGTGTGG	65	2571
501183	20301	20320	TCACTTGCTTGAGGTCAGGG	83	2572
501184	20306	20325	CAAAATCACTTGCTTGAGGT	72	2573
501185	20311	20330	AGAGGCAAAATCACTTGCTT	59	2574
501186	20397	20416	CCACAGCACTCTCTGGGAAG	30	2575
501187	20402	20421	CCGTCCCACAGCACTCTCTG	27	2576
501188	20407	20426	CTTCACCGTCCCACAGCACT	39	2577
501189	20442	20461	GGAAAGCAATCCCCTTCTCC	41	2578
501190	20447	20466	CACCCGGAAAGCAATCCCCT	18	2579
501191	20452	20471	TTTACCACCCGGAAAGCAAT	12	2580
501192	20457	20476	GCTCTTTTACCACCCGGAAA	55	2581
501193	20462	20481	GAGCAGCTCTTTTACCACCC	66	2582
501194	20541	20560	GCAGCACTTGCTTTACACAC	60	2583
501195	20546	20565	CCCAGGCAGCACTTGCTTTA	33	2584
501196	20551	20570	CTGCTCCCAGGCAGCACTTG	0	2585
501197	20639	20658	ACAACCCTGCTACCTACAGA	23	2586
501198	20644	20663	GGAACACAACCCTGCTACCT	37	2587
501199	20668	20687	GTACAAGTTTCTCCACCTAT	80	2588

501200	20673	20692	CCTAGGTACAAGTTTCTCCA	79	2589
501201	20714	20733	GGACTGACCCCAGAGATGGG	22	2590
501202	20719	20738	ACTGAGGACTGACCCCAGAG	0	2591
501203	20724	20743	CCATCACTGAGGACTGACCC	33	2592
501204	20729	20748	CAGCCCCATCACTGAGGACT	18	2593
501205	20771	20790	GGATGCCCAAGTTAGACTGG	24	2594
495670	20776	20795	GGCCTGGATGCCCAAGTTAG	69	1943
501206	20802	20821	CCAGAGCAGCCTCAGAGGCA	55	2595
501207	20807	20826	CAAATCCAGAGCAGCCTCAG	13	2596
501208	20812	20831	ATAAGCAAATCCAGAGCAGC	18	2597
501209	20817	20836	AATCCATAAGCAAATCCAGA	60	2598
501210	20822	20841	GAGCAAATCCATAAGCAAAT	70	2599
501211	20827	20846	TAGCTGAGCAAATCCATAAG	58	2600
501212	20832	20851	CTGCATAGCTGAGCAAATCC	79	2601
501213	20837	20856	GTTTACTGCATAGCTGAGCA	84	2602
501214	20842	20861	TAGAGGTTTACTGCATAGCT	75	2603
501215	20868	20887	GATTCATCTGTGGTAAGAGG	55	2604
501216	20873	20892	TACCTGATTCATCTGTGGTA	44	2605
501217	20878	20897	CTTGGTACCTGATTCATCTG	64	2606
501218	20884	20903	CCAGGACTTGGTACCTGATT	54	2607
501219	20889	20908	GGGTGCCAGGACTTGGTACC	26	2608
501220	20913	20932	GCCATCCCACTGCCAGTGAC	23	2609
501221	20937	20956	ACAGCACCAATGTCACTTTA	55	2610
501222	20950	20969	TCTGCACACTCCCACAGCAC	52	2611
501223	20955	20974	CTCTCTCTGCACACTCCCAC	59	2612
501224	20960	20979	CTGCACTCTCTCTGCACACT	76	2613
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	77	425

Table 39

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
501075	16484	16503	GTCCTGGCCTCTACCCTGAA	57	2614
501076	16510	16529	GAAGGACTGGGATGCTAGGT	65	2615
501077	16515	16534	GGCATGAAGGACTGGGATGC	49	2616
501078	16520	16539	AGGGAGGCATGAAGGACTGG	22	2617
501079	16525	16544	GAAACAGGGAGGCATGAAGG	21	2618
501080	16530	16549	GTAGAGAAACAGGGAGGCAT	34	2619
501081	16535	16554	GAAAAGTAGAGAAACAGGGA	0	2620
501082	16540	16559	AGTTGGAAAAGTAGAGAAAC	11	2621
501083	16546	16565	GAGTCTAGTTGGAAAAGTAG	1	2622

501084	16551	16570	ACTGTGAGTCTAGTTGGAAA	33	2623
501085	16556	16575	CAGAGACTGTGAGTCTAGTT	51	2624
501086	16561	16580	CAGCACAGAGACTGTGAGTC	59	2625
501087	16566	16585	GACTGCAGCACAGAGACTGT	29	2626
501088	16571	16590	AGTCAGACTGCAGCACAGAG	25	2627
501089	16576	16595	AGTTTAGTCAGACTGCAGCA	35	2628
501090	16673	16692	GATGCCTTCCAGGAGGAAGG	19	2629
501091	16678	16697	TTAGGGATGCCTTCCAGGAG	31	2630
501092	16683	16702	TGTTCTTAGGGATGCCTTCC	44	2631
501093	16808	16827	AGGCTGAGTTCTGCTCCTGG	72	2632
501094	16813	16832	GCTAGAGGCTGAGTTCTGCT	83	2633
501095	16818	16837	CATCTGCTAGAGGCTGAGTT	67	2634
501096	16823	16842	TTGGGCATCTGCTAGAGGCT	65	2635
501097	16828	16847	GCTTCTTGGGCATCTGCTAG	75	2636
501098	16833	16852	CCTCTGCTTCTTGGGCATCT	84	2637
501099	16896	16915	TTTCTAAGTACCCTTTACAC	34	2638
501100	16901	16920	AGTGCTTTCTAAGTACCCTT	86	2639
501101	16941	16960	GGAGAGAGAAGGGTGGAACC	26	2640
501102	16949	16968	AGAGGAAGGGAGAGAGAAGG	13	2641
501103	17007	17026	GGGAAAGGTCTTCTCCAGCT	89	2642
501104	17012	17031	CAGGAGGGAAAGGTCTTCTC	60	2643
501105	17017	17036	GGAATCAGGAGGGAAAGGTC	25	2644
501106	17038	17057	GGGTCAAGCAGAGCTTTCTG	66	2645
501107	17109	17128	ATGAATAAACAGGGCCTAGA	37	2646
501108	17114	17133	CTGTGATGAATAAACAGGGC	67	2647
501109	17138	17157	TGAATGACTGAATGCTTGAG	39	2648
501110	17143	17162	TTTGCTGAATGACTGAATGC	53	2649
501111	17207	17226	TCTCATTCATCTGGGCCCTG	72	2650
501112	17244	17263	TGGGAAAAGGTATGTGTGTG	16	2651
501113	17249	17268	CATTATGGGAAAAGGTATGT	8	2652
501114	17254	17273	TTTCTCATTATGGGAAAAGG	38	2653
501115	17259	17278	AGCCCTTTCTCATTATGGGA	47	2654
501116	17264	17283	TACTCAGCCCTTTCTCATTA	43	2655
501117	17269	17288	CCCTGTACTCAGCCCTTTCT	65	2656
501118	17274	17293	CTCACCCCTGTACTCAGCCC	73	2657
501119	17279	17298	CCCATCTCACCCCTGTACTC	66	2658
501120	17284	17303	CCTGTCCCATCTCACCCCTG	13	2659
501121	17289	17308	CCCTGCCTGTCCCATCTCAC	36	2660
501122	17328	17347	AGTCTTCCTTCTCCTCCACC	75	2661
501123	17333	17352	TGGAAAGTCTTCCTTCTCCT	72	2662
501124	17338	17357	TTCTCTGGAAAGTCTTCCTT	66	2663
501125	17420	17439	TTGGTCAGTCTTTTAGCACA	64	2664

501126	17425	17444	CTAGTTTGGTCAGTCTTTTA	68	2665
501127	17450	17469	AGGTAGAGTTCTATTGCTTC	81	2666
501128	17530	17549	GTCTCCACTTGGTGCCTCAC	72	2667
501129	17535	17554	AAGCTGTCTCCACTTGGTGC	61	2668
501130	17540	17559	ACAGGAAGCTGTCTCCACTT	69	2669
501131	17545	17564	CTCACACAGGAAGCTGTCTC	44	2670
501132	17614	17633	AGCTGCCATCTCTGGAGGGT	15	2671
501133	17619	17638	GGCAAAGCTGCCATCTCTGG	52	2672
501134	17624	17643	GTCATGGCAAAGCTGCCATC	7	2673
501135	17664	17683	CCTTTCAGCGGGAGTCCACA	44	2674
501136	17687	17706	TTCCAGGCTCCTCCAGGCAG	36	2675
501137	17692	17711	CTCTCTTCCAGGCTCCTCCA	44	2676
501138	17720	17739	ATGCCACTTCATCAAGGCTG	33	2677
501139	17725	17744	AAGAGATGCCACTTCATCAA	36	2678
501140	17730	17749	TGCCAAAGAGATGCCACTTC	63	2679
501141	17735	17754	CCAAGTGCCAAAGAGATGCC	39	2680
501142	17740	17759	TCAGGCCAAGTGCCAAAGAG	30	2681
501143	17745	17764	GGAAGTCAGGCCAAGTGCCA	38	2682
501144	17750	17769	GTCTAGGAAGTCAGGCCAAG	46	2683
501145	17755	17774	GGGAGGTCTAGGAAGTCAGG	19	2684
501146	17760	17779	CCCCAGGGAGGTCTAGGAAG	32	2685
501147	17765	17784	TCCAGCCCCAGGGAGGTCTA	30	2686
501148	17770	17789	GCTCTTCCAGCCCCAGGGAG	36	2687
501149	17804	17823	AGAGTGAGGGTCAGTACATA	15	2688
501150	17809	17828	GTAGCAGAGTGAGGGTCAGT	28	2689
501151	17933	17952	TAGGTGAGTGAGAAAGTCAC	16	2690
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	78	425

Table 40

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
500994	15257	15276	CATCTGCACCATAATCTGCA	72	2691
500995	15292	15311	TTTACCCAAAAGGTTCACAG	64	2692
500996	15297	15316	ATTGATTTACCCAAAAGGTT	32	2693
500997	15318	15337	GAGTTTGTGTTTCCCATTTC	69	2694
500998	15323	15342	AAAAGGAGTTTGTGTTTCCC	81	2695
500999	15328	15347	ATAAGAAAAGGAGTTTGTGT	30	2696
501000	15333	15352	CTCTAATAAGAAAAGGAGTT	33	2697
501001	15338	15357	TTCTGCTCTAATAAGAAAAG	12	2698
501002	15343	15362	GCTAATTCTGCTCTAATAAG	28	2699

501003	15348	15367	GAATGGCTAATTCTGCTCTA	48	2700
501004	15353	15372	GCTTAGAATGGCTAATTCTG	69	2701
501005	15358	15377	GCAGGGCTTAGAATGGCTAA	59	2702
501006	15363	15382	CAGAGGCAGGGCTTAGAATG	56	2703
501007	15368	15387	GGAAGCAGAGGCAGGGCTTA	68	2704
501008	15373	15392	ACATGGGAAGCAGAGGCAGG	66	2705
501009	15378	15397	AGGTCACATGGGAAGCAGAG	57	2706
501010	15431	15450	TCCTCACTGTGCAGATGAGA	30	2707
501011	15436	15455	AGTCCTCCTCACTGTGCAGA	48	2708
501012	15441	15460	CAACCAGTCCTCCTCACTGT	33	2709
501013	15446	15465	CATCTCAACCAGTCCTCCTC	52	2710
501014	15504	15523	TTAGGGACAAGAATGGAATC	23	2711
501015	15509	15528	AGCAGTTAGGGACAAGAATG	10	2712
501016	15514	15533	CCCACAGCAGTTAGGGACAA	63	2713
501017	15568	15587	TTTTCACAAGGAGAAGCTGA	47	2714
501018	15573	15592	CACCATTTTCACAAGGAGAA	76	2715
501019	15578	15597	GAGTGCACCATTTTCACAAG	71	2716
501020	15646	15665	ATCACAATATATGGGCAAGC	82	2717
501021	15651	15670	TCCCCATCACAATATATGGG	39	2718
501022	15671	15690	CAAGGAATCTCCAAAATACG	37	2719
501023	15703	15722	ATGGCAACACTACTAGCTTG	27	2720
501024	15708	15727	CTGCCATGGCAACACTACTA	56	2721
501025	15729	15748	TAGCTACTGCAGTGGAAGGG	71	2722
501026	15734	15753	AAAAGTAGCTACTGCAGTGG	69	2723
501027	15739	15758	ATTCAAAAAGTAGCTACTGC	59	2724
501028	15744	15763	AGCACATTCAAAAAGTAGCT	59	2725
501029	15804	15823	CTGGACATGATTGCTGAGGA	63	2726
501030	15809	15828	GGACCCTGGACATGATTGCT	74	2727
501031	15814	15833	ATCCAGGACCCTGGACATGA	69	2728
501032	15839	15858	TTCCTGATACCGAACATGGA	22	2729
501033	15876	15895	GGTAAGGCCAAGGAAGTGAG	78	2730
501034	15881	15900	CAAGAGGTAAGGCCAAGGAA	80	2731
501035	15933	15952	ACCTGGGTTTTTGTGTATTC	82	2732
501036	15938	15957	CATACACCTGGGTTTTTGTG	57	2733
501037	15943	15962	TACTCCATACACCTGGGTTT	69	2734
501038	15991	16010	TTATCCACAGAAGATCTCCC	75	2735
501039	16046	16065	CTGAGTGCTGCTAACTTGGG	70	2736
501040	16051	16070	GAAATCTGAGTGCTGCTAAC	78	2737
501041	16082	16101	CACTAAATTAGGAAGCTGGG	79	2738
501043	16105	16124	CCCTCTCTAGGTTTCCCCAT	63	2739
501045	16110	16129	TCCTCCCCTCTCTAGGTTTC	34	2740
501047	16115	16134	CCTCTTCCTCCCCTCTCTAG	24	2741

501049	16120	16139	CTAAGCCTCTTCCTCCCCTC	33	2742
501050	16171	16190	GCCTGCTGCAGGGAGCCAGG	4	2743
501051	16208	16227	GGCCATCAGGACCCTGCAGG	30	2744
501052	16213	16232	AAGTGGGCCATCAGGACCCT	5	2745
501053	16227	16246	GTGTGCCAGGTGGGAAGTGG	0	2746
501054	16232	16251	GCTAGGTGTGCCAGGTGGGA	38	2747
501055	16237	16256	GCTATGCTAGGTGTGCCAGG	62	2748
501056	16242	16261	ACACAGCTATGCTAGGTGTG	22	2749
501057	16247	16266	CCAGCACACAGCTATGCTAG	25	2750
501058	16252	16271	GAGAGCCAGCACACAGCTAT	44	2751
501059	16257	16276	TACTGGAGAGCCAGCACACA	57	2752
501060	16262	16281	CAAACTACTGGAGAGCCAGC	59	2753
501061	16288	16307	TGGGACATCTGGCCCAAAGG	67	2754
501062	16293	16312	CCCACTGGGACATCTGGCCC	77	2755
501063	16305	16324	CTTAAAGCAGGGCCCACTGG	49	2756
501064	16310	16329	GTATCCTTAAAGCAGGGCCC	80	2757
501065	16364	16383	TTCTTTTCTGAAAAGATTAA	16	2758
501066	16369	16388	GTGAGTTCTTTTCTGAAAAG	48	2759
501067	16428	16447	ACTGGTGCCTAAGAGCCCTA	76	2760
501068	16433	16452	CCTCCACTGGTGCCTAAGAG	66	2761
501069	16438	16457	CACTCCCTCCACTGGTGCCT	71	2762
501070	16459	16478	AGAAGACAGCCAGTCAGAGC	67	2763
501071	16464	16483	GGCAGAGAAGACAGCCAGTC	53	2764
501072	16469	16488	CTGAAGGCAGAGAAGACAGC	11	2765
501073	16474	16493	CTACCCTGAAGGCAGAGAAG	0	2766
501074	16479	16498	GGCCTCTACCCTGAAGGCAG	1	2767
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	79	425

Table 41

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
500917	12407	12426	TGTCAGAAAGGACTCCTCTG	37	2768
500918	12412	12431	ACAGCTGTCAGAAAGGACTC	47	2769
500919	12417	12436	CCTCAACAGCTGTCAGAAAG	22	2770
500920	12439	12458	ACCCACCCCAGCCTGTTGCA	56	2771
500921	12474	12493	CAAGCAGATCCACAGTGATG	16	2772
500922	12479	12498	AGTTTCAAGCAGATCCACAG	37	2773
500923	12500	12519	CCCCCAACAATCTAGCCACT	41	2774
500924	12505	12524	AGTTACCCCCAACAATCTAG	16	2775
500925	12510	12529	TTCCCAGTTACCCCCAACAA	16	2776

500926	12515	12534	CTCAGTTCCCAGTTACCCCC	44	2777
500927	12520	12539	CAACCCTCAGTTCCCAGTTA	26	2778
500928	12549	12568	TCTGACTTAGGACTAGGTTA	70	2779
500929	12554	12573	CTCATTCTGACTTAGGACTA	64	2780
500930	12559	12578	ATGTTCTCATTCTGACTTAG	44	2781
500931	12564	12583	GAGTAATGTTCTCATTCTGA	44	2782
500932	12569	12588	CATGAGAGTAATGTTCTCAT	44	2783
500933	12618	12637	GGAAGTGATGTAGGTGAGGG	23	2784
500934	12671	12690	AGCCTAGATGAGCCCTTGGT	65	2785
500935	12676	12695	TTCTCAGCCTAGATGAGCCC	69	2786
500936	12681	12700	CTCCTTTCTCAGCCTAGATG	52	2787
500937	12686	12705	TGGCCCTCCTTTCTCAGCCT	54	2788
500938	12691	12710	ACTCTTGGCCCTCCTTTCTC	26	2789
500939	12696	12715	ACATTACTCTTGGCCCTCCT	59	2790
500940	12779	12798	TTGCTGTTGAATTTGAGGGC	53	2791
500941	12784	12803	AGTACTTGCTGTTGAATTTG	45	2792
500942	12806	12825	CAGCACTAATTTTTACAACT	78	2793
500943	12834	12853	ATCTGTAACATGAGGGTTGG	36	2794
500944	12839	12858	ATCCCATCTGTAACATGAGG	69	2795
500945	12844	12863	CAGTGATCCCATCTGTAACA	67	2796
500946	12890	12909	GCCTGGCTTTGATAACCCTG	63	2797
500947	12895	12914	TTCTAGCCTGGCTTTGATAA	20	2798
500948	12917	12936	CAGACTGGGAGATGGATCTG	31	2799
500949	12922	12941	GGCCACAGACTGGGAGATGG	47	2800
500950	12927	12946	AGTCAGGCCACAGACTGGGA	72	2801
500951	12932	12951	TAAGGAGTCAGGCCACAGAC	47	2802
500952	12937	12956	TGGCTTAAGGAGTCAGGCCA	43	2803
500953	12942	12961	TCTCTTGGCTTAAGGAGTCA	71	2804
500954	12977	12996	GCCCTGCACTCAGCCCTTCA	19	2805
500955	12982	13001	ACAGAGCCCTGCACTCAGCC	54	2806
500956	13026	13045	GACAACCTTCACTCATTCAG	35	2807
500957	13098	13117	ATCCACTAGGGCAGGCTTGG	69	2808
500958	13202	13221	GGCCAGGAGGAAGAGTTTGG	39	2809
500959	13207	13226	TCATAGGCCAGGAGGAAGAG	20	2810
500960	13212	13231	TTACTTCATAGGCCAGGAGG	63	2811
500961	13239	13258	TGGCAGTGGAGGCTGTTCAC	63	2812
500962	13306	13325	GCAGGAACAGGAAGACCACC	0	2813
500963	13311	13330	ATGCTGCAGGAACAGGAAGA	51	2814
500964	13316	13335	GAGTAATGCTGCAGGAACAG	35	2815
500965	13321	13340	ATTGGGAGTAATGCTGCAGG	55	2816
500966	13441	13460	TGGCTCTCTAGATAGGGTGG	75	2817
500967	13485	13504	TAAAAGAAGATGTGGTGATT	0	2818

500968	13490	13509	AAAAATAAAAGAAGATGTGG	0	2819
500969	13495	13514	GCTATAAAAATAAAAGAAGA	0	2820
500970	13500	13519	TAAAGGCTATAAAAATAAAA	0	2821
500971	13542	13561	ATTGCTTAAACAGATAAGCA	6	2822
500972	13547	13566	AGACAATTGCTTAAACAGAT	32	2823
500973	13916	13935	GTTCCTGTTTCCAAGGGACT	59	2824
500974	13921	13940	ACAAGGTTCCTGTTTCCAAG	69	2825
500975	13926	13945	GACAGACAAGGTTCCTGTTT	72	2826
500976	13931	13950	AGAAAGACAGACAAGGTTCC	51	2827
500977	13936	13955	CACTGAGAAAGACAGACAAG	0	2828
500978	13941	13960	CACAGCACTGAGAAAGACAG	36	2829
500979	13962	13981	GCCAGGCACTGTGCTAGATG	63	2830
500980	13967	13986	CCAGTGCCAGGCACTGTGCT	37	2831
500981	13972	13991	TATTACCAGTGCCAGGCACT	13	2832
500982	13977	13996	GTACCTATTACCAGTGCCAG	64	2833
500983	13982	14001	ACTAAGTACCTATTACCAGT	7	2834
500984	14054	14073	AGCTAAAAGCAGGGCTTCCT	0	2835
500985	14177	14196	GCTCCTTGCCAGACTGTGGG	60	2836
500986	14182	14201	AGCCAGCTCCTTGCCAGACT	75	2837
500987	14187	14206	CTTGGAGCCAGCTCCTTGCC	54	2838
500988	14192	14211	TCAGCCTTGGAGCCAGCTCC	35	2839
500989	14197	14216	GCCACTCAGCCTTGGAGCCA	76	2840
500990	14239	14258	GGAAGCAGTAAGGGTGACCA	73	2841
500991	14246	14265	AGCCCTGGGAAGCAGTAAGG	11	2842
500992	14251	14270	TAATAAGCCCTGGGAAGCAG	0	2843
500993	14327	14346	ATCCCCAGAGAGGAAGTGAA	0	2844
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	80	425

Table 42

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
500840	11204	11223	ATAACCACAGCGATAATCAC	45	2845
500841	11209	11228	GGCAGATAACCACAGCGATA	79	2846
500842	11228	11247	CAGCACCCACACCAAGAGGG	38	2847
500843	11318	11337	TCAGAGGCTACTGGCTGGAT	69	2848
500844	11323	11342	GGCTGTCAGAGGCTACTGGC	75	2849
500845	11346	11365	AAAAGGACTCAAGTGAGAGA	24	2850
500846	11351	11370	AACAGAAAAGGACTCAAGTG	4	2851
500847	11356	11375	CAGGGAACAGAAAAGGACTC	30	2852
500848	11361	11380	GGACACAGGGAACAGAAAAG	2	2853

500849	11366	11385	TCAAAGGACACAGGGAACAG	24	2854
500850	11371	11390	GGACATCAAAGGACACAGGG	3	2855
500851	11376	11395	CCTAAGGACATCAAAGGACA	3	2856
500852	11413	11432	GCATGAACAAGGGCAAGTCC	74	2857
500853	11457	11476	AGAACATCCCTATCCCACTG	37	2858
500854	11462	11481	CACAGAGAACATCCCTATCC	59	2859
500855	11509	11528	CCTGTGGATGGCAGAGCCGA	32	2860
500856	11514	11533	CCCAGCCTGTGGATGGCAGA	21	2861
500857	11519	11538	CAGCTCCCAGCCTGTGGATG	0	2862
500858	11553	11572	CATGACAGCCAGGGTCACTG	57	2863
500859	11559	11578	CAAAAACATGACAGCCAGGG	80	2864
500860	11564	11583	TAAGTCAAAAACATGACAGC	24	2865
500861	11569	11588	AACTCTAAGTCAAAAACATG	0	2866
500862	11574	11593	GAACAAACTCTAAGTCAAAA	5	2867
500863	11579	11598	CTAAGGAACAAACTCTAAGT	19	2868
500864	11584	11603	TTCTCCTAAGGAACAAACTC	31	2869
500865	11589	11608	ACAAGTTCTCCTAAGGAACA	28	2870
500866	11594	11613	AGAGTACAAGTTCTCCTAAG	66	2871
500867	11599	11618	TCGCTAGAGTACAAGTTCTC	81	2872
500868	11635	11654	TCCTGACATGATATTAAGTG	50	2873
500869	11640	11659	AATGTTCCTGACATGATATT	5	2874
500870	11707	11726	ATGATGTAAATCCTTGCACC	68	2875
500871	11712	11731	ATTCCATGATGTAAATCCTT	63	2876
500872	11717	11736	CCTACATTCCATGATGTAAA	45	2877
500873	11722	11741	CCCTTCCTACATTCCATGAT	56	2878
500874	11727	11746	ACCAGCCCTTCCTACATTCC	54	2879
500875	11732	11751	TTCATACCAGCCCTTCCTAC	22	2880
500876	11755	11774	AAGCTGAACTGACTGGTTTG	41	2881
500877	11760	11779	CCAGAAAGCTGAACTGACTG	0	2882
500878	11765	11784	AGATCCCAGAAAGCTGAACT	29	2883
500879	11770	11789	AAAGTAGATCCCAGAAAGCT	15	2884
500880	11775	11794	TCACCAAAGTAGATCCCAGA	58	2885
500881	11780	11799	ATCTTTCACCAAAGTAGATC	33	2886
500882	11785	11804	ACCCAATCTTTCACCAAAGT	18	2887
500883	11790	11809	ACTCCACCCAATCTTTCACC	49	2888
500884	11795	11814	CCCCTACTCCACCCAATCTT	14	2889
500885	11800	11819	GCCCTCCCCTACTCCACCCA	32	2890
500886	11805	11824	TCAGTGCCCTCCCCTACTCC	26	2891
500887	11827	11846	TGCCCAGATAACAAAATGTG	29	2892
500888	11832	11851	GGAGATGCCCAGATAACAAA	56	2893
500889	11857	11876	CAAGGATCTAGAAGGCAGGT	59	2894
500890	11862	11881	AGGACCAAGGATCTAGAAGG	28	2895

500891	11867	11886	CTTCAAGGACCAAGGATCTA	30	2896
500892	11872	11891	AGTATCTTCAAGGACCAAGG	72	2897
500893	11893	11912	AGGCAAACTAGGCCACTGGG	20	2898
500894	11898	11917	CACAGAGGCAAACTAGGCCA	4	2899
500895	11920	11939	CTCACAACAGTGGGACCTTA	69	2900
500896	11925	11944	ACCAGCTCACAACAGTGGGA	43	2901
500897	11930	11949	TGTTCACCAGCTCACAACAG	8	2902
500898	11964	11983	CATGGTCTCTACTTGAATAC	14	2903
500899	11969	11988	GAATCCATGGTCTCTACTTG	18	2904
500900	11974	11993	TCACAGAATCCATGGTCTCT	42	2905
500901	11979	11998	TCCCTTCACAGAATCCATGG	36	2906
500902	11984	12003	GGACTTCCCTTCACAGAATC	23	2907
500903	11989	12008	TCACAGGACTTCCCTTCACA	47	2908
500904	12070	12089	ACCTACCCATACTCCCACAG	31	2909
500905	12075	12094	CACCCACCTACCCATACTCC	15	2910
500906	12080	12099	GCATGCACCCACCTACCCAT	41	2911
500907	12085	12104	CCCCAGCATGCACCCACCTA	14	2912
500908	12090	12109	GCTTCCCCCAGCATGCACCC	36	2913
500909	12138	12157	GGCACAGGACAGCCCTCCAA	54	2914
500910	12169	12188	TGTCCTGATGAACTCTGCAA	54	2915
500911	12242	12261	TGTCAGAGGGCTCTTCTGAA	0	2916
500912	12247	12266	GCAGGTGTCAGAGGGCTCTT	60	2917
500913	12285	12304	TCTCATGCTAGGTCCTGTGC	80	2918
500914	12392	12411	CTCTGCTACATCAAAACTTG	25	2919
500915	12397	12416	GACTCCTCTGCTACATCAAA	38	2920
500916	12402	12421	GAAAGGACTCCTCTGCTACA	23	2921
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	75	425

Table 43

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
501824	27442	27461	TTGGGTCTGATCAATTATTA	14	2922
501825	27447	27466	TGTGGTTGGGTCTGATCAAT	50	2923
501826	27458	27477	GGTTTCTGGGCTGTGGTTGG	20	2924
501827	27469	27488	GATGCTGGGCCGGTTTCTGG	40	2925
501828	27551	27570	CAGGAGATCTGCCTGTCCAA	48	2926
501829	27556	27575	TAGCTCAGGAGATCTGCCTG	32	2927
501830	27561	27580	AGCAGTAGCTCAGGAGATCT	50	2928
501831	27566	27585	TAATTAGCAGTAGCTCAGGA	65	2929
501832	27613	27632	AGGTTTGAGAGGCAGAGGGA	6	2930

501833	27618	27637	CCAGCAGGTTTGAGAGGCAG	29	2931
501834	27623	27642	TTCTGCCAGCAGGTTTGAGA	40	2932
501835	27628	27647	TGAGCTTCTGCCAGCAGGTT	64	2933
501836	27633	27652	CCAGGTGAGCTTCTGCCAGC	43	2934
501837	27638	27657	GCTTGCCAGGTGAGCTTCTG	61	2935
501838	27643	27662	TCTTTGCTTGCCAGGTGAGC	67	2936
501839	27673	27692	TCCAGGGAGAGACCAACAGG	7	2937
501840	27678	27697	TCTGGTCCAGGGAGAGACCA	0	2938
501841	27683	27702	AAATCTCTGGTCCAGGGAGA	26	2939
501842	27688	27707	GTGAAAAATCTCTGGTCCAG	12	2940
501843	27693	27712	AAGTGGTGAAAAATCTCTGG	5	2941
501844	27698	27717	GCACAAAGTGGTGAAAAATC	41	2942
501845	27703	27722	CCATGGCACAAAGTGGTGAA	41	2943
501846	27708	27727	GGGTTCCATGGCACAAAGTG	1	2944
501847	27761	27780	ATTAAATACTCTAAAACACT	0	2945
501848	27766	27785	CTTGTATTAAATACTCTAAA	5	2946
501849	27771	27790	TGCACCTTGTATTAAATACT	77	2947
501850	27776	27795	TCCAATGCACCTTGTATTAA	79	2948
501851	27781	27800	TGAAATCCAATGCACCTTGT	69	2949
501852	27786	27805	TCCTTTGAAATCCAATGCAC	76	2950
501853	27791	27810	TAGTTTCCTTTGAAATCCAA	64	2951
501854	27849	27868	TGTTACTACATGTCTAATCA	32	2952
501855	27854	27873	GCACCTGTTACTACATGTCT	87	2953
501856	27859	27878	AAAAGGCACCTGTTACTACA	57	2954
501857	27864	27883	TAATAAAAAGGCACCTGTTA	32	2955
501858	27992	28011	AAATAACAAAGGTATTTTCA	1	2956
501859	27997	28016	CAAATAAATAACAAAGGTAT	14	2957
501860	28002	28021	TGACACAAATAAATAACAAA	18	2958
501861	28026	28045	TCACAGAATTATCAGCAGTA	92	2959
501862	28031	28050	ATAAATCACAGAATTATCAG	0	2960
501863	28054	28073	CATTTCCTTCACTTACCAAT	41	2961
501864	28078	28097	CACTTATCTCTTATGGAAAT	47	2962
501865	28083	28102	ATTTTCACTTATCTCTTATG	35	2963
501866	28088	28107	TCTAAATTTTCACTTATCTC	48	2964
501867	28093	28112	TGACATCTAAATTTTCACTT	63	2965
501868	28098	28117	ACAAATGACATCTAAATTTT	0	2966
501869	28103	28122	GGGAAACAAATGACATCTAA	58	2967
501870	28127	28146	ACACAATATCCATGGACTTG	59	2968
501871	28132	28151	CTGACACACAATATCCATGG	75	2969
501872	28185	28204	ATTTCCTTACAGGGTATTGG	53	2970
501873	28210	28229	GGCCAAGCCCCATTCCTAAG	7	2971
501874	28215	28234	TTGCTGGCCAAGCCCCATTC	0	2972

501875	28220	28239	GCCACTTGCTGGCCAAGCCC	22	2973
501876	28269	28288	GGTGAAGAGCATGGACTCTG	41	2974
501877	28293	28312	GCAGGGAAGGCAGCAGTGTG	39	2975
501878	28298	28317	CAATGGCAGGGAAGGCAGCA	55	2976
501879	28358	28377	ACTTGTGATACAAAATTCTG	41	2977
501880	28363	28382	AAGACACTTGTGATACAAAA	66	2978
501881	28454	28473	AAGCTTAGAAGGCCCTGCTT	44	2979
501882	28459	28478	ATGAGAAGCTTAGAAGGCCC	41	2980
501883	28464	28483	AGCTCATGAGAAGCTTAGAA	74	2981
501884	28469	28488	TGCTGAGCTCATGAGAAGCT	82	2982
501885	28474	28493	ACTGTTGCTGAGCTCATGAG	37	2983
501886	28479	28498	AAACCACTGTTGCTGAGCTC	78	2984
501887	28484	28503	AGTAAAAACCACTGTTGCTG	60	2985
501888	28489	28508	GCTGCAGTAAAAACCACTGT	66	2986
501889	28515	28534	CTGGTTCCATGCTCTTAGGT	63	2987
501890	28520	28539	AGGCTCTGGTTCCATGCTCT	71	2988
501891	28525	28544	ACAACAGGCTCTGGTTCCAT	38	2989
501892	28530	28549	TCTGAACAACAGGCTCTGGT	19	2990
501893	28535	28554	TGTCCTCTGAACAACAGGCT	52	2991
501894	28540	28559	ATCCTTGTCCTCTGAACAAC	36	2992
501895	28545	28564	GCCTAATCCTTGTCCTCTGA	54	2993
501896	28550	28569	TCAGAGCCTAATCCTTGTCC	53	2994
501897	28555	28574	CTTTCTCAGAGCCTAATCCT	39	2995
501898	28560	28579	CCTTCCTTTCTCAGAGCCTA	50	2996
501899	28565	28584	AATGACCTTCCTTTCTCAGA	19	2997
501900	28570	28589	CACCAAATGACCTTCCTTTC	66	2998
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	79	425

Table 44

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
501901	28575	28594	AAATCCACCAAATGACCTTC	42	2999
501902	28580	28599	GAACTAAATCCACCAAATGA	13	3000
501903	28585	28604	AGGATGAACTAAATCCACCA	65	3001
501904	28590	28609	GCAAAAGGATGAACTAAATC	4	3002
501905	28595	28614	GAAGAGCAAAAGGATGAACT	0	3003
501906	28600	28619	CACAGGAAGAGCAAAAGGAT	0	3004
501907	28605	28624	CCAAACACAGGAAGAGCAAA	0	3005
501908	28610	28629	AGAAACCAAACACAGGAAGA	33	3006
501909	28615	28634	GCCCCAGAAACCAAACACAG	20	3007

501910	28620	28639	CTCCAGCCCCAGAAACCAAA	45	3008
501911	28625	28644	AATCTCTCCAGCCCCAGAAA	36	3009
501912	28787	28806	CCTGGCCTTTCTCAGCTGGG	25	3010
501913	28792	28811	TCTAGCCTGGCCTTTCTCAG	0	3011
501914	28797	28816	TGAATTCTAGCCTGGCCTTT	44	3012
501915	28802	28821	GAGACTGAATTCTAGCCTGG	48	3013
501916	28807	28826	ATCCAGAGACTGAATTCTAG	71	3014
501917	28829	28848	AGAAGAAGAGGCCTGATGGG	29	3015
501918	28834	28853	GATGGAGAAGAAGAGGCCTG	59	3016
501919	28839	28858	GCCTGGATGGAGAAGAAGAG	0	3017
501920	28844	28863	AGGCAGCCTGGATGGAGAAG	5	3018
501921	28849	28868	TGCTGAGGCAGCCTGGATGG	26	3019
501922	28854	28873	TCTGCTGCTGAGGCAGCCTG	12	3020
501923	28859	28878	CTTACTCTGCTGCTGAGGCA	47	3021
501924	28864	28883	TTGTCCTTACTCTGCTGCTG	55	3022
501925	28901	28920	GGCTGGTCTCTCTGGGAAGG	25	3023
501926	28906	28925	TAGAGGGCTGGTCTCTCTGG	40	3024
501927	28911	28930	CTGCTTAGAGGGCTGGTCTC	40	3025
501928	28916	28935	CCCCACTGCTTAGAGGGCTG	34	3026
501929	28921	28940	CCAGGCCCCACTGCTTAGAG	26	3027
501930	28926	28945	GAGCTCCAGGCCCCACTGCT	7	3028
501931	28986	29005	GGAAACCTAGCTTCCAGAAA	53	3029
501932	29010	29029	TTTAGGCTATGGTCTGAGCA	78	3030
501933	29015	29034	TGAGGTTTAGGCTATGGTCT	68	3031
501934	29044	29063	GATGCTCCAGGTGGGCCAGA	68	3032
501935	29049	29068	AGGTGGATGCTCCAGGTGGG	0	3033
501936	29054	29073	CCTCTAGGTGGATGCTCCAG	18	3034
501937	29059	29078	GGCATCCTCTAGGTGGATGC	22	3035
501938	29064	29083	CTAGTGGCATCCTCTAGGTG	50	3036
501939	29069	29088	CTCCTCTAGTGGCATCCTCT	33	3037
501940	29074	29093	CCAGGCTCCTCTAGTGGCAT	55	3038
501941	29079	29098	GGCATCCAGGCTCCTCTAGT	53	3039
501942	29103	29122	GACTCTAGCCCCCCAGACTC	29	3040
501943	29139	29158	TCTGCCTGATTCCCTTTCTT	30	3041
501944	29144	29163	AGCAGTCTGCCTGATTCCCT	81	3042
501945	29149	29168	TGTTCAGCAGTCTGCCTGAT	50	3043
501946	29154	29173	CTTACTGTTCAGCAGTCTGC	70	3044
501947	29159	29178	TCATACTTACTGTTCAGCAG	65	3045
501948	29164	29183	CAAAGTCATACTTACTGTTC	29	3046
501949	29169	29188	GCCTACAAAGTCATACTTAC	17	3047
501950	29193	29212	GGTGAATAGCTATGTCTAAA	80	3048
501951	29198	29217	AGCTTGGTGAATAGCTATGT	76	3049

501952	29222	29241	AGCAAACTGTGAAAAGCTTA	59	3050
501953	29227	29246	TTAAAAGCAAACTGTGAAAA	2	3051
501954	29232	29251	GCCTGTTAAAAGCAAACTGT	48	3052
501955	29237	29256	CAAGAGCCTGTTAAAAGCAA	12	3053
501956	29242	29261	GCCTACAAGAGCCTGTTAAA	30	3054
501957	29247	29266	GTGCAGCCTACAAGAGCCTG	69	3055
501958	29252	29271	AGCATGTGCAGCCTACAAGA	57	3056
501959	29257	29276	AGGGAAGCATGTGCAGCCTA	76	3057
501960	29262	29281	TTTCTAGGGAAGCATGTGCA	76	3058
501961	29267	29286	ACAAGTTTCTAGGGAAGCAT	40	3059
501962	29272	29291	GGAAGACAAGTTTCTAGGGA	52	3060
501963	29277	29296	AGAAGGGAAGACAAGTTTCT	30	3061
501964	29282	29301	ATCGCAGAAGGGAAGACAAG	28	3062
501965	29327	29346	AGTGACGAGATGTCCAATTT	59	3063
501966	29361	29380	ACAACTCTCTTGTTGGGAGG	71	3064
501967	29366	29385	AGGGTACAACTCTCTTGTTG	59	3065
501968	29371	29390	AAAACAGGGTACAACTCTCT	73	3066
501969	29376	29395	AGCTAAAAACAGGGTACAAC	13	3067
501970	29383	29402	CCAGGGTAGCTAAAAACAGG	3	3068
501971	29388	29407	TCTCCCCAGGGTAGCTAAAA	0	3069
501972	29393	29412	CAGCCTCTCCCCAGGGTAGC	33	3070
501973	29417	29436	TAGCCCTGTTCTAGACTCCT	36	3071
501974	29440	29459	TAGCCCCTTGTTGCCCCCCA	43	3072
501975	29445	29464	AATGGTAGCCCCTTGTTGCC	11	3073
501976	29450	29469	AGGGAAATGGTAGCCCCTTG	63	3074
501977	29475	29494	GTAGACTCTCCATGAGCCTA	60	3075
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	77	425

Table 45

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
501978	30937	30956	GGGCCCACAAACCCTGAGAA	20	3076
501979	30962	30981	AGGCACACCCAGGGCCATGG	68	3077
501980	30967	30986	AAGCTAGGCACACCCAGGGC	48	3078
501981	30972	30991	GCACTAAGCTAGGCACACCC	77	3079
501982	30977	30996	CTGTGGCACTAAGCTAGGCA	78	3080
501983	30982	31001	GTTTACTGTGGCACTAAGCT	80	3081
501984	30987	31006	TGAGTGTTTACTGTGGCACT	56	3082
501985	31026	31045	ACTGGGCTTCATCTCCCCTC	0	3083
501986	31031	31050	GTCCTACTGGGCTTCATCTC	28	3084

501987	31074	31093	GGCACTGCAGGCCACTCCTG	41	3085
501988	31185	31204	AAGGGAGGCCTTGCACTTAC	26	3086
501989	31236	31255	GCCCTTCAGCTTGTGCAGGG	36	3087
501990	31241	31260	ATGAGGCCCTTCAGCTTGTG	57	3088
501991	31246	31265	TCAGGATGAGGCCCTTCAGC	67	3089
501992	31251	31270	AGCACTCAGGATGAGGCCCT	50	3090
501993	31274	31293	ACAAAGTGGGTGTTAAAAGA	22	3091
501994	31279	31298	TTTTCACAAAGTGGGTGTTA	40	3092
501995	31315	31334	GCTTTTAACCTCCCCCCAAA	6	3093
501996	31366	31385	CCTCGACTGAGTGTGAACTC	66	3094
501997	31371	31390	CAAACCCTCGACTGAGTGTG	46	3095
501998	31376	31395	TTATGCAAACCCTCGACTGA	24	3096
501999	31490	31509	ACATTTGGGCAAGGCAGACA	14	3097
502000	31525	31544	AGGGAATAAAATACAGAGTT	0	3098
502001	31530	31549	CTTCCAGGGAATAAAATACA	0	3099
502002	31535	31554	GCCACCTTCCAGGGAATAAA	0	3100
502003	31540	31559	CTCCTGCCACCTTCCAGGGA	0	3101
502004	31545	31564	GTGACCTCCTGCCACCTTCC	54	3102
502005	31606	31625	TTTACCTGGATGGGAAAGTA	0	3103
502006	31612	31631	CAGCACTTTACCTGGATGGG	2	3104
502007	31617	31636	ACTCACAGCACTTTACCTGG	0	3105
502008	31622	31641	ACAACACTCACAGCACTTTA	1	3106
502009	31688	31707	ACTTGCTTCCCTGTGGGTGG	0	3107
502010	31693	31712	TCTAAACTTGCTTCCCTGTG	16	3108
502011	31698	31717	CTTGGTCTAAACTTGCTTCC	60	3109
502012	31703	31722	ACCAACTTGGTCTAAACTTG	57	3110
502013	31768	31787	GGATACTCAGAAGAGCAGTG	79	3111
502014	31792	31811	CCTCAGGGCTGGCCCAAAGA	61	3112
502015	31797	31816	CAGGACCTCAGGGCTGGCCC	74	3113
502016	31802	31821	CCTGTCAGGACCTCAGGGCT	40	3114
502017	31807	31826	ATTTCCCTGTCAGGACCTCA	46	3115
502018	31828	31847	TGAAAGCCAAACTGAGCCAC	55	3116
502019	31866	31885	AGCTTGCAGACCAGGCAGGG	60	3117
502020	31871	31890	AGCCCAGCTTGCAGACCAGG	55	3118
502021	31876	31895	TCACCAGCCCAGCTTGCAGA	30	3119
502022	31881	31900	GTGCCTCACCAGCCCAGCTT	49	3120
502023	31904	31923	ACATGCATCAGGGCCAGATG	35	3121
502024	31932	31951	AGTTATCCTCAATTCACCAG	66	3122
502025	31937	31956	GCCAGAGTTATCCTCAATTC	76	3123
502026	31942	31961	ATCCTGCCAGAGTTATCCTC	71	3124
502027	31947	31966	TCAGGATCCTGCCAGAGTTA	63	3125
502028	31952	31971	AACCTTCAGGATCCTGCCAG	60	3126

502029	31957	31976	GGGAAAACCTTCAGGATCCT	51	3127
502030	31975	31994	ACAGGTCTTTCCCCTGTGGG	31	3128
502031	31980	31999	GCCAGACAGGTCTTTCCCCT	65	3129
502032	32052	32071	CTTCAGCACCCCTACCTTCT	45	3130
502033	32057	32076	CCACTCTTCAGCACCCCTAC	53	3131
502034	32062	32081	TGCCTCCACTCTTCAGCACC	60	3132
502035	32110	32129	ATATACACCACCCTGCACCC	30	3133
502036	32115	32134	AGCAAATATACACCACCCTG	67	3134
502037	32120	32139	ACAACAGCAAATATACACCA	73	3135
502038	32125	32144	GACTCACAACAGCAAATATA	68	3136
502039	32130	32149	TCACTGACTCACAACAGCAA	60	3137
502040	32135	32154	CTCAGTCACTGACTCACAAC	83	3138
502041	32140	32159	AGGATCTCAGTCACTGACTC	68	3139
502042	32146	32165	CACACCAGGATCTCAGTCAC	61	3140
502043	32167	32186	CCAGCCACTGCCCCCAGGCA	38	3141
502044	32172	32191	GTTACCCAGCCACTGCCCCC	33	3142
502045	32177	32196	GCAGGGTTACCCAGCCACTG	76	3143
502046	32182	32201	AGGATGCAGGGTTACCCAGC	80	3144
502047	32187	32206	AGTGAAGGATGCAGGGTTAC	13	3145
502048	32192	32211	AATGCAGTGAAGGATGCAGG	52	3146
502049	32223	32242	AGGAGCTGGCCCTGCCACCC	48	3147
502050	32228	32247	GCAGAAGGAGCTGGCCCTGC	64	3148
502051	32233	32252	GATGAGCAGAAGGAGCTGGC	56	3149
502052	32238	32257	CTAAGGATGAGCAGAAGGAG	42	3150
502053	32243	32262	TTAGGCTAAGGATGAGCAGA	60	3151
502054	32248	32267	TGGGCTTAGGCTAAGGATGA	53	3152
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	79	425

Table 46

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	77	425
502055	33408	33427	TCTTCATTACATGATTACTG	66	3153
502056	33413	33432	GCAGATCTTCATTACATGAT	81	3154
502057	33449	33468	ACCAGGAAGGGAGTAGGTGG	0	3155
502058	33454	33473	GTCCCACCAGGAAGGGAGTA	0	3156
502059	33459	33478	CCAGAGTCCCACCAGGAAGG	0	3157
502060	33464	33483	AAAGACCAGAGTCCCACCAG	15	3158
502061	33489	33508	GGGCCAGATGAGCTGTTCTG	26	3159
502062	33513	33532	GTGCCAACAGAAGGGATACA	68	3160

502063	33518	33537	CACCTGTGCCAACAGAAGGG	36	3161
502064	33523	33542	AACCCCACCTGTGCCAACAG	53	3162
502065	33557	33576	GGCTGGTGGTCTCGGTGGCT	61	3163
502066	33562	33581	CAGGTGGCTGGTGGTCTCGG	38	3164
502067	33567	33586	TCTTCCAGGTGGCTGGTGGT	32	3165
502068	33572	33591	GCTCCTCTTCCAGGTGGCTG	61	3166
502069	33577	33596	TGTCTGCTCCTCTTCCAGGT	63	3167
502070	33582	33601	GGCACTGTCTGCTCCTCTTC	64	3168
502071	33636	33655	TTCCTAGTCTCCTCTCCAAG	24	3169
502072	33658	33677	ATTCTAAGCTTAGAGAGAGT	28	3170
502073	33663	33682	AGGTGATTCTAAGCTTAGAG	53	3171
502074	33668	33687	TGGACAGGTGATTCTAAGCT	66	3172
502075	33673	33692	GCAGATGGACAGGTGATTCT	72	3173
502076	33678	33697	ATGAGGCAGATGGACAGGTG	66	3174
502077	33683	33702	GTGAAATGAGGCAGATGGAC	52	3175
502078	33688	33707	TATCAGTGAAATGAGGCAGA	16	3176
502079	33693	33712	AAGCCTATCAGTGAAATGAG	8	3177
502080	33698	33717	TCAGTAAGCCTATCAGTGAA	0	3178
502081	33703	33722	GTGCCTCAGTAAGCCTATCA	56	3179
502082	33708	33727	TCTCTGTGCCTCAGTAAGCC	32	3180
502083	33729	33748	TGACCTTGGGATAGTCCCTC	84	3181
502084	33734	33753	CTTTGTGACCTTGGGATAGT	61	3182
502085	33740	33759	CTTAAGCTTTGTGACCTTGG	69	3183
502086	33745	33764	TACTACTTAAGCTTTGTGAC	59	3184
502087	33750	33769	CCTGCTACTACTTAAGCTTT	30	3185
502088	33755	33774	CTAGTCCTGCTACTACTTAA	43	3186
502089	33760	33779	CTACACTAGTCCTGCTACTA	16	3187
502090	33765	33784	GGTTCCTACACTAGTCCTGC	59	3188
502091	33802	33821	CAGGAGTAAGACCATGGGCC	59	3189
502092	33807	33826	TAACACAGGAGTAAGACCAT	57	3190
502093	33812	33831	GAAAGTAACACAGGAGTAAG	45	3191
502094	33817	33836	ATGGTGAAAGTAACACAGGA	54	3192
502095	33846	33865	TGCTTAAGTTTACACAGCAC	66	3193
502096	33851	33870	AGGCTTGCTTAAGTTTACAC	62	3194
502097	33856	33875	AGCAAAGGCTTGCTTAAGTT	65	3195
502098	33861	33880	AGAAGAGCAAAGGCTTGCTT	79	3196
502099	33866	33885	CCCACAGAAGAGCAAAGGCT	80	3197
502100	33871	33890	TCAGACCCACAGAAGAGCAA	69	3198
502101	33893	33912	AGCAGTGCATAGAGGAAAAA	16	3199
502102	33898	33917	ACCACAGCAGTGCATAGAGG	60	3200
502103	33903	33922	GTCCCACCACAGCAGTGCAT	49	3201
502104	33908	33927	GGCTTGTCCCACCACAGCAG	42	3202

502105	33913	33932	AGATAGGCTTGTCCCACCAC	54	3203
502106	33918	33937	TGCTCAGATAGGCTTGTCCC	71	3204
502107	33958	33977	CAAGTCACTCTTTATACCCT	53	3205
502108	33963	33982	CCTATCAAGTCACTCTTTAT	18	3206
502109	33968	33987	ACATTCCTATCAAGTCACTC	58	3207
502110	34017	34036	CCCAACACGATGCCCAGGCC	70	3208
502111	34053	34072	TCCTCTTGCTGCCTGTTTCC	34	3209
502112	34058	34077	TTGTGTCCTCTTGCTGCCTG	59	3210
502113	34063	34082	TGCTCTTGTGTCCTCTTGCT	68	3211
502114	34098	34117	AAGGATACCGCCAATGAAGG	65	3212
502115	34155	34174	TCATGTCACACTCCCCTCCC	58	3213
502116	34179	34198	CATCTGACCAGCTCTGATCT	52	3214
502117	34184	34203	GTAGGCATCTGACCAGCTCT	68	3215
502118	34189	34208	AGAATGTAGGCATCTGACCA	57	3216
502119	34211	34230	TGCCCTTGCTGTAGGACCCA	84	3217
502120	34216	34235	GTCAATGCCCTTGCTGTAGG	70	3218
502121	34221	34240	TGCAAGTCAATGCCCTTGCT	44	3219
502122	34226	34245	CACAGTGCAAGTCAATGCCC	62	3220
502123	34231	34250	TGGGACACAGTGCAAGTCAA	55	3221
502124	34267	34286	AGGCTCTGATGGGACATTTG	65	3222
502125	34301	34320	CAGGTGGCTCTTTAAATCAT	59	3223
502126	34306	34325	GGCCCCAGGTGGCTCTTTAA	32	3224
502127	34312	34331	CCAGTGGGCCCCAGGTGGCT	63	3225
502128	34317	34336	GTCACCCAGTGGGCCCCAGG	46	3226
502129	34340	34359	CCTGGGCTGCTGGATGAAGA	0	3227
502130	34345	34364	TTTTCCCTGGGCTGCTGGAT	28	3228
502131	34350	34369	TGCACTTTTCCCTGGGCTGC	70	3229

Table 47

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	78	425
502132	34391	34410	TCACAGCAAATTATCCTGCA	49	3230
502133	34396	34415	GGAGGTCACAGCAAATTATC	41	3231
502134	34401	34420	CCTGTGGAGGTCACAGCAAA	52	3232
502135	34460	34479	TAAGCCATTCCTTGGATGAC	72	3233
502136	34465	34484	AGGTCTAAGCCATTCCTTGG	58	3234
502137	34470	34489	CTGAAAGGTCTAAGCCATTC	59	3235
502138	34553	34572	TTTGTCCCCTTCCTATGGCT	49	3236
502139	34605	34624	CAGGCCTGGGATAGTTACCC	8	3237

502140	34610	34629	ATGGCCAGGCCTGGGATAGT	33	3238
502141	34615	34634	AGCTGATGGCCAGGCCTGGG	7	3239
502142	34620	34639	TCCTGAGCTGATGGCCAGGC	40	3240
502143	34625	34644	CTTGCTCCTGAGCTGATGGC	20	3241
502144	34630	34649	GGAAACTTGCTCCTGAGCTG	62	3242
502145	34635	34654	AACTTGGAAACTTGCTCCTG	52	3243
502146	34640	34659	TGGGAAACTTGGAAACTTGC	66	3244
502147	34676	34695	GGCATTGAGGGAAGAGCTGG	42	3245
502148	34681	34700	AGGCAGGCATTGAGGGAAGA	53	3246
502149	34686	34705	AAGGCAGGCAGGCATTGAGG	62	3247
502150	34691	34710	TGAAAAAGGCAGGCAGGCAT	63	3248
502151	34696	34715	TTTGATGAAAAAGGCAGGCA	49	3249
502152	34701	34720	CTAGTTTTGATGAAAAAGGC	53	3250
502153	34706	34725	TTGTGCTAGTTTTGATGAAA	41	3251
502154	34739	34758	TAGCTCTCAGTGAAGCTGGA	83	3252
502155	34826	34845	GAGCAGATCTCAAAATCTCG	70	3253
502156	34868	34887	ACAGCAGCAGTCTAATCCAT	73	3254
502157	34873	34892	GGGAAACAGCAGCAGTCTAA	49	3255
502158	34878	34897	TAAATGGGAAACAGCAGCAG	62	3256
502159	34883	34902	CCAAATAAATGGGAAACAGC	15	3257
502160	34888	34907	ACTCCCCAAATAAATGGGAA	13	3258
502161	34893	34912	CAGCTACTCCCCAAATAAAT	0	3259
502162	34898	34917	ACTCTCAGCTACTCCCCAAA	56	3260
502163	34903	34922	AACCAACTCTCAGCTACTCC	76	3261
502164	34931	34950	CAAACAGATTAAAGTTGCTC	80	3262
502165	35006	35025	AATGTGAGCAAGACTCCCTC	58	3263
502166	35167	35186	TTGGGAGCCTCCTGGCAGAG	0	3264
502167	35192	35211	GCCCAGGTTTTCTGTGACTC	65	3265
502168	35197	35216	CAAGAGCCCAGGTTTTCTGT	53	3266
502169	35220	35239	GTCACTGGCCACCAGCAGAA	44	3267
502170	35225	35244	GCAGAGTCACTGGCCACCAG	59	3268
502171	35230	35249	TGGAAGCAGAGTCACTGGCC	48	3269
502172	35263	35282	TGCAAAGTGCCCCTTCCCTG	67	3270
502173	35268	35287	AGTGCTGCAAAGTGCCCCTT	61	3271
502174	35273	35292	ACCTGAGTGCTGCAAAGTGC	61	3272
502175	35278	35297	CTCCCACCTGAGTGCTGCAA	83	3273
502176	35283	35302	TGACACTCCCACCTGAGTGC	60	3274
502177	35288	35307	ATCAATGACACTCCCACCTG	59	3275
502178	35318	35337	TTTTGGCTGCCCTGCCTCAA	36	3276
502179	35323	35342	GGTCTTTTTGGCTGCCCTGC	82	3277
502180	35345	35364	GATAACAAGGAATGAACACG	8	3278
502181	35350	35369	TCCTGGATAACAAGGAATGA	36	3279

502182	35356	35375	TACAATTCCTGGATAACAAG	0	3280
502183	35361	35380	AGAAATACAATTCCTGGATA	9	3281
502184	35366	35385	CTTCTAGAAATACAATTCCT	37	3282
502185	35371	35390	ACAAACTTCTAGAAATACAA	0	3283
502186	35376	35395	GTGAAACAAACTTCTAGAAA	62	3284
502187	35401	35420	TTTGTCCACATATCTGATTG	40	3285
502188	35406	35425	TTATCTTTGTCCACATATCT	44	3286
502189	35411	35430	ATACCTTATCTTTGTCCACA	81	3287
502190	35416	35435	AATAAATACCTTATCTTTGT	0	3288
502191	35421	35440	GCTTCAATAAATACCTTATC	88	3289
502192	35426	35445	GTAATGCTTCAATAAATACC	67	3290
502193	35431	35450	TAGAAGTAATGCTTCAATAA	0	3291
502194	35436	35455	CCTCTTAGAAGTAATGCTTC	75	3292
502195	35441	35460	ATTTCCCTCTTAGAAGTAAT	30	3293
502196	35446	35465	CCAAAATTTCCCTCTTAGAA	39	3294
502197	35519	35538	TATTCTACAGCACAGCTCTC	24	3295
502198	35560	35579	TCAAAATCCCTCAGTTCCAT	25	3296
502199	35565	35584	CCTTATCAAAATCCCTCAGT	53	3297
502200	35570	35589	TCTGTCCTTATCAAAATCCC	23	3298
502201	35575	35594	AGCTATCTGTCCTTATCAAA	8	3299
502202	35607	35626	ATCATTTTTATATCATTTTC	0	3300
502203	35612	35631	TTGATATCATTTTTATATCA	0	3301
502204	35617	35636	ATGGGTTGATATCATTTTTA	61	3302
502205	35622	35641	GTTATATGGGTTGATATCAT	48	3303
502206	35627	35646	TTGAGGTTATATGGGTTGAT	68	3304
502207	35632	35651	CAAAATTGAGGTTATATGGG	19	3305
502208	35656	35675	ATACATGCTCTTTTTCAAAA	45	3306

Table 48

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition (RTS2988_MGB)	% inhibition (RTS2367)	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	72	77	425
502209	37525	37544	CATCTCCCAATGCAGGCCCA	37	34	3307
502210	37555	37574	GCCCTGACCCACCATGTCTG	0	27	3308
502211	37560	37579	CCTCAGCCCTGACCCACCAT	19	51	3309
502212	37565	37584	CTCCTCCTCAGCCCTGACCC	0	8	3310
502213	37570	37589	CAGCTCTCCTCCTCAGCCCT	20	33	3311
502214	37575	37594	ATGGACAGCTCTCCTCCTCA	31	46	3312
502215	37580	37599	ACCATATGGACAGCTCTCCT	57	68	3313
502216	37695	37714	GTGCCATGGACAACAATCAG	0	0	3314

502217	37700	37719	TTACAGTGCCATGGACAACA	0	23	3315
502218	37705	37724	GACAATTACAGTGCCATGGA	15	7	3316
502219	37740	37759	AATGCATCAGTCTGGTGGGA	53	59	3317
502220	37745	37764	ATCCCAATGCATCAGTCTGG	66	73	3318
502221	37804	37823	TGCATTTGGCAAACATTCCC	36	50	3319
502222	37809	37828	ACTCATGCATTTGGCAAACA	42	0	3320
502223	37814	37833	TGGGAACTCATGCATTTGGC	62	65	3321
502224	37819	37838	TGTTTTGGGAACTCATGCAT	3	25	3322
502225	37824	37843	AAGGTTGTTTTGGGAACTCA	44	42	3323
502226	37829	37848	GATACAAGGTTGTTTTGGGA	29	44	3324
502227	37834	37853	CTAATGATACAAGGTTGTTT	29	41	3325
502228	37839	37858	TGCAGCTAATGATACAAGGT	68	67	3326
502229	37844	37863	TAAAATGCAGCTAATGATAC	21	18	3327
502230	37849	37868	ATCTGTAAAATGCAGCTAAT	13	38	3328
502231	37854	37873	TCCTCATCTGTAAAATGCAG	48	43	3329
502232	37859	37878	CAGTTTCCTCATCTGTAAAA	8	19	3330
502233	37864	37883	AGCCTCAGTTTCCTCATCTG	42	44	3331
502234	37869	37888	TTCTGAGCCTCAGTTTCCTC	34	54	3332
502235	37874	37893	CATTTTTCTGAGCCTCAGTT	46	45	3333
502236	37879	37898	CTATTCATTTTTCTGAGCCT	56	65	3334
502237	37884	37903	GTAAGCTATTCATTTTTCTG	50	53	3335
502238	37889	37908	TCTGTGTAAGCTATTCATTT	44	55	3336
502239	37894	37913	CTGGTTCTGTGTAAGCTATT	55	55	3337
502240	37899	37918	GTTGTCTGGTTCTGTGTAAG	31	38	3338
502241	37904	37923	TTGGAGTTGTCTGGTTCTGT	52	52	3339
502242	37989	38008	TGGATCCACTCCCCATCCCC	0	30	3340
502243	37994	38013	GCCCATGGATCCACTCCCCA	0	0	3341
502244	37999	38018	GGGTTGCCCATGGATCCACT	0	10	3342
502245	38004	38023	AGTCAGGGTTGCCCATGGAT	9	13	3343
502246	38270	38289	CCAAGGAGTCTGCTGCCCTG	15	16	3344
502247	38292	38311	GTCTGGGTCCTGTCTTCAGG	17	15	3345
502248	38326	38345	CAGAATGACTGACTCCCTTC	10	19	3346
502249	38356	38375	GCAGTCTGGGCTCCAACATC	0	5	3347
502250	38361	38380	ACTGTGCAGTCTGGGCTCCA	0	7	3348
502251	38366	38385	CCCACACTGTGCAGTCTGGG	5	10	3349
502252	38371	38390	CTTGGCCCACACTGTGCAGT	4	8	3350
502253	38376	38395	GCAAACTTGGCCCACACTGT	2	0	3351
502254	38381	38400	CATGGGCAAACTTGGCCCAC	21	22	3352
502255	38386	38405	ACACACATGGGCAAACTTGG	0	0	3353
502256	38391	38410	CCCAGACACACATGGGCAAA	0	0	3354
502257	38396	38415	GCCCACCCAGACACACATGG	0	5	3355
502258	38401	38420	TCTGTGCCCACCCAGACACA	0	13	3356

502259	38406	38425	TTGCATCTGTGCCCACCCAG	5	22	3357
502260	38411	38430	ACAGGTTGCATCTGTGCCCA	33	45	3358
502261	38478	38497	GGCCCCAGGTGGTCCAGTCC	0	4	3359
502262	38483	38502	ATTCTGGCCCCAGGTGGTCC	0	10	3360
502263	38505	38524	TGGTCTCCCAGCAAAATGAT	0	0	3361
502264	38510	38529	CCTCCTGGTCTCCCAGCAAA	0	0	3362
502265	38515	38534	CCTGACCTCCTGGTCTCCCA	0	7	3363
502266	38520	38539	TCCTTCCTGACCTCCTGGTC	3	16	3364
502267	38525	38544	CACCCTCCTTCCTGACCTCC	0	3	3365
502268	38595	38614	TTCCAAAGCCTGAGGTAAGG	18	36	3366
502269	38600	38619	TCTTCTTCCAAAGCCTGAGG	14	40	3367
502270	38605	38624	CAGCCTCTTCTTCCAAAGCC	10	9	3368
502271	38630	38649	CTGGCCCAGGGCTGAGCCTG	0	0	3369
502272	38676	38695	TCCCTGAAGGCAGGGACTGG	0	10	3370
502273	38681	38700	GGTGCTCCCTGAAGGCAGGG	24	28	3371
502274	38686	38705	CCCTTGGTGCTCCCTGAAGG	0	15	3372
502275	38726	38745	CACACTGTGTTGTCACTGTC	41	44	3373
502276	38731	38750	CTCAGCACACTGTGTTGTCA	38	48	3374
502277	38736	38755	ACAGTCTCAGCACACTGTGT	6	21	3375
502278	38759	38778	AGCCCTGGACTCACCATTGT	0	4	3376
502279	38764	38783	CTCTCAGCCCTGGACTCACC	6	8	3377
502280	38809	38828	GCCTCTGCCAGGAAGTTCTC	8	6	3378
502281	38814	38833	GGCCTGCCTCTGCCAGGAAG	0	51	3379
502282	38819	38838	TGCAGGGCCTGCCTCTGCCA	9	2	3380
502283	38843	38862	GAATGCCTGTTTTCCACCTC	34	53	3381
502284	38848	38867	CTCTGGAATGCCTGTTTTCC	19	27	3382
502285	38874	38893	AGGCAAAGGGAAGGCTGAGC	4	23	3383

Table 49

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition (RTS2988_MGB)	% inhibition (RTS2367)	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	74	73	425
502286	38879	38898	CCCCCAGGCAAAGGGAAGGC	0	16	3384
502287	38928	38947	GCCTTCTGCCCCACTGCTAG	0	6	3385
502288	38933	38952	GATGGGCCTTCTGCCCCACT	0	0	3386
502289	38938	38957	GTTCTGATGGGCCTTCTGCC	0	15	3387
502290	38943	38962	ACCAGGTTCTGATGGGCCTT	0	42	3388
502291	38948	38967	TCTCTACCAGGTTCTGATGG	0	2	3389
502292	39030	39049	GGCCCTGGACACTGGCCAAG	0	12	3390
502293	39035	39054	CTAGAGGCCCTGGACACTGG	0	16	3391

502294	39041	39060	GTCAGCCTAGAGGCCCTGGA	18	40	3392
502295	39082	39101	CCAGGGTCTGTCATACCCTA	0	0	3393
502296	39087	39106	AGAGGCCAGGGTCTGTCATA	0	0	3394
502297	39097	39116	TCTGGAAGGGAGAGGCCAGG	0	0	3395
502298	39301	39320	ACCAACAGTGGTGATGGGCT	7	24	3396
502299	39306	39325	GGCTTACCAACAGTGGTGAT	0	0	3397
502300	39337	39356	GTTCAGGACAGCCCTTGGTC	25	35	3398
502301	39342	39361	CCTGTGTTCAGGACAGCCCT	26	31	3399
502302	39347	39366	GGCACCCTGTGTTCAGGACA	41	52	3400
502303	39377	39396	AATCCCGTCTCTACTGCTGA	18	39	3401
502304	39401	39420	TCAGAGCCAGGTGGCCTGCA	30	27	3402
502305	39406	39425	GGCCATCAGAGCCAGGTGGC	0	33	3403
502306	39411	39430	GGCATGGCCATCAGAGCCAG	0	12	3404
502307	39416	39435	CTAAGGGCATGGCCATCAGA	0	23	3405
502308	39421	39440	CATGGCTAAGGGCATGGCCA	0	10	3406
502309	39426	39445	GTCCTCATGGCTAAGGGCAT	26	29	3407
502310	39431	39450	TCAAAGTCCTCATGGCTAAG	0	37	3408
502311	39436	39455	ACACTTCAAAGTCCTCATGG	33	52	3409
502312	39441	39460	ACCCAACACTTCAAAGTCCT	44	57	3410
502313	39446	39465	TCAGCACCCAACACTTCAAA	35	47	3411
502314	39514	39533	ATCACAGAGCTTGGTTCATC	61	62	3412
502315	39539	39558	GACTGCAGATTTTCTTTCCT	18	40	3413
502316	39577	39596	GTCTTCCCTGATAGACTAGT	43	46	3414
502317	39614	39633	TCCTCATCACATTCCCCCAC	37	59	3415
502318	39665	39684	AGAGTTACCTCCTCCCTGGG	14	25	3416
502319	39670	39689	GTGCAAGAGTTACCTCCTCC	71	81	3417
502320	39675	39694	TAGCAGTGCAAGAGTTACCT	61	67	3418
502321	39680	39699	TCAGTTAGCAGTGCAAGAGT	38	53	3419
502322	39685	39704	TCCTATCAGTTAGCAGTGCA	73	75	3420
502323	39690	39709	ATAATTCCTATCAGTTAGCA	32	35	3421
502324	39695	39714	GCTAGATAATTCCTATCAGT	25	17	3422
502325	39700	39719	ATTTTGCTAGATAATTCCTA	0	0	3423
502326	39705	39724	CCTCTATTTTGCTAGATAAT	1	26	3424
502327	39727	39746	TTCTGATAAAAATTCTCTTC	10	13	3425
502328	39732	39751	ATTGTTTCTGATAAAAATTC	0	0	3426
502329	39737	39756	AGGCTATTGTTTCTGATAAA	34	31	3427
502330	39813	39832	CTATGCTGCAGTCATATTAA	35	26	3428
502331	39818	39837	CAGGTCTATGCTGCAGTCAT	58	45	3429
502332	39823	39842	TCTGACAGGTCTATGCTGCA	46	50	3430
502333	39828	39847	ACTCTTCTGACAGGTCTATG	47	50	3431
502334	39833	39852	TTTCCACTCTTCTGACAGGT	54	72	3432
502335	39906	39925	ATTCTTTAGAATCCTCTAAA	0	10	3433

502336	39911	39930	AGGTAATTCTTTAGAATCCT	41	62	3434
502337	39965	39984	AAGGGCCCATGTGCTCCTGG	14	33	3435
502338	39970	39989	CTGCCAAGGGCCCATGTGCT	10	30	3436
502339	39975	39994	GTCCACTGCCAAGGGCCCAT	37	51	3437
502340	39980	39999	CTCAAGTCCACTGCCAAGGG	0	9	3438
502341	39985	40004	GGCCCCTCAAGTCCACTGCC	0	14	3439
502342	39990	40009	GCTTTGGCCCCTCAAGTCCA	13	27	3440
502343	40041	40060	TAAAAGTACAAGGCAGGACA	26	25	3441
502344	40063	40082	TCCCTGTTGCTTTGTCTCTA	20	26	3442
502345	40068	40087	CTGCCTCCCTGTTGCTTTGT	24	31	3443
502346	40073	40092	TCCTGCTGCCTCCCTGTTGC	0	21	3444
502347	40078	40097	AATGTTCCTGCTGCCTCCCT	0	0	3445
502348	40083	40102	ATGGAAATGTTCCTGCTGCC	33	33	3446
502349	40088	40107	TGTGCATGGAAATGTTCCTG	39	38	3447
502350	40093	40112	ACACCTGTGCATGGAAATGT	7	24	3448
502351	40098	40117	CAGCCACACCTGTGCATGGA	56	54	3449
502352	40103	40122	CTCCCCAGCCACACCTGTGC	10	21	3450
502353	40108	40127	AGCCCCTCCCCAGCCACACC	2	0	3451
502354	40130	40149	CTTCACATTGCCCACAGGAC	39	41	3452
502355	40135	40154	AATTCCTTCACATTGCCCAC	14	19	3453
502356	40140	40159	GAGCAAATTCCTTCACATTG	0	0	3454
502357	40145	40164	GTGAAGAGCAAATTCCTTCA	0	13	3455
502358	40150	40169	TCAAGGTGAAGAGCAAATTC	0	7	3456
502359	40155	40174	CATTCTCAAGGTGAAGAGCA	32	20	3457
502360	40160	40179	CTCTCCATTCTCAAGGTGAA	0	0	3458
502361	40182	40201	CCTCCCAAACACTCTCTGGT	11	11	3459
502362	40187	40206	CTTCCCCTCCCAAACACTCT	2	15	3460

Table 50

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
507659	26616	26635	AGTCCTGATGATCCCCTACC	44	3384
507660	26617	26636	AAGTCCTGATGATCCCCTAC	54	3385
507661	26618	26637	TAAGTCCTGATGATCCCCTA	53	3386
507662	26619	26638	GTAAGTCCTGATGATCCCCT	59	3387
507663	26621	26640	TGGTAAGTCCTGATGATCCC	73	3388
507664	26622	26641	ATGGTAAGTCCTGATGATCC	49	3389
507665	26623	26642	CATGGTAAGTCCTGATGATC	68	3390
507666	26624	26643	ACATGGTAAGTCCTGATGAT	35	3391
495752	26631	26650	AGCACTGACATGGTAAGTCC	67	3392

495753	26632	26651	CAGCACTGACATGGTAAGTC	75	3393
495754	26633	26652	TCAGCACTGACATGGTAAGT	50	3394
495755	26634	26653	CTCAGCACTGACATGGTAAG	35	3395
507667	26636	26655	TGCTCAGCACTGACATGGTA	60	3396
507668	26637	26656	CTGCTCAGCACTGACATGGT	56	3397
507669	26638	26657	GCTGCTCAGCACTGACATGG	69	3398
507670	26639	26658	AGCTGCTCAGCACTGACATG	54	3399
507671	26712	26731	TGTGAAGTTCTATCCCTTGG	52	3400
507672	26713	26732	CTGTGAAGTTCTATCCCTTG	40	3401
507673	26714	26733	CCTGTGAAGTTCTATCCCTT	28	3402
507674	26715	26734	ACCTGTGAAGTTCTATCCCT	27	3403
495756	26779	26798	CTGCCATTTAATGAGCTTCA	80	3404
495757	26780	26799	TCTGCCATTTAATGAGCTTC	56	3405
495758	26781	26800	CTCTGCCATTTAATGAGCTT	22	3406
495759	26782	26801	ACTCTGCCATTTAATGAGCT	13	3407
507675	26812	26831	GGAATGCACTGAGTTTCTGC	64	3408
507676	26813	26832	GGGAATGCACTGAGTTTCTG	39	3409
507677	26850	26869	TCACTAATTCTGGGCTTCCA	66	3410
507678	26851	26870	TTCACTAATTCTGGGCTTCC	51	3411
507679	26852	26871	GTTCACTAATTCTGGGCTTC	70	3412
507680	26853	26872	AGTTCACTAATTCTGGGCTT	37	3413
507681	26880	26899	AAGGTGAAGACTGGCTGTTT	4	3414
507682	26881	26900	AAAGGTGAAGACTGGCTGTT	43	3415
507683	26882	26901	TAAAGGTGAAGACTGGCTGT	46	3416
507684	26883	26902	CTAAAGGTGAAGACTGGCTG	70	3417
507685	26885	26904	GCCTAAAGGTGAAGACTGGC	42	3418
507686	26886	26905	GGCCTAAAGGTGAAGACTGG	18	3419
507687	26887	26906	GGGCCTAAAGGTGAAGACTG	31	3420
507688	26888	26907	TGGGCCTAAAGGTGAAGACT	37	3421
507689	27047	27066	AGTTCTTCCAACCAGTGTTT	66	3422
507690	27048	27067	CAGTTCTTCCAACCAGTGTT	69	3423
507691	27049	27068	TCAGTTCTTCCAACCAGTGT	63	3424
507692	27050	27069	CTCAGTTCTTCCAACCAGTG	83	3425
507693	27052	27071	TGCTCAGTTCTTCCAACCAG	79	3426
507694	27053	27072	TTGCTCAGTTCTTCCAACCA	80	3427
507695	27054	27073	TTTGCTCAGTTCTTCCAACC	78	3428
507696	27055	27074	GTTTGCTCAGTTCTTCCAAC	85	3429
507697	27057	27076	TAGTTTGCTCAGTTCTTCCA	30	3430
507698	27058	27077	TTAGTTTGCTCAGTTCTTCC	55	3431
507699	27059	27078	TTTAGTTTGCTCAGTTCTTC	27	3432
507700	27060	27079	GTTTAGTTTGCTCAGTTCTT	48	3433
507701	27217	27236	GTACTTTCTTCTCATGTGAC	9	3434

507702	27218	27237	AGTACTTTCTTCTCATGTGA	0	3435
507703	27219	27238	CAGTACTTTCTTCTCATGTG	0	3436
507704	27220	27239	CCAGTACTTTCTTCTCATGT	53	3437
507705	27222	27241	TCCCAGTACTTTCTTCTCAT	67	3438
507706	27223	27242	GTCCCAGTACTTTCTTCTCA	57	3439
507707	27224	27243	GGTCCCAGTACTTTCTTCTC	58	3440
507708	27225	27244	TGGTCCCAGTACTTTCTTCT	49	3441
507709	27227	27246	CCTGGTCCCAGTACTTTCTT	65	3442
507710	27228	27247	TCCTGGTCCCAGTACTTTCT	77	3443
507711	27229	27248	GTCCTGGTCCCAGTACTTTC	69	3444
507712	27230	27249	TGTCCTGGTCCCAGTACTTT	64	3445
507713	27232	27251	CTTGTCCTGGTCCCAGTACT	61	3446
507714	27233	27252	TCTTGTCCTGGTCCCAGTAC	61	3447
507715	27234	27253	TTCTTGTCCTGGTCCCAGTA	67	3448
507716	27235	27254	GTTCTTGTCCTGGTCCCAGT	76	3449
507717	27237	27256	GGGTTCTTGTCCTGGTCCCA	80	3450
507718	27238	27257	TGGGTTCTTGTCCTGGTCCC	71	3451
507719	27239	27258	CTGGGTTCTTGTCCTGGTCC	62	3452
507720	27240	27259	CCTGGGTTCTTGTCCTGGTC	55	3453
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	69	425
507721	35662	35681	AAAAATATACATGCTCTTTT	0	3461
507722	35663	35682	CAAAAATATACATGCTCTTT	29	3462
507723	35664	35683	TCAAAAATATACATGCTCTT	45	3463
507724	35665	35684	CTCAAAAATATACATGCTCT	74	3464
507725	35667	35686	TACTCAAAAATATACATGCT	51	3465
507726	35668	35687	CTACTCAAAAATATACATGC	63	3466
507727	35669	35688	TCTACTCAAAAATATACATG	0	3467

Table 51

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
522363	12807	12826	CCAGCACTAATTTTTACAAC	72	3468
522364	12808	12827	TCCAGCACTAATTTTTACAA	49	3469
522365	12809	12828	ATCCAGCACTAATTTTTACA	65	3470
522366	13442	13461	GTGGCTCTCTAGATAGGGTG	80	3471
522367	14193	14212	CTCAGCCTTGGAGCCAGCTC	59	3472
522368	14194	14213	ACTCAGCCTTGGAGCCAGCT	72	3473
522369	14195	14214	CACTCAGCCTTGGAGCCAGC	63	3474
522370	14196	14215	CCACTCAGCCTTGGAGCCAG	71	3475
522371	14198	14217	TGCCACTCAGCCTTGGAGCC	67	3476

522372	14199	14218	TTGCCACTCAGCCTTGGAGC	62	3477
522373	15319	15338	GGAGTTTGTGTTTCCCATTT	83	3478
522374	15321	15340	AAGGAGTTTGTGTTTCCCAT	83	3479
522375	15322	15341	AAAGGAGTTTGTGTTTCCCA	83	3480
522376	15324	15343	GAAAAGGAGTTTGTGTTTCC	50	3481
522377	15325	15344	AGAAAAGGAGTTTGTGTTTC	17	3482
522378	15326	15345	AAGAAAAGGAGTTTGTGTTT	30	3483
522379	15327	15346	TAAGAAAAGGAGTTTGTGTT	21	3484
522380	15569	15588	ATTTTCACAAGGAGAAGCTG	40	3485
522381	15570	15589	CATTTTCACAAGGAGAAGCT	44	3486
522382	15571	15590	CCATTTTCACAAGGAGAAGC	32	3487
522383	15574	15593	GCACCATTTTCACAAGGAGA	84	3488
522384	15575	15594	TGCACCATTTTCACAAGGAG	77	3489
522385	15576	15595	GTGCACCATTTTCACAAGGA	72	3490
522386	15577	15596	AGTGCACCATTTTCACAAGG	65	3491
522387	15647	15666	CATCACAATATATGGGCAAG	44	3492
522388	15648	15667	CCATCACAATATATGGGCAA	51	3493
522389	15649	15668	CCCATCACAATATATGGGCA	60	3494
522390	15650	15669	CCCCATCACAATATATGGGC	55	3495
522391	15877	15896	AGGTAAGGCCAAGGAAGTGA	69	3496
522392	15878	15897	GAGGTAAGGCCAAGGAAGTG	50	3497
522393	15879	15898	AGAGGTAAGGCCAAGGAAGT	43	3498
522394	15880	15899	AAGAGGTAAGGCCAAGGAAG	57	3499
522395	15934	15953	CACCTGGGTTTTTGTGTATT	66	3500
522396	15935	15954	ACACCTGGGTTTTTGTGTAT	61	3501
522397	15936	15955	TACACCTGGGTTTTTGTGTA	37	3502
522398	15937	15956	ATACACCTGGGTTTTTGTGT	69	3503
522399	16047	16066	TCTGAGTGCTGCTAACTTGG	77	3504
522400	16048	16067	ATCTGAGTGCTGCTAACTTG	65	3505
522401	16049	16068	AATCTGAGTGCTGCTAACTT	62	3506
522402	16050	16069	AAATCTGAGTGCTGCTAACT	60	3507
522403	16052	16071	TGAAATCTGAGTGCTGCTAA	68	3508
522404	16053	16072	TTGAAATCTGAGTGCTGCTA	74	3509
522405	16054	16073	GTTGAAATCTGAGTGCTGCT	78	3510
522406	16083	16102	GCACTAAATTAGGAAGCTGG	77	3511
522407	16084	16103	AGCACTAAATTAGGAAGCTG	65	3512
522408	16289	16308	CTGGGACATCTGGCCCAAAG	72	3513
522409	16290	16309	ACTGGGACATCTGGCCCAAA	71	3514
522410	16291	16310	CACTGGGACATCTGGCCCAA	66	3515
522411	16292	16311	CCACTGGGACATCTGGCCCA	71	3516
522412	16294	16313	GCCCACTGGGACATCTGGCC	61	3517
522413	16295	16314	GGCCCACTGGGACATCTGGC	68	3518

522414	16306	16325	CCTTAAAGCAGGGCCCACTG	50	3519
522415	16307	16326	TCCTTAAAGCAGGGCCCACT	58	3520
522416	16308	16327	ATCCTTAAAGCAGGGCCCAC	67	3521
522417	16309	16328	TATCCTTAAAGCAGGGCCCA	63	3522
522418	16429	16448	CACTGGTGCCTAAGAGCCCT	70	3523
522419	16430	16449	CCACTGGTGCCTAAGAGCCC	63	3524
522420	16431	16450	TCCACTGGTGCCTAAGAGCC	61	3525
522421	16432	16451	CTCCACTGGTGCCTAAGAGC	73	3526
522422	16809	16828	GAGGCTGAGTTCTGCTCCTG	77	3527
522423	16810	16829	AGAGGCTGAGTTCTGCTCCT	59	3528
522424	16811	16830	TAGAGGCTGAGTTCTGCTCC	71	3529
522425	16812	16831	CTAGAGGCTGAGTTCTGCTC	60	3530
522426	16814	16833	TGCTAGAGGCTGAGTTCTGC	65	3531
522427	16815	16834	CTGCTAGAGGCTGAGTTCTG	71	3532
522428	16816	16835	TCTGCTAGAGGCTGAGTTCT	74	3533
522429	16817	16836	ATCTGCTAGAGGCTGAGTTC	67	3534
522430	16824	16843	CTTGGGCATCTGCTAGAGGC	69	3535
522431	16825	16844	TCTTGGGCATCTGCTAGAGG	66	3536
522432	16826	16845	TTCTTGGGCATCTGCTAGAG	65	3537
522433	16827	16846	CTTCTTGGGCATCTGCTAGA	62	3538
522434	16829	16848	TGCTTCTTGGGCATCTGCTA	71	3539
522435	16830	16849	CTGCTTCTTGGGCATCTGCT	81	3540
522436	16831	16850	TCTGCTTCTTGGGCATCTGC	80	3541
522437	16832	16851	CTCTGCTTCTTGGGCATCTG	82	3542
522438	16834	16853	TCCTCTGCTTCTTGGGCATC	67	3543
522439	16835	16854	CTCCTCTGCTTCTTGGGCAT	68	3544
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	82	425

Table 52

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
522440	16836	16855	TCTCCTCTGCTTCTTGGGCA	78	3545
522441	16897	16916	CTTTCTAAGTACCCTTTACA	37	3546
522442	16898	16917	GCTTTCTAAGTACCCTTTAC	71	3547
522443	16899	16918	TGCTTTCTAAGTACCCTTTA	62	3548
522444	16900	16919	GTGCTTTCTAAGTACCCTTT	85	3549
522445	16902	16921	CAGTGCTTTCTAAGTACCCT	86	3550
522446	17008	17027	AGGGAAAGGTCTTCTCCAGC	74	3551
522447	17009	17028	GAGGGAAAGGTCTTCTCCAG	67	3552
522448	17010	17029	GGAGGGAAAGGTCTTCTCCA	62	3553

522449	17011	17030	AGGAGGGAAAGGTCTTCTCC	60	3554
522450	17208	17227	GTCTCATTCATCTGGGCCCT	80	3555
522451	17209	17228	TGTCTCATTCATCTGGGCCC	65	3556
522452	17210	17229	ATGTCTCATTCATCTGGGCC	72	3557
522453	17270	17289	CCCCTGTACTCAGCCCTTTC	49	3558
522454	17271	17290	ACCCCTGTACTCAGCCCTTT	60	3559
522455	17272	17291	CACCCCTGTACTCAGCCCTT	51	3560
522456	17273	17292	TCACCCCTGTACTCAGCCCT	61	3561
522457	17275	17294	TCTCACCCCTGTACTCAGCC	70	3562
522458	17276	17295	ATCTCACCCCTGTACTCAGC	58	3563
522459	17277	17296	CATCTCACCCCTGTACTCAG	51	3564
522460	17278	17297	CCATCTCACCCCTGTACTCA	54	3565
522461	17329	17348	AAGTCTTCCTTCTCCTCCAC	65	3566
522462	17330	17349	AAAGTCTTCCTTCTCCTCCA	71	3567
522463	17331	17350	GAAAGTCTTCCTTCTCCTCC	75	3568
522464	17332	17351	GGAAAGTCTTCCTTCTCCTC	75	3569
522465	17451	17470	CAGGTAGAGTTCTATTGCTT	80	3570
522466	17452	17471	CCAGGTAGAGTTCTATTGCT	77	3571
522467	19361	19380	GGCTACTGGCATTGCTCCTC	74	3572
522468	19362	19381	TGGCTACTGGCATTGCTCCT	56	3573
522469	19363	19382	GTGGCTACTGGCATTGCTCC	68	3574
522470	19364	19383	GGTGGCTACTGGCATTGCTC	74	3575
522471	19909	19928	ACATGCCTGAGGGCAGCAGT	68	3576
522472	19910	19929	CACATGCCTGAGGGCAGCAG	69	3577
522473	19911	19930	TCACATGCCTGAGGGCAGCA	81	3578
522474	19912	19931	CTCACATGCCTGAGGGCAGC	79	3579
522475	19984	20003	AATATCTGATATCAAAGTGA	14	3580
522476	19985	20004	CAATATCTGATATCAAAGTG	14	3581
522477	19986	20005	CCAATATCTGATATCAAAGT	41	3582
522478	19987	20006	CCCAATATCTGATATCAAAG	74	3583
522479	19989	20008	TGCCCAATATCTGATATCAA	73	3584
522480	19990	20009	TTGCCCAATATCTGATATCA	65	3585
522481	20297	20316	TTGCTTGAGGTCAGGGTGTG	62	3586
522482	20298	20317	CTTGCTTGAGGTCAGGGTGT	72	3587
522483	20299	20318	ACTTGCTTGAGGTCAGGGTG	68	3588
522484	20300	20319	CACTTGCTTGAGGTCAGGGT	84	3589
522485	20302	20321	ATCACTTGCTTGAGGTCAGG	82	3590
522486	20303	20322	AATCACTTGCTTGAGGTCAG	77	3591
522487	20304	20323	AAATCACTTGCTTGAGGTCA	75	3592
522488	20305	20324	AAAATCACTTGCTTGAGGTC	71	3593
522489	20669	20688	GGTACAAGTTTCTCCACCTA	75	3594
522490	20670	20689	AGGTACAAGTTTCTCCACCT	74	3595

522491	20671	20690	TAGGTACAAGTTTCTCCACC	47	3596
522492	20672	20691	CTAGGTACAAGTTTCTCCAC	72	3597
522493	20828	20847	ATAGCTGAGCAAATCCATAA	63	3598
522494	20829	20848	CATAGCTGAGCAAATCCATA	73	3599
522495	20830	20849	GCATAGCTGAGCAAATCCAT	80	3600
522496	20831	20850	TGCATAGCTGAGCAAATCCA	72	3601
522497	20833	20852	ACTGCATAGCTGAGCAAATC	63	3602
522498	20834	20853	TACTGCATAGCTGAGCAAAT	67	3603
522499	20835	20854	TTACTGCATAGCTGAGCAAA	65	3604
522500	20836	20855	TTTACTGCATAGCTGAGCAA	65	3605
522501	20838	20857	GGTTTACTGCATAGCTGAGC	85	3606
522502	20839	20858	AGGTTTACTGCATAGCTGAG	65	3607
522503	20840	20859	GAGGTTTACTGCATAGCTGA	72	3608
522504	20841	20860	AGAGGTTTACTGCATAGCTG	75	3609
522505	20843	20862	ATAGAGGTTTACTGCATAGC	71	3610
522506	20844	20863	CATAGAGGTTTACTGCATAG	65	3611
522507	20956	20975	ACTCTCTCTGCACACTCCCA	62	3612
522508	20957	20976	CACTCTCTCTGCACACTCCC	61	3613
522509	20958	20977	GCACTCTCTCTGCACACTCC	80	3614
522510	20959	20978	TGCACTCTCTCTGCACACTC	76	3615
522511	21934	21953	TGCTGATTACAAGCTGATTC	64	3616
522512	21935	21954	CTGCTGATTACAAGCTGATT	67	3617
522513	21936	21955	ACTGCTGATTACAAGCTGAT	61	3618
522514	21937	21956	AACTGCTGATTACAAGCTGA	55	3619
522515	22152	22171	TGGTGATAAGGCAGCAGTCT	53	3620
522516	22153	22172	ATGGTGATAAGGCAGCAGTC	62	3621
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	81	425

Table 53

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
522517	22154	22173	GATGGTGATAAGGCAGCAGT	67	3622
522518	22155	22174	AGATGGTGATAAGGCAGCAG	71	3623
522519	22157	22176	AGAGATGGTGATAAGGCAGC	58	3624
522520	22158	22177	CAGAGATGGTGATAAGGCAG	38	3625
522521	22159	22178	CCAGAGATGGTGATAAGGCA	60	3626
522522	22160	22179	CCCAGAGATGGTGATAAGGC	67	3627
522523	23856	23875	AGACTTGCCCAGCAACCCAT	49	3628
522524	23857	23876	CAGACTTGCCCAGCAACCCA	58	3629
522525	23858	23877	CCAGACTTGCCCAGCAACCC	61	3630

522526	23859	23878	TCCAGACTTGCCCAGCAACC	57	3631
522527	24120	24139	AAACCTAGGTTCAGACTTTG	51	3632
522528	24121	24140	CAAACCTAGGTTCAGACTTT	48	3633
522529	24123	24142	GTCAAACCTAGGTTCAGACT	84	3634
522530	24125	24144	GAGTCAAACCTAGGTTCAGA	66	3635
522531	24126	24145	AGAGTCAAACCTAGGTTCAG	48	3636
522532	24127	24146	AAGAGTCAAACCTAGGTTCA	50	3637
522533	24128	24147	GAAGAGTCAAACCTAGGTTC	61	3638
522534	25019	25038	GAGCATCCCCAATCCCTGCT	72	3639
522535	25020	25039	TGAGCATCCCCAATCCCTGC	63	3640
522536	25021	25040	TTGAGCATCCCCAATCCCTG	56	3641
522537	25022	25041	TTTGAGCATCCCCAATCCCT	48	3642
522538	25024	25043	ACTTTGAGCATCCCCAATCC	42	3643
522539	25025	25044	TACTTTGAGCATCCCCAATC	53	3644
522540	25026	25045	GTACTTTGAGCATCCCCAAT	70	3645
522541	25027	25046	TGTACTTTGAGCATCCCCAA	68	3646
522542	25029	25048	AGTGTACTTTGAGCATCCCC	77	3647
522543	25030	25049	AAGTGTACTTTGAGCATCCC	70	3648
522544	25031	25050	CAAGTGTACTTTGAGCATCC	73	3649
522545	25032	25051	CCAAGTGTACTTTGAGCATC	76	3650
522546	25034	25053	CTCCAAGTGTACTTTGAGCA	82	3651
522547	25070	25089	CAGAGGTTCAACATCCAATT	74	3652
522548	25071	25090	ACAGAGGTTCAACATCCAAT	74	3653
522549	25072	25091	GACAGAGGTTCAACATCCAA	73	3654
522550	25073	25092	GGACAGAGGTTCAACATCCA	82	3655
522551	25076	25095	CAAGGACAGAGGTTCAACAT	53	3656
522552	25077	25096	CCAAGGACAGAGGTTCAACA	72	3657
522553	25078	25097	GCCAAGGACAGAGGTTCAAC	84	3658
522554	25079	25098	GGCCAAGGACAGAGGTTCAA	82	3659
522555	25081	25100	GAGGCCAAGGACAGAGGTTC	80	3660
522556	25082	25101	TGAGGCCAAGGACAGAGGTT	82	3661
522557	25083	25102	GTGAGGCCAAGGACAGAGGT	67	3662
522558	25084	25103	TGTGAGGCCAAGGACAGAGG	63	3663
522559	25086	25105	TCTGTGAGGCCAAGGACAGA	54	3664
522560	25087	25106	GTCTGTGAGGCCAAGGACAG	58	3665
522561	25088	25107	TGTCTGTGAGGCCAAGGACA	71	3666
522562	25089	25108	CTGTCTGTGAGGCCAAGGAC	74	3667
522563	25184	25203	AGTCTCTCATAATTGCCAGT	69	3668
522564	25185	25204	AAGTCTCTCATAATTGCCAG	69	3669
522565	25186	25205	GAAGTCTCTCATAATTGCCA	71	3670
522566	25187	25206	GGAAGTCTCTCATAATTGCC	46	3671
522567	25189	25208	TGGGAAGTCTCTCATAATTG	37	3672

522568	25190	25209	TTGGGAAGTCTCTCATAATT	22	3673
522569	25191	25210	CTTGGGAAGTCTCTCATAAT	23	3674
522570	25192	25211	CCTTGGGAAGTCTCTCATAA	35	3675
522571	25194	25213	GGCCTTGGGAAGTCTCTCAT	51	3676
522572	25195	25214	AGGCCTTGGGAAGTCTCTCA	55	3677
522573	25196	25215	TAGGCCTTGGGAAGTCTCTC	61	3678
522574	25197	25216	CTAGGCCTTGGGAAGTCTCT	43	3679
522575	25242	25261	CATTTTGGAGACCACATGAA	31	3680
522576	25243	25262	TCATTTTGGAGACCACATGA	41	3681
522577	25244	25263	GTCATTTTGGAGACCACATG	60	3682
522578	25245	25264	GGTCATTTTGGAGACCACAT	70	3683
522579	25268	25287	AATGGGAATGGTATCGCACT	84	3684
522580	25269	25288	CAATGGGAATGGTATCGCAC	87	3685
522581	25270	25289	ACAATGGGAATGGTATCGCA	85	3686
522582	25271	25290	CACAATGGGAATGGTATCGC	86	3687
522583	25377	25396	AGCTATAGAATCAGACAGAC	53	3688
522584	25378	25397	CAGCTATAGAATCAGACAGA	56	3689
522585	25379	25398	TCAGCTATAGAATCAGACAG	48	3690
522586	25381	25400	CATCAGCTATAGAATCAGAC	64	3691
522587	25783	25802	GCACTTGATCTGGGACCCAA	87	3692
522588	25784	25803	AGCACTTGATCTGGGACCCA	88	3693
522589	25785	25804	GAGCACTTGATCTGGGACCC	86	3694
522590	25786	25805	AGAGCACTTGATCTGGGACC	76	3695
522591	25788	25807	GTAGAGCACTTGATCTGGGA	74	3696
522592	25789	25808	GGTAGAGCACTTGATCTGGG	79	3697
522593	25790	25809	GGGTAGAGCACTTGATCTGG	61	3698
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	84	425

Table 54

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
522594	25842	25861	AACTATCACACCACCTCCCA	44	3699
522595	25843	25862	GAACTATCACACCACCTCCC	42	3700
522596	25844	25863	GGAACTATCACACCACCTCC	47	3701
522597	25845	25864	GGGAACTATCACACCACCTC	61	3702
522598	25847	25866	ATGGGAACTATCACACCACC	64	3703
522599	25848	25867	AATGGGAACTATCACACCAC	33	3704
522600	25849	25868	AAATGGGAACTATCACACCA	37	3705
522601	25850	25869	TAAATGGGAACTATCACACC	16	3706
522602	25901	25920	TGACCTTGGGCAAGTTACCT	74	3707

522603	25902	25921	GTGACCTTGGGCAAGTTACC	76	3708
522604	25903	25922	TGTGACCTTGGGCAAGTTAC	77	3709
522605	25904	25923	GTGTGACCTTGGGCAAGTTA	78	3710
522606	25906	25925	CTGTGTGACCTTGGGCAAGT	80	3711
522607	25907	25926	TCTGTGTGACCTTGGGCAAG	81	3712
522608	25908	25927	ATCTGTGTGACCTTGGGCAA	81	3713
522609	25909	25928	AATCTGTGTGACCTTGGGCA	87	3714
522610	25911	25930	CAAATCTGTGTGACCTTGGG	85	3715
522611	25912	25931	TCAAATCTGTGTGACCTTGG	69	3716
522612	25913	25932	TTCAAATCTGTGTGACCTTG	75	3717
522613	25914	25933	ATTCAAATCTGTGTGACCTT	79	3718
522614	25916	25935	GGATTCAAATCTGTGTGACC	75	3719
522615	25917	25936	GGGATTCAAATCTGTGTGAC	54	3720
522616	25918	25937	AGGGATTCAAATCTGTGTGA	57	3721
522617	25919	25938	CAGGGATTCAAATCTGTGTG	63	3722
522618	25951	25970	GGGAAAGGCACAGGCTTTGG	81	3723
522619	25952	25971	TGGGAAAGGCACAGGCTTTG	70	3724
522620	25954	25973	TGTGGGAAAGGCACAGGCTT	66	3725
522621	26006	26025	AGGCAAAGTAACATACCTGC	87	3726
522622	26007	26026	AAGGCAAAGTAACATACCTG	76	3727
522623	26008	26027	TAAGGCAAAGTAACATACCT	62	3728
522624	26009	26028	TTAAGGCAAAGTAACATACC	69	3729
522625	26011	26030	CCTTAAGGCAAAGTAACATA	73	3730
522626	26012	26031	ACCTTAAGGCAAAGTAACAT	45	3731
522627	26166	26185	ATTTCTTATCTTCAATCCTC	84	3732
522628	26167	26186	CATTTCTTATCTTCAATCCT	64	3733
522629	26168	26187	TCATTTCTTATCTTCAATCC	62	3734
522630	26169	26188	CTCATTTCTTATCTTCAATC	81	3735
522631	26171	26190	CTCTCATTTCTTATCTTCAA	86	3736
522632	26172	26191	GCTCTCATTTCTTATCTTCA	90	3737
522633	26173	26192	TGCTCTCATTTCTTATCTTC	78	3738
522634	26174	26193	GTGCTCTCATTTCTTATCTT	80	3739
522635	26176	26195	AGGTGCTCTCATTTCTTATC	78	3740
522636	26177	26196	CAGGTGCTCTCATTTCTTAT	73	3741
522637	26178	26197	CCAGGTGCTCTCATTTCTTA	74	3742
522638	26179	26198	GCCAGGTGCTCTCATTTCTT	84	3743
522639	26201	26220	GCCCATCATGACCAGGCCCT	60	3744
522640	26202	26221	GGCCCATCATGACCAGGCCC	21	3745
522641	26203	26222	GGGCCCATCATGACCAGGCC	41	3746
522642	26301	26320	CAGGCCTCGGGAAGCACCTG	71	3747
522643	26302	26321	GCAGGCCTCGGGAAGCACCT	86	3748
522644	26303	26322	AGCAGGCCTCGGGAAGCACC	77	3749

522645	26304	26323	GAGCAGGCCTCGGGAAGCAC	80	3750
522646	26354	26373	CAGAAAAAGCAACCAAAGCA	31	3751
522647	26355	26374	GCAGAAAAAGCAACCAAAGC	31	3752
522648	26356	26375	TGCAGAAAAAGCAACCAAAG	34	3753
522649	26357	26376	CTGCAGAAAAAGCAACCAAA	52	3754
522650	26359	26378	ACCTGCAGAAAAAGCAACCA	32	3755
522651	26360	26379	GACCTGCAGAAAAAGCAACC	24	3756
522652	26361	26380	AGACCTGCAGAAAAAGCAAC	17	3757
522653	26362	26381	CAGACCTGCAGAAAAAGCAA	23	3758
522654	26386	26405	ACCTAAGGAGTGAGGGTATC	46	3759
522655	26387	26406	AACCTAAGGAGTGAGGGTAT	58	3760
522656	26388	26407	CAACCTAAGGAGTGAGGGTA	59	3761
522657	26389	26408	GCAACCTAAGGAGTGAGGGT	73	3762
522658	27639	27658	TGCTTGCCAGGTGAGCTTCT	76	3763
522659	27640	27659	TTGCTTGCCAGGTGAGCTTC	65	3764
522660	27641	27660	TTTGCTTGCCAGGTGAGCTT	65	3765
522661	27642	27661	CTTTGCTTGCCAGGTGAGCT	77	3766
522662	27644	27663	GTCTTTGCTTGCCAGGTGAG	74	3767
522663	27645	27664	GGTCTTTGCTTGCCAGGTGA	75	3768
522664	27767	27786	CCTTGTATTAAATACTCTAA	59	3769
522665	27768	27787	ACCTTGTATTAAATACTCTA	57	3770
522666	27769	27788	CACCTTGTATTAAATACTCT	78	3771
522667	27770	27789	GCACCTTGTATTAAATACTC	83	3772
522668	27772	27791	ATGCACCTTGTATTAAATAC	69	3773
522669	27773	27792	AATGCACCTTGTATTAAATA	41	3774
522670	27774	27793	CAATGCACCTTGTATTAAAT	59	3775
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	83	425

Table 55

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
522671	27775	27794	CCAATGCACCTTGTATTAAA	83	3776
522672	27777	27796	ATCCAATGCACCTTGTATTA	85	3777
522673	27778	27797	AATCCAATGCACCTTGTATT	77	3778
522674	27779	27798	AAATCCAATGCACCTTGTAT	80	3779
522675	27780	27799	GAAATCCAATGCACCTTGTA	85	3780
522676	27782	27801	TTGAAATCCAATGCACCTTG	86	3781
522677	27783	27802	TTTGAAATCCAATGCACCTT	87	3782
522678	27784	27803	CTTTGAAATCCAATGCACCT	82	3783
522679	27785	27804	CCTTTGAAATCCAATGCACC	88	3784

522680	27787	27806	TTCCTTTGAAATCCAATGCA	82	3785
522681	27788	27807	TTTCCTTTGAAATCCAATGC	82	3786
522682	27789	27808	GTTTCCTTTGAAATCCAATG	87	3787
522683	27790	27809	AGTTTCCTTTGAAATCCAAT	82	3788
522684	27850	27869	CTGTTACTACATGTCTAATC	61	3789
522685	27851	27870	CCTGTTACTACATGTCTAAT	51	3790
522686	27852	27871	ACCTGTTACTACATGTCTAA	68	3791
522687	27853	27872	CACCTGTTACTACATGTCTA	82	3792
522688	27855	27874	GGCACCTGTTACTACATGTC	90	3793
522689	27856	27875	AGGCACCTGTTACTACATGT	88	3794
522690	27857	27876	AAGGCACCTGTTACTACATG	82	3795
522691	27858	27877	AAAGGCACCTGTTACTACAT	80	3796
522692	28027	28046	ATCACAGAATTATCAGCAGT	84	3797
522693	28028	28047	AATCACAGAATTATCAGCAG	79	3798
522694	28029	28048	AAATCACAGAATTATCAGCA	86	3799
522695	28030	28049	TAAATCACAGAATTATCAGC	64	3800
522696	28128	28147	CACACAATATCCATGGACTT	80	3801
522697	28129	28148	ACACACAATATCCATGGACT	88	3802
522698	28130	28149	GACACACAATATCCATGGAC	89	3803
522699	28131	28150	TGACACACAATATCCATGGA	75	3804
522700	28133	28152	CCTGACACACAATATCCATG	80	3805
522701	28134	28153	GCCTGACACACAATATCCAT	79	3806
522702	28135	28154	AGCCTGACACACAATATCCA	72	3807
522703	28460	28479	CATGAGAAGCTTAGAAGGCC	59	3808
522704	28462	28481	CTCATGAGAAGCTTAGAAGG	63	3809
522705	28463	28482	GCTCATGAGAAGCTTAGAAG	83	3810
522706	28465	28484	GAGCTCATGAGAAGCTTAGA	70	3811
522707	28466	28485	TGAGCTCATGAGAAGCTTAG	60	3812
522708	28467	28486	CTGAGCTCATGAGAAGCTTA	69	3813
522709	28468	28487	GCTGAGCTCATGAGAAGCTT	80	3814
522710	28470	28489	TTGCTGAGCTCATGAGAAGC	74	3815
522711	28471	28490	GTTGCTGAGCTCATGAGAAG	66	3816
522712	28472	28491	TGTTGCTGAGCTCATGAGAA	60	3817
522713	28473	28492	CTGTTGCTGAGCTCATGAGA	65	3818
522714	28475	28494	CACTGTTGCTGAGCTCATGA	73	3819
522715	28476	28495	CCACTGTTGCTGAGCTCATG	86	3820
522716	28477	28496	ACCACTGTTGCTGAGCTCAT	86	3821
522717	28478	28497	AACCACTGTTGCTGAGCTCA	87	3822
522718	28480	28499	AAAACCACTGTTGCTGAGCT	80	3823
522719	28481	28500	AAAAACCACTGTTGCTGAGC	83	3824
522720	28482	28501	TAAAAACCACTGTTGCTGAG	69	3825
522721	28483	28502	GTAAAAACCACTGTTGCTGA	69	3826

522722	28516	28535	TCTGGTTCCATGCTCTTAGG	70	3827
522723	28517	28536	CTCTGGTTCCATGCTCTTAG	74	3828
522724	28518	28537	GCTCTGGTTCCATGCTCTTA	78	3829
522725	28519	28538	GGCTCTGGTTCCATGCTCTT	75	3830
522726	28521	28540	CAGGCTCTGGTTCCATGCTC	73	3831
522727	28522	28541	ACAGGCTCTGGTTCCATGCT	78	3832
522728	28523	28542	AACAGGCTCTGGTTCCATGC	78	3833
522729	28581	28600	TGAACTAAATCCACCAAATG	22	3834
522730	28582	28601	ATGAACTAAATCCACCAAAT	46	3835
522731	28583	28602	GATGAACTAAATCCACCAAA	46	3836
522732	28584	28603	GGATGAACTAAATCCACCAA	67	3837
522733	28586	28605	AAGGATGAACTAAATCCACC	65	3838
522734	28587	28606	AAAGGATGAACTAAATCCAC	43	3839
522735	28588	28607	AAAAGGATGAACTAAATCCA	33	3840
522736	28589	28608	CAAAAGGATGAACTAAATCC	16	3841
522737	28803	28822	AGAGACTGAATTCTAGCCTG	59	3842
522738	28804	28823	CAGAGACTGAATTCTAGCCT	67	3843
522739	28805	28824	CCAGAGACTGAATTCTAGCC	67	3844
522740	28806	28825	TCCAGAGACTGAATTCTAGC	77	3845
522741	28808	28827	TATCCAGAGACTGAATTCTA	52	3846
522742	28809	28828	GTATCCAGAGACTGAATTCT	46	3847
522743	28810	28829	GGTATCCAGAGACTGAATTC	50	3848
522744	28811	28830	GGGTATCCAGAGACTGAATT	65	3849
522745	29011	29030	GTTTAGGCTATGGTCTGAGC	90	3850
522746	29012	29031	GGTTTAGGCTATGGTCTGAG	78	3851
522747	29013	29032	AGGTTTAGGCTATGGTCTGA	71	3852
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	84	425

Table 56

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
522748	29014	29033	GAGGTTTAGGCTATGGTCTG	71	3853
522749	29016	29035	ATGAGGTTTAGGCTATGGTC	67	3854
522750	29045	29064	GGATGCTCCAGGTGGGCCAG	59	3855
522751	29046	29065	TGGATGCTCCAGGTGGGCCA	52	3856
522752	29047	29066	GTGGATGCTCCAGGTGGGCC	57	3857
522753	29048	29067	GGTGGATGCTCCAGGTGGGC	52	3858
522754	29140	29159	GTCTGCCTGATTCCCTTTCT	75	3859
522755	29141	29160	AGTCTGCCTGATTCCCTTTC	58	3860
522756	29142	29161	CAGTCTGCCTGATTCCCTTT	59	3861

522757	29143	29162	GCAGTCTGCCTGATTCCCTT	85	3862
522758	29145	29164	CAGCAGTCTGCCTGATTCCC	79	3863
522759	29146	29165	TCAGCAGTCTGCCTGATTCC	72	3864
522760	29147	29166	TTCAGCAGTCTGCCTGATTC	61	3865
522761	29148	29167	GTTCAGCAGTCTGCCTGATT	71	3866
522762	29150	29169	CTGTTCAGCAGTCTGCCTGA	55	3867
522763	29151	29170	ACTGTTCAGCAGTCTGCCTG	62	3868
522764	29152	29171	TACTGTTCAGCAGTCTGCCT	64	3869
522765	29153	29172	TTACTGTTCAGCAGTCTGCC	61	3870
522766	29155	29174	ACTTACTGTTCAGCAGTCTG	73	3871
522767	29156	29175	TACTTACTGTTCAGCAGTCT	75	3872
522768	29157	29176	ATACTTACTGTTCAGCAGTC	74	3873
522769	29158	29177	CATACTTACTGTTCAGCAGT	74	3874
522770	29160	29179	GTCATACTTACTGTTCAGCA	89	3875
522771	29161	29180	AGTCATACTTACTGTTCAGC	74	3876
522772	29162	29181	AAGTCATACTTACTGTTCAG	39	3877
522773	29163	29182	AAAGTCATACTTACTGTTCA	43	3878
522774	29194	29213	TGGTGAATAGCTATGTCTAA	54	3879
522775	29195	29214	TTGGTGAATAGCTATGTCTA	58	3880
522776	29196	29215	CTTGGTGAATAGCTATGTCT	71	3881
522777	29197	29216	GCTTGGTGAATAGCTATGTC	77	3882
522778	29199	29218	TAGCTTGGTGAATAGCTATG	70	3883
522779	29200	29219	GTAGCTTGGTGAATAGCTAT	50	3884
522780	29201	29220	GGTAGCTTGGTGAATAGCTA	71	3885
522781	29243	29262	AGCCTACAAGAGCCTGTTAA	39	3886
522782	29244	29263	CAGCCTACAAGAGCCTGTTA	67	3887
522783	29245	29264	GCAGCCTACAAGAGCCTGTT	82	3888
522784	29246	29265	TGCAGCCTACAAGAGCCTGT	82	3889
522785	29248	29267	TGTGCAGCCTACAAGAGCCT	64	3890
522786	29249	29268	ATGTGCAGCCTACAAGAGCC	59	3891
522787	29250	29269	CATGTGCAGCCTACAAGAGC	39	3892
522788	29251	29270	GCATGTGCAGCCTACAAGAG	64	3893
522789	29253	29272	AAGCATGTGCAGCCTACAAG	70	3894
522790	29254	29273	GAAGCATGTGCAGCCTACAA	66	3895
522791	29255	29274	GGAAGCATGTGCAGCCTACA	78	3896
522792	29256	29275	GGGAAGCATGTGCAGCCTAC	69	3897
522793	29258	29277	TAGGGAAGCATGTGCAGCCT	74	3898
522794	29259	29278	CTAGGGAAGCATGTGCAGCC	72	3899
522795	29260	29279	TCTAGGGAAGCATGTGCAGC	65	3900
522796	29261	29280	TTCTAGGGAAGCATGTGCAG	61	3901
522797	29263	29282	GTTTCTAGGGAAGCATGTGC	72	3902
522798	29264	29283	AGTTTCTAGGGAAGCATGTG	40	3903

522799	29265	29284	AAGTTTCTAGGGAAGCATGT	46	3904
522800	29266	29285	CAAGTTTCTAGGGAAGCATG	42	3905
522801	29362	29381	TACAACTCTCTTGTTGGGAG	70	3906
522802	29363	29382	GTACAACTCTCTTGTTGGGA	73	3907
522803	29364	29383	GGTACAACTCTCTTGTTGGG	63	3908
522804	29365	29384	GGGTACAACTCTCTTGTTGG	57	3909
522805	29367	29386	CAGGGTACAACTCTCTTGTT	64	3910
522806	29368	29387	ACAGGGTACAACTCTCTTGT	57	3911
522807	29369	29388	AACAGGGTACAACTCTCTTG	85	3912
522808	29370	29389	AAACAGGGTACAACTCTCTT	63	3913
522809	29372	29391	AAAAACAGGGTACAACTCTC	62	3914
522810	29373	29392	TAAAAACAGGGTACAACTCT	32	3915
522811	29374	29393	CTAAAAACAGGGTACAACTC	21	3916
522812	29375	29394	GCTAAAAACAGGGTACAACT	31	3917
522813	29476	29495	TGTAGACTCTCCATGAGCCT	65	3918
522814	29477	29496	ATGTAGACTCTCCATGAGCC	45	3919
522815	29478	29497	GATGTAGACTCTCCATGAGC	25	3920
522816	29479	29498	GGATGTAGACTCTCCATGAG	42	3921
522817	30968	30987	TAAGCTAGGCACACCCAGGG	43	3922
522818	30969	30988	CTAAGCTAGGCACACCCAGG	23	3923
522819	30970	30989	ACTAAGCTAGGCACACCCAG	33	3924
522820	30971	30990	CACTAAGCTAGGCACACCCA	48	3925
522821	30973	30992	GGCACTAAGCTAGGCACACC	78	3926
522822	30975	30994	GTGGCACTAAGCTAGGCACA	69	3927
522823	30976	30995	TGTGGCACTAAGCTAGGCAC	66	3928
522824	30978	30997	ACTGTGGCACTAAGCTAGGC	69	3929
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	85	425

Table 57

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
522825	30979	30998	TACTGTGGCACTAAGCTAGG	53	3930
522826	30980	30999	TTACTGTGGCACTAAGCTAG	36	3931
522827	30981	31000	TTTACTGTGGCACTAAGCTA	40	3932
522828	30983	31002	TGTTTACTGTGGCACTAAGC	59	3933
522829	30984	31003	GTGTTTACTGTGGCACTAAG	68	3934
522830	30985	31004	AGTGTTTACTGTGGCACTAA	67	3935
522831	30986	31005	GAGTGTTTACTGTGGCACTA	72	3936
522832	31770	31789	ATGGATACTCAGAAGAGCAG	34	3937
522833	31771	31790	GATGGATACTCAGAAGAGCA	46	3938

522834	31793	31812	ACCTCAGGGCTGGCCCAAAG	47	3939
522835	31794	31813	GACCTCAGGGCTGGCCCAAA	67	3940
522836	31795	31814	GGACCTCAGGGCTGGCCCAA	66	3941
522837	31796	31815	AGGACCTCAGGGCTGGCCCA	68	3942
522838	31798	31817	TCAGGACCTCAGGGCTGGCC	78	3943
522839	31799	31818	GTCAGGACCTCAGGGCTGGC	66	3944
522840	31800	31819	TGTCAGGACCTCAGGGCTGG	53	3945
522841	31801	31820	CTGTCAGGACCTCAGGGCTG	49	3946
522842	31933	31952	GAGTTATCCTCAATTCACCA	74	3947
522843	31934	31953	AGAGTTATCCTCAATTCACC	59	3948
522844	31936	31955	CCAGAGTTATCCTCAATTCA	71	3949
522845	31938	31957	TGCCAGAGTTATCCTCAATT	52	3950
522846	31939	31958	CTGCCAGAGTTATCCTCAAT	62	3951
522847	31940	31959	CCTGCCAGAGTTATCCTCAA	64	3952
522848	31941	31960	TCCTGCCAGAGTTATCCTCA	68	3953
522849	31943	31962	GATCCTGCCAGAGTTATCCT	69	3954
522850	31944	31963	GGATCCTGCCAGAGTTATCC	62	3955
522851	31945	31964	AGGATCCTGCCAGAGTTATC	45	3956
522852	31946	31965	CAGGATCCTGCCAGAGTTAT	60	3957
522853	32116	32135	CAGCAAATATACACCACCCT	70	3958
522854	32117	32136	ACAGCAAATATACACCACCC	66	3959
522855	32118	32137	AACAGCAAATATACACCACC	56	3960
522856	32119	32138	CAACAGCAAATATACACCAC	66	3961
522857	32121	32140	CACAACAGCAAATATACACC	70	3962
522858	32122	32141	TCACAACAGCAAATATACAC	55	3963
522859	32123	32142	CTCACAACAGCAAATATACA	41	3964
522860	32124	32143	ACTCACAACAGCAAATATAC	48	3965
522861	32126	32145	TGACTCACAACAGCAAATAT	21	3966
522862	32127	32146	CTGACTCACAACAGCAAATA	33	3967
522863	32128	32147	ACTGACTCACAACAGCAAAT	44	3968
522864	32129	32148	CACTGACTCACAACAGCAAA	54	3969
522865	32131	32150	GTCACTGACTCACAACAGCA	85	3970
522866	32132	32151	AGTCACTGACTCACAACAGC	80	3971
522867	32133	32152	CAGTCACTGACTCACAACAG	62	3972
522868	32134	32153	TCAGTCACTGACTCACAACA	62	3973
522869	32136	32155	TCTCAGTCACTGACTCACAA	71	3974
522870	32137	32156	ATCTCAGTCACTGACTCACA	77	3975
522871	32138	32157	GATCTCAGTCACTGACTCAC	75	3976
522872	32139	32158	GGATCTCAGTCACTGACTCA	73	3977
522873	32173	32192	GGTTACCCAGCCACTGCCCC	65	3978
522874	32174	32193	GGGTTACCCAGCCACTGCCC	54	3979
522875	32175	32194	AGGGTTACCCAGCCACTGCC	61	3980

522876	32176	32195	CAGGGTTACCCAGCCACTGC	65	3981
522877	32178	32197	TGCAGGGTTACCCAGCCACT	74	3982
522878	32179	32198	ATGCAGGGTTACCCAGCCAC	73	3983
522879	32180	32199	GATGCAGGGTTACCCAGCCA	67	3984
522880	32181	32200	GGATGCAGGGTTACCCAGCC	69	3985
522881	32183	32202	AAGGATGCAGGGTTACCCAG	58	3986
522882	32184	32203	GAAGGATGCAGGGTTACCCA	58	3987
522883	32185	32204	TGAAGGATGCAGGGTTACCC	51	3988
522884	32186	32205	GTGAAGGATGCAGGGTTACC	43	3989
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	80	425
522885	33409	33428	ATCTTCATTACATGATTACT	59	3990
522886	33410	33429	GATCTTCATTACATGATTAC	58	3991
522887	33411	33430	AGATCTTCATTACATGATTA	69	3992
522888	33412	33431	CAGATCTTCATTACATGATT	81	3993
522889	33414	33433	GGCAGATCTTCATTACATGA	83	3994
522890	33669	33688	ATGGACAGGTGATTCTAAGC	69	3995
522891	33670	33689	GATGGACAGGTGATTCTAAG	56	3996
522892	33672	33691	CAGATGGACAGGTGATTCTA	62	3997
522893	33674	33693	GGCAGATGGACAGGTGATTC	67	3998
522894	33675	33694	AGGCAGATGGACAGGTGATT	76	3999
522895	33676	33695	GAGGCAGATGGACAGGTGAT	69	4000
522896	33677	33696	TGAGGCAGATGGACAGGTGA	50	4001
522897	33730	33749	GTGACCTTGGGATAGTCCCT	88	4002
522898	33731	33750	TGTGACCTTGGGATAGTCCC	76	4003
522899	33732	33751	TTGTGACCTTGGGATAGTCC	69	4004
522900	33733	33752	TTTGTGACCTTGGGATAGTC	52	4005
522901	33857	33876	GAGCAAAGGCTTGCTTAAGT	60	4006

Table 58

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	77	425
522902	33858	33877	AGAGCAAAGGCTTGCTTAAG	40	4007
522903	33859	33878	AAGAGCAAAGGCTTGCTTAA	41	4008
522904	33860	33879	GAAGAGCAAAGGCTTGCTTA	67	4009
522905	33862	33881	CAGAAGAGCAAAGGCTTGCT	74	4010
522906	33863	33882	ACAGAAGAGCAAAGGCTTGC	61	4011
522907	33864	33883	CACAGAAGAGCAAAGGCTTG	33	4012
522908	33865	33884	CCACAGAAGAGCAAAGGCTT	58	4013
522909	33867	33886	ACCCACAGAAGAGCAAAGGC	63	4014

522910	33868	33887	GACCCACAGAAGAGCAAAGG	40	4015
522911	33869	33888	AGACCCACAGAAGAGCAAAG	37	4016
522912	33870	33889	CAGACCCACAGAAGAGCAAA	37	4017
522913	34212	34231	ATGCCCTTGCTGTAGGACCC	84	4018
522914	34213	34232	AATGCCCTTGCTGTAGGACC	69	4019
522915	34214	34233	CAATGCCCTTGCTGTAGGAC	59	4020
522916	34215	34234	TCAATGCCCTTGCTGTAGGA	56	4021
522917	34740	34759	TTAGCTCTCAGTGAAGCTGG	76	4022
522918	34869	34888	AACAGCAGCAGTCTAATCCA	49	4023
522919	34870	34889	AAACAGCAGCAGTCTAATCC	50	4024
522920	34871	34890	GAAACAGCAGCAGTCTAATC	30	4025
522921	34872	34891	GGAAACAGCAGCAGTCTAAT	33	4026
522922	34899	34918	AACTCTCAGCTACTCCCCAA	46	4027
522923	34900	34919	CAACTCTCAGCTACTCCCCA	56	4028
522924	34901	34920	CCAACTCTCAGCTACTCCCC	75	4029
522925	34902	34921	ACCAACTCTCAGCTACTCCC	75	4030
522926	34932	34951	GCAAACAGATTAAAGTTGCT	55	4031
522927	34933	34952	GGCAAACAGATTAAAGTTGC	63	4032
522928	35274	35293	CACCTGAGTGCTGCAAAGTG	47	4033
522929	35275	35294	CCACCTGAGTGCTGCAAAGT	55	4034
522930	35276	35295	CCCACCTGAGTGCTGCAAAG	58	4035
522931	35277	35296	TCCCACCTGAGTGCTGCAAA	60	4036
522932	35279	35298	ACTCCCACCTGAGTGCTGCA	77	4037
522933	35280	35299	CACTCCCACCTGAGTGCTGC	62	4038
522934	35281	35300	ACACTCCCACCTGAGTGCTG	64	4039
522935	35282	35301	GACACTCCCACCTGAGTGCT	69	4040
522936	35319	35338	TTTTTGGCTGCCCTGCCTCA	35	4041
522937	35320	35339	CTTTTTGGCTGCCCTGCCTC	56	4042
522938	35321	35340	TCTTTTTGGCTGCCCTGCCT	58	4043
522939	35322	35341	GTCTTTTTGGCTGCCCTGCC	74	4044
522940	35324	35343	TGGTCTTTTTGGCTGCCCTG	72	4045
522941	35325	35344	TTGGTCTTTTTGGCTGCCCT	79	4046
522942	35326	35345	GTTGGTCTTTTTGGCTGCCC	81	4047
522943	35327	35346	CGTTGGTCTTTTTGGCTGCC	79	4048
522944	35407	35426	CTTATCTTTGTCCACATATC	57	4049
522945	35408	35427	CCTTATCTTTGTCCACATAT	66	4050
522946	35409	35428	ACCTTATCTTTGTCCACATA	60	4051
522947	35410	35429	TACCTTATCTTTGTCCACAT	75	4052
522948	35412	35431	AATACCTTATCTTTGTCCAC	67	4053
522949	35413	35432	AAATACCTTATCTTTGTCCA	61	4054
522950	35414	35433	TAAATACCTTATCTTTGTCC	71	4055
522951	35415	35434	ATAAATACCTTATCTTTGTC	16	4056

522952	35417	35436	CAATAAATACCTTATCTTTG	22	4057
522953	35418	35437	TCAATAAATACCTTATCTTT	3	4058
522954	35419	35438	TTCAATAAATACCTTATCTT	12	4059
522955	35420	35439	CTTCAATAAATACCTTATCT	47	4060
522956	35422	35441	TGCTTCAATAAATACCTTAT	65	4061
522957	35423	35442	ATGCTTCAATAAATACCTTA	55	4062
522958	35424	35443	AATGCTTCAATAAATACCTT	42	4063
522959	35425	35444	TAATGCTTCAATAAATACCT	42	4064
522960	35432	35451	TTAGAAGTAATGCTTCAATA	37	4065
522961	35433	35452	CTTAGAAGTAATGCTTCAAT	44	4066
522962	35434	35453	TCTTAGAAGTAATGCTTCAA	44	4067
522963	35435	35454	CTCTTAGAAGTAATGCTTCA	59	4068
522964	35437	35456	CCCTCTTAGAAGTAATGCTT	80	4069
522965	35438	35457	TCCCTCTTAGAAGTAATGCT	73	4070
522966	35439	35458	TTCCCTCTTAGAAGTAATGC	59	4071
522967	35440	35459	TTTCCCTCTTAGAAGTAATG	48	4072
522968	37835	37854	GCTAATGATACAAGGTTGTT	57	4073
522969	37836	37855	AGCTAATGATACAAGGTTGT	54	4074
522970	37838	37857	GCAGCTAATGATACAAGGTT	65	4075
522971	37840	37859	ATGCAGCTAATGATACAAGG	57	4076
522972	37841	37860	AATGCAGCTAATGATACAAG	33	4077
522973	37842	37861	AAATGCAGCTAATGATACAA	24	4078
522974	37843	37862	AAAATGCAGCTAATGATACA	22	4079
522975	39666	39685	AAGAGTTACCTCCTCCCTGG	30	4080
522976	39667	39686	CAAGAGTTACCTCCTCCCTG	36	4081
522977	39668	39687	GCAAGAGTTACCTCCTCCCT	62	4082
522978	39669	39688	TGCAAGAGTTACCTCCTCCC	61	4083

Table 59

Inhibition of DGAT2 mRNA by 3-10-4 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
525386	10047	10063	CCACAGGGCCCTTTCCA	49	4141
525387	10048	10064	GCCACAGGGCCCTTTCC	53	4142
525388	10215	10231	GTTCTCGAATATCCCTA	67	4143
525389	10216	10232	AGTTCTCGAATATCCCT	55	4144
525390	10217	10233	GAGTTCTCGAATATCCC	52	4145
525391	10218	10234	GGAGTTCTCGAATATCC	60	4146
525392	10219	10235	AGGAGTTCTCGAATATC	34	4147
525393	10220	10236	GAGGAGTTCTCGAATAT	41	4148
525394	10490	10506	GGTCCTCTCCGCTGCCT	62	4149

525395	10491	10507	GGGTCCTCTCCGCTGCC	70	4150
525396	10492	10508	AGGGTCCTCTCCGCTGC	57	4151
525397	10529	10545	TTCACTGAGGACCTCAG	29	4152
525398	10530	10546	ATTCACTGAGGACCTCA	44	4153
525399	10531	10547	GATTCACTGAGGACCTC	66	4154
525400	10532	10548	CGATTCACTGAGGACCT	48	4155
525401	10533	10549	GCGATTCACTGAGGACC	83	4156
525402	10534	10550	CGCGATTCACTGAGGAC	71	4157
525403	10535	10551	GCGCGATTCACTGAGGA	68	4158
525404	10536	10552	TGCGCGATTCACTGAGG	65	4159
525405	10537	10553	CTGCGCGATTCACTGAG	60	4160
525406	10538	10554	TCTGCGCGATTCACTGA	45	4161
525407	10650	10666	TCCTCCCACTTCAGTTT	28	4162
525408	10651	10667	TTCCTCCCACTTCAGTT	18	4163
525409	10652	10668	CTTCCTCCCACTTCAGT	30	4164
525410	10654	10670	TGCTTCCTCCCACTTCA	30	4165
525411	10655	10671	ATGCTTCCTCCCACTTC	37	4166
525412	10656	10672	CATGCTTCCTCCCACTT	32	4167
525413	10657	10673	GCATGCTTCCTCCCACT	59	4168
525414	10658	10674	GGCATGCTTCCTCCCAC	69	4169
525415	10659	10675	AGGCATGCTTCCTCCCA	71	4170
525416	10660	10676	TAGGCATGCTTCCTCCC	62	4171
525417	10661	10677	TTAGGCATGCTTCCTCC	53	4172
525418	10662	10678	CTTAGGCATGCTTCCTC	53	4173
525419	10663	10679	ACTTAGGCATGCTTCCT	63	4174
525420	10664	10680	AACTTAGGCATGCTTCC	62	4175
525421	10665	10681	AAACTTAGGCATGCTTC	50	4176
525422	10666	10682	AAAACTTAGGCATGCTT	58	4177
525423	10667	10683	GAAAACTTAGGCATGCT	68	4178
525424	10668	10684	GGAAAACTTAGGCATGC	65	4179
525425	10669	10685	AGGAAAACTTAGGCATG	41	4180
525426	10670	10686	AAGGAAAACTTAGGCAT	15	4181
525427	10671	10687	TAAGGAAAACTTAGGCA	15	4182
525428	10672	10688	CTAAGGAAAACTTAGGC	12	4183
525429	10728	10744	GATGACTTCCCAGGGTC	32	4184
525430	10729	10745	TGATGACTTCCCAGGGT	41	4185
525431	10730	10746	GTGATGACTTCCCAGGG	78	4186
525432	10731	10747	TGTGATGACTTCCCAGG	51	4187
525433	10732	10748	CTGTGATGACTTCCCAG	41	4188
525434	10733	10749	GCTGTGATGACTTCCCA	63	4189
525435	10734	10750	AGCTGTGATGACTTCCC	61	4190
525436	10735	10751	CAGCTGTGATGACTTCC	60	4191

525437	10736	10752	ACAGCTGTGATGACTTC	31	4192
525438	10737	10753	GACAGCTGTGATGACTT	0	4193
525439	10816	10832	TGTCAGAGAGGCTCAGC	59	4194
525440	10817	10833	ATGTCAGAGAGGCTCAG	41	4195
525441	10818	10834	CATGTCAGAGAGGCTCA	60	4196
525442	10819	10835	CCATGTCAGAGAGGCTC	73	4197
525443	10820	10836	TCCATGTCAGAGAGGCT	75	4198
525444	10821	10837	ATCCATGTCAGAGAGGC	64	4199
525445	10822	10838	AATCCATGTCAGAGAGG	44	4200
525446	10823	10839	AAATCCATGTCAGAGAG	10	4201
525447	10940	10956	TAGTCGATTTACCAGAA	31	4202
525448	10941	10957	ATAGTCGATTTACCAGA	31	4203
525449	10942	10958	GATAGTCGATTTACCAG	43	4204
525450	10943	10959	GGATAGTCGATTTACCA	62	4205
525451	10944	10960	TGGATAGTCGATTTACC	48	4206
525452	10945	10961	TTGGATAGTCGATTTAC	36	4207
525453	10946	10962	TTTGGATAGTCGATTTA	16	4208
525454	11074	11090	CGATGTTACATTAAGGG	26	4209
525455	11075	11091	TCGATGTTACATTAAGG	24	4210
525456	11076	11092	CTCGATGTTACATTAAG	11	4211
496041	31122	31138	CACAGCGATGAGCCAGC	52	1096
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	69	425
525765	36860	36876	ATTATTCTAAAACTCAA	11	4212
525766	36861	36877	GATTATTCTAAAACTCA	6	4213
525767	36862	36878	TGATTATTCTAAAACTC	7	4214
525768	37022	37038	GGGCAGTCACCATTTGC	14	4215
525769	37023	37039	TGGGCAGTCACCATTTG	12	4216
525770	37024	37040	TTGGGCAGTCACCATTT	7	4217

Table 60

Inhibition of DGAT2 mRNA by 3-10-4 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
525457	11077	11093	CCTCGATGTTACATTAA	44	4218
525458	11127	11143	TATTGCAACCACTAGGA	36	4219
525459	11128	11144	TTATTGCAACCACTAGG	41	4220
525460	11129	11145	GTTATTGCAACCACTAG	49	4221
525461	11130	11146	GGTTATTGCAACCACTA	61	4222
525462	11158	11174	AGTTAAAGTGTGGTACA	4	4223
525463	11159	11175	CAGTTAAAGTGTGGTAC	37	4224
525464	11160	11176	ACAGTTAAAGTGTGGTA	14	4225

525465	11171	11187	ATGCCTAGGTCACAGTT	55	4226
525466	11172	11188	AATGCCTAGGTCACAGT	48	4227
525467	11173	11189	CAATGCCTAGGTCACAG	44	4228
525468	11174	11190	CCAATGCCTAGGTCACA	73	4229
525469	11175	11191	GCCAATGCCTAGGTCAC	89	4230
525470	11176	11192	TGCCAATGCCTAGGTCA	82	4231
525471	11177	11193	ATGCCAATGCCTAGGTC	79	4232
525472	11178	11194	AATGCCAATGCCTAGGT	76	4233
525473	11179	11195	CAATGCCAATGCCTAGG	69	4234
525474	11180	11196	GCAATGCCAATGCCTAG	78	4235
525475	11199	11215	AGCGATAATCACACAAG	54	4236
525476	11200	11216	CAGCGATAATCACACAA	58	4237
525477	11201	11217	ACAGCGATAATCACACA	72	4238
525478	11202	11218	CACAGCGATAATCACAC	49	4239
525479	11203	11219	CCACAGCGATAATCACA	79	4240
525480	11204	11220	ACCACAGCGATAATCAC	76	4241
525481	11205	11221	AACCACAGCGATAATCA	40	4242
525482	14503	14519	GGTCTGCCACTCTCTAC	49	4243
525483	14504	14520	GGGTCTGCCACTCTCTA	47	4244
525484	14505	14521	AGGGTCTGCCACTCTCT	64	4245
525485	14648	14664	AGTCATCTTGTGTACAT	60	4246
525486	14649	14665	CAGTCATCTTGTGTACA	49	4247
525487	14650	14666	ACAGTCATCTTGTGTAC	52	4248
525488	14663	14679	CAGATCACTCTGCACAG	62	4249
525489	14664	14680	TCAGATCACTCTGCACA	65	4250
525490	14665	14681	CTCAGATCACTCTGCAC	61	4251
525491	14667	14683	TGCTCAGATCACTCTGC	60	4252
525492	14668	14684	TTGCTCAGATCACTCTG	51	4253
525493	14669	14685	ATTGCTCAGATCACTCT	54	4254
525494	14745	14761	ACCTCTTCCAGGAAGAC	41	4255
525495	14746	14762	CACCTCTTCCAGGAAGA	44	4256
525496	14747	14763	TCACCTCTTCCAGGAAG	28	4257
525497	14755	14771	ACTGAATGTCACCTCTT	57	4258
525498	14756	14772	GACTGAATGTCACCTCT	62	4259
525499	14757	14773	GGACTGAATGTCACCTC	71	4260
525500	14758	14774	CGGACTGAATGTCACCT	74	4261
525501	14759	14775	CCGGACTGAATGTCACC	80	4262
525502	14760	14776	TCCGGACTGAATGTCAC	39	4263
525503	14770	14786	TCTTTCCAGATCCGGAC	53	4264
525504	14771	14787	ATCTTTCCAGATCCGGA	62	4265
525505	14772	14788	CATCTTTCCAGATCCGG	70	4266
525506	14773	14789	TCATCTTTCCAGATCCG	71	4267

525507	14774	14790	TTCATCTTTCCAGATCC	63	4268
525508	14775	14791	ATTCATCTTTCCAGATC	23	4269
525509	14996	15012	TCTCAAGTCTTCCTCCT	33	4270
525510	14997	15013	CTCTCAAGTCTTCCTCC	46	4271
525511	14998	15014	GCTCTCAAGTCTTCCTC	65	4272
525512	14999	15015	AGCTCTCAAGTCTTCCT	72	4273
525513	15000	15016	GAGCTCTCAAGTCTTCC	73	4274
525514	15001	15017	TGAGCTCTCAAGTCTTC	64	4275
525515	15250	15266	ATAATCTGCACAGGTTC	72	4276
525516	15251	15267	CATAATCTGCACAGGTT	67	4277
525517	15252	15268	CCATAATCTGCACAGGT	69	4278
525518	15253	15269	ACCATAATCTGCACAGG	68	4279
525519	15254	15270	CACCATAATCTGCACAG	49	4280
525520	15255	15271	GCACCATAATCTGCACA	60	4281
525521	18156	18172	TTAATCCAGGATTGTCA	55	4282
525522	18157	18173	TTTAATCCAGGATTGTC	57	4283
525523	18158	18174	CTTTAATCCAGGATTGT	26	4284
525524	18161	18177	TAGCTTTAATCCAGGAT	42	4285
525525	18162	18178	TTAGCTTTAATCCAGGA	28	4286
525526	18163	18179	CTTAGCTTTAATCCAGG	45	4287
525527	18164	18180	CCTTAGCTTTAATCCAG	27	4288
525528	18165	18181	TCCTTAGCTTTAATCCA	60	4289
525529	18166	18182	CTCCTTAGCTTTAATCC	23	4290
525530	18167	18183	CCTCCTTAGCTTTAATC	32	4291
525531	18168	18184	TCCTCCTTAGCTTTAAT	28	4292
525532	18174	18190	TCAGTGTCCTCCTTAGC	39	4293
525533	18175	18191	CTCAGTGTCCTCCTTAG	32	4294
496041	31122	31138	CACAGCGATGAGCCAGC	64	1096
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	78	425

Table 61

Inhibition of DGAT2 mRNA by 3-10-4 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
525534	18176	18192	ACTCAGTGTCCTCCTTA	35	4295
525535	18177	18193	GACTCAGTGTCCTCCTT	64	4296
525536	18178	18194	GGACTCAGTGTCCTCCT	73	4297
525537	18180	18196	TGGGACTCAGTGTCCTC	62	4298
525538	18181	18197	CTGGGACTCAGTGTCCT	59	4299
525539	18182	18198	CCTGGGACTCAGTGTCC	63	4300
525540	18308	18324	CTGTTTGATGGGTAAAA	20	4301

525541	18309	18325	CCTGTTTGATGGGTAAA	62	4302
525542	18310	18326	TCCTGTTTGATGGGTAA	68	4303
525543	18311	18327	CTCCTGTTTGATGGGTA	39	4304
525544	18312	18328	TCTCCTGTTTGATGGGT	73	4305
525545	18313	18329	CTCTCCTGTTTGATGGG	47	4306
525546	18314	18330	CCTCTCCTGTTTGATGG	43	4307
525547	18321	18337	TCGGTGTCCTCTCCTGT	63	4308
525548	18322	18338	CTCGGTGTCCTCTCCTG	64	4309
525549	18323	18339	CCTCGGTGTCCTCTCCT	60	4310
525550	18324	18340	GCCTCGGTGTCCTCTCC	68	4311
525551	18325	18341	AGCCTCGGTGTCCTCTC	78	4312
525552	18326	18342	AAGCCTCGGTGTCCTCT	73	4313
525553	18327	18343	TAAGCCTCGGTGTCCTC	70	4314
525554	18328	18344	GTAAGCCTCGGTGTCCT	75	4315
525555	18329	18345	AGTAAGCCTCGGTGTCC	64	4316
525556	18417	18433	CCAGATTGTTGTGGGAA	66	4317
525557	18418	18434	ACCAGATTGTTGTGGGA	68	4318
525558	18419	18435	CACCAGATTGTTGTGGG	63	4319
525559	18432	18448	CTAATACCTACCTCACC	35	4320
525560	18433	18449	GCTAATACCTACCTCAC	25	4321
525561	18434	18450	GGCTAATACCTACCTCA	34	4322
525562	18450	18466	CTCATCTATACAGTGGG	58	4323
525563	18451	18467	CCTCATCTATACAGTGG	51	4324
525564	18452	18468	TCCTCATCTATACAGTG	28	4325
525565	18581	18597	ACTGGCATCTGGCAGGG	69	4326
525566	18582	18598	TACTGGCATCTGGCAGG	52	4327
525567	18583	18599	ATACTGGCATCTGGCAG	31	4328
525568	18591	18607	TCACCTCCATACTGGCA	21	4329
525569	18592	18608	CTCACCTCCATACTGGC	20	4330
525570	18593	18609	CCTCACCTCCATACTGG	6	4331
525571	18828	18844	ATGCTTAACTTCTGCTG	48	4332
525572	18829	18845	GATGCTTAACTTCTGCT	46	4333
525573	18830	18846	GGATGCTTAACTTCTGC	53	4334
525574	18831	18847	AGGATGCTTAACTTCTG	40	4335
525575	18832	18848	TAGGATGCTTAACTTCT	40	4336
525576	18833	18849	TTAGGATGCTTAACTTC	20	4337
525577	18869	18885	GGCCTGGATGCCCAAGT	65	4338
	20779	20795			
525578	18870	18886	AGGCCTGGATGCCCAAG	71	4339
	20780	20796			
525579	18871	18887	TAGGCCTGGATGCCCAA	66	4340
	20781	20797			

525580	18900	18916	CAGATGATGTCCTGCCT	25	4341
525581	18901	18917	GCAGATGATGTCCTGCC	55	4342
525582	18902	18918	AGCAGATGATGTCCTGC	38	4343
525583	19018	19034	TAGTCAAAGGTGGCTTC	44	4344
525584	19019	19035	GTAGTCAAAGGTGGCTT	57	4345
525585	19020	19036	AGTAGTCAAAGGTGGCT	55	4346
525589	22548	22564	AACAAGTGGGAAATGCA	17	4347
525590	22549	22565	CAACAAGTGGGAAATGC	19	4348
525591	22550	22566	CCAACAAGTGGGAAATG	23	4349
525592	22771	22787	AGCTTATTAGGTGTCTT	42	4350
525593	22772	22788	AAGCTTATTAGGTGTCT	53	4351
525594	22773	22789	TAAGCTTATTAGGTGTC	44	4352
525595	22774	22790	CTAAGCTTATTAGGTGT	36	4353
525596	22886	22902	CCCCCATGCAGCTTGGA	29	4354
525597	22887	22903	GCCCCCATGCAGCTTGG	43	4355
525598	22888	22904	AGCCCCCATGCAGCTTG	50	4356
525599	23096	23112	CCAAACACTCAGGTAGG	49	4357
525600	23097	23113	TCCAAACACTCAGGTAG	41	4358
525601	23098	23114	GTCCAAACACTCAGGTA	54	4359
525602	23100	23116	CAGTCCAAACACTCAGG	47	4360
525603	23101	23117	TCAGTCCAAACACTCAG	57	4361
525604	23102	23118	TTCAGTCCAAACACTCA	49	4362
525605	23239	23255	GAACAGCAGCATCAGCA	47	4363
525606	23240	23256	GGAACAGCAGCATCAGC	67	4364
525607	23241	23257	GGGAACAGCAGCATCAG	40	4365
525608	23242	23258	TGGGAACAGCAGCATCA	44	4366
525609	23243	23259	CTGGGAACAGCAGCATC	69	4367
525610	23244	23260	TCTGGGAACAGCAGCAT	65	4368
525586	36855	36871	TCTAAAACTCAAATCCA	0	4369
525587	36856	36872	TTCTAAAACTCAAATCC	0	4370
525588	36857	36873	ATTCTAAAACTCAAATC	0	4371
496041	31122	31138	CACAGCGATGAGCCAGC	64	1096
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	78	425

Table 62

Inhibition of DGAT2 mRNA by 3-10-4 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
525611	23245	23261	GTCTGGGAACAGCAGCA	65	4372
525612	23246	23262	GGTCTGGGAACAGCAGC	83	4373
525613	23247	23263	TGGTCTGGGAACAGCAG	42	4374

525614	23427	23443	ACAAGTCATCTTCCAGC	16	4375
525615	23428	23444	GACAAGTCATCTTCCAG	24	4376
525616	23429	23445	GGACAAGTCATCTTCCA	37	4377
525617	23551	23567	ATCCTTGAGGGTCTCAT	55	4378
525618	23552	23568	TATCCTTGAGGGTCTCA	55	4379
525619	23553	23569	TTATCCTTGAGGGTCTC	65	4380
525620	23554	23570	CTTATCCTTGAGGGTCT	46	4381
525621	26400	26416	CCTGGATGGCAACCTAA	42	4382
525622	26401	26417	GCCTGGATGGCAACCTA	33	4383
525623	26402	26418	GGCCTGGATGGCAACCT	43	4384
525624	26484	26500	CTGCTATGCTGAGAGCA	44	4385
525625	26485	26501	CCTGCTATGCTGAGAGC	42	4386
525626	26486	26502	ACCTGCTATGCTGAGAG	8	4387
525627	26516	26532	GTTCATCTGCCTTGACG	44	4388
525628	26517	26533	GGTTCATCTGCCTTGAC	56	4389
525629	26518	26534	AGGTTCATCTGCCTTGA	33	4390
525630	26519	26535	CAGGTTCATCTGCCTTG	55	4391
525631	26520	26536	GCAGGTTCATCTGCCTT	75	4392
525632	26521	26537	AGCAGGTTCATCTGCCT	62	4393
525633	26536	26552	TCTGTGATGCTCTGGAG	33	4394
525634	26537	26553	CTCTGTGATGCTCTGGA	43	4395
525635	26538	26554	ACTCTGTGATGCTCTGG	46	4396
525636	26539	26555	CACTCTGTGATGCTCTG	39	4397
525637	26627	26643	ACATGGTAAGTCCTGAT	38	4398
525638	26628	26644	GACATGGTAAGTCCTGA	55	4399
525639	26629	26645	TGACATGGTAAGTCCTG	58	4400
525640	26630	26646	CTGACATGGTAAGTCCT	55	4401
525641	26631	26647	ACTGACATGGTAAGTCC	35	4402
525642	26632	26648	CACTGACATGGTAAGTC	48	4403
525643	26783	26799	TCTGCCATTTAATGAGC	19	4404
525644	26784	26800	CTCTGCCATTTAATGAG	22	4405
525645	26785	26801	ACTCTGCCATTTAATGA	12	4406
525646	26788	26804	CCAACTCTGCCATTTAA	43	4407
525647	26789	26805	CCCAACTCTGCCATTTA	47	4408
525648	26790	26806	TCCCAACTCTGCCATTT	35	4409
525649	26926	26942	AGGGTTCATGGATCCCC	69	4410
525650	26927	26943	AAGGGTTCATGGATCCC	67	4411
525651	26928	26944	TAAGGGTTCATGGATCC	44	4412
525652	27251	27267	CTGGAGTCCCTGGGTTC	45	4413
525653	27252	27268	GCTGGAGTCCCTGGGTT	30	4414
525654	27253	27269	GGCTGGAGTCCCTGGGT	31	4415
525655	27352	27368	AGCCAGGCCCAGACCCA	32	4416

525656	27353	27369	CAGCCAGGCCCAGACCC	22	4417
525657	27354	27370	CCAGCCAGGCCCAGACC	11	4418
525658	27382	27398	GGTGTTCTACAAGCTGC	61	4419
525659	27383	27399	TGGTGTTCTACAAGCTG	50	4420
525660	27384	27400	CTGGTGTTCTACAAGCT	49	4421
525661	27387	27403	GAGCTGGTGTTCTACAA	34	4422
525662	27388	27404	TGAGCTGGTGTTCTACA	47	4423
525663	27389	27405	GTGAGCTGGTGTTCTAC	55	4424
525664	27437	27453	GATCAATTATTAACCTA	14	4425
525665	27438	27454	TGATCAATTATTAACCT	0	4426
525666	27439	27455	CTGATCAATTATTAACC	5	4427
525667	29678	29694	GCAGGTACTCATGTTTG	50	4428
525668	29679	29695	AGCAGGTACTCATGTTT	39	4429
525669	29680	29696	CAGCAGGTACTCATGTT	31	4430
525670	29782	29798	CCAATATCATACTATCT	5	4431
525671	29783	29799	CCCAATATCATACTATC	13	4432
525672	29784	29800	CCCCAATATCATACTAT	40	4433
525673	29828	29844	AACCTTTAAGGCCTATC	16	4434
525674	29829	29845	CAACCTTTAAGGCCTAT	23	4435
525675	29830	29846	CCAACCTTTAAGGCCTA	35	4436
525676	29831	29847	CCCAACCTTTAAGGCCT	40	4437
525677	29839	29855	ATTTTTTACCCAACCTT	30	4438
525678	29840	29856	CATTTTTTACCCAACCT	24	4439
525679	29841	29857	CCATTTTTTACCCAACC	50	4440
525680	29842	29858	TCCATTTTTTACCCAAC	40	4441
525681	29843	29859	TTCCATTTTTTACCCAA	24	4442
525682	30483	30499	GCTTTAGAAATTCACCA	45	4443
525683	30484	30500	GGCTTTAGAAATTCACC	68	4444
525684	30485	30501	AGGCTTTAGAAATTCAC	39	4445
496041	31122	31138	CACAGCGATGAGCCAGC	58	1096
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	76	425
525685	32431	32447	TGGACAAGTCCTGCCCA	47	4446
525686	32432	32448	CTGGACAAGTCCTGCCC	58	4447
525687	32433	32449	CCTGGACAAGTCCTGCC	60	4448

Table 63

Inhibition of DGAT2 mRNA by 3-10-4 MOE gapmers targeting SEQ ID NO: 2

ISIS NO	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence	% inhibition	SEQ ID NO
496041	31122	31138	CACAGCGATGAGCCAGC	44	1096
413433	32431	32450	GCCTGGACAAGTCCTGCCCA	74	425

525688	32434	32450	GCCTGGACAAGTCCTGC	77	4449
525689	32435	32451	AGCCTGGACAAGTCCTG	50	4450
525690	32447	32463	ACTAGACTATGCAGCCT	62	4451
525691	32448	32464	TACTAGACTATGCAGCC	55	4452
525692	32449	32465	ATACTAGACTATGCAGC	37	4453
525693	32450	32466	CATACTAGACTATGCAG	17	4454
525694	32451	32467	TCATACTAGACTATGCA	20	4455
525695	32452	32468	ATCATACTAGACTATGC	20	4456
525696	32453	32469	CATCATACTAGACTATG	13	4457
525697	32454	32470	CCATCATACTAGACTAT	32	4458
525698	32455	32471	GCCATCATACTAGACTA	58	4459
525699	32456	32472	TGCCATCATACTAGACT	51	4460
525700	32457	32473	TTGCCATCATACTAGAC	40	4461
525701	32458	32474	GTTGCCATCATACTAGA	51	4462
525702	32460	32476	ATGTTGCCATCATACTA	52	4463
525703	32461	32477	AATGTTGCCATCATACT	28	4464
525704	32462	32478	CAATGTTGCCATCATAC	40	4465
525705	32463	32479	GCAATGTTGCCATCATA	73	4466
525706	32464	32480	TGCAATGTTGCCATCAT	62	4467
525707	32465	32481	TTGCAATGTTGCCATCA	61	4468
525708	32466	32482	GTTGCAATGTTGCCATC	79	4469
525709	32467	32483	GGTTGCAATGTTGCCAT	69	4470
525710	32468	32484	TGGTTGCAATGTTGCCA	66	4471
525711	32469	32485	GTGGTTGCAATGTTGCC	73	4472
525712	32470	32486	GGTGGTTGCAATGTTGC	45	4473
525713	32476	32492	CTGGATGGTGGTTGCAA	20	4474
525714	32477	32493	CCTGGATGGTGGTTGCA	59	4475
525715	32478	32494	GCCTGGATGGTGGTTGC	58	4476
525716	32479	32495	AGCCTGGATGGTGGTTG	34	4477
525717	32619	32635	GAGATCTCCAGCAGCAA	52	4478
525718	32620	32636	TGAGATCTCCAGCAGCA	57	4479
525719	32621	32637	CTGAGATCTCCAGCAGC	51	4480
525720	32622	32638	ACTGAGATCTCCAGCAG	16	4481
525721	32645	32661	GGAGTGACAGGGCAGGA	42	4482
525722	32646	32662	TGGAGTGACAGGGCAGG	42	4483
525723	32647	32663	ATGGAGTGACAGGGCAG	35	4484
525724	32752	32768	AAGTCTATCAGGATGCA	43	4485
525725	32753	32769	AAAGTCTATCAGGATGC	37	4486
525726	32754	32770	CAAAGTCTATCAGGATG	20	4487
525727	32755	32771	ACAAAGTCTATCAGGAT	0	4488
525728	32757	32773	TGACAAAGTCTATCAGG	25	4489
525729	32758	32774	GTGACAAAGTCTATCAG	51	4490

525730	32759	32775	AGTGACAAAGTCTATCA	28	4491
525731	33180	33196	CCTAGTGCCCCAGGGAG	29	4492
525732	33181	33197	TCCTAGTGCCCCAGGGA	25	4493
525733	33182	33198	GTCCTAGTGCCCCAGGG	74	4494
525734	33183	33199	TGTCCTAGTGCCCCAGG	53	4495
525735	36248	36264	GGTATTCTGCTCATAAA	43	4496
525736	36249	36265	GGGTATTCTGCTCATAA	50	4497
525737	36250	36266	AGGGTATTCTGCTCATA	65	4498
525738	36251	36267	AAGGGTATTCTGCTCAT	55	4499
525739	36252	36268	TAAGGGTATTCTGCTCA	58	4500
525740	36253	36269	GTAAGGGTATTCTGCTC	64	4501
525741	36254	36270	AGTAAGGGTATTCTGCT	60	4502
525742	36263	36279	GAGACAATGAGTAAGGG	25	4503
525743	36264	36280	AGAGACAATGAGTAAGG	19	4504
525744	36265	36281	GAGAGACAATGAGTAAG	11	4505
525745	36522	36538	AAGCGACAGCCCTGTGC	17	4506
525746	36523	36539	CAAGCGACAGCCCTGTG	16	4507
525747	36524	36540	ACAAGCGACAGCCCTGT	28	4508
525748	36652	36668	AATGAGACAGGCAGCCC	40	4509
525749	36653	36669	GAATGAGACAGGCAGCC	35	4510
525750	36654	36670	AGAATGAGACAGGCAGC	37	4511
525751	36679	36695	CTCTGTGGGCTCCTCCA	25	4512
525752	36680	36696	GCTCTGTGGGCTCCTCC	57	4513
525753	36681	36697	TGCTCTGTGGGCTCCTC	46	4514
525754	36682	36698	GTGCTCTGTGGGCTCCT	76	4515
525755	36683	36699	TGTGCTCTGTGGGCTCC	59	4516
525756	36686	36702	CCCTGTGCTCTGTGGGC	30	4517
525757	36687	36703	GCCCTGTGCTCTGTGGG	32	4518
525758	36688	36704	GGCCCTGTGCTCTGTGG	40	4519
525759	36738	36754	CCACTGTCAGTCTCTCC	40	4520
525760	36739	36755	CCCACTGTCAGTCTCTC	46	4521
525761	36740	36756	CCCCACTGTCAGTCTCT	29	4522
525762	36758	36774	CTTGGCTGCAAGCTCTG	22	4523
525763	36759	36775	CCTTGGCTGCAAGCTCT	37	4524
525764	36760	36776	GCCTTGGCTGCAAGCTC	30	4525

Example 5: Antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Antisense oligonucleotides were designed targeting a diacylglycerol acyltransferase 2 (DGAT2) nucleic acid and were tested for their effects on DGAT2 mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were

transfected using electroporation with 1,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. ISIS 413433, which consistently demonstrated higher potency than any of the previously disclosed oligonucleotides in the studies above was included in this study as a benchmark oligonucleotide. Antisense oligonucleotides that demonstrated about the same or greater potency than ISIS 413433 were therefore considered for further experimentation.

The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE gapmers. The gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to the human DGAT2 genomic sequence, designated herein as SEQ ID NO: 2 (RefSeq No. NT_033927.5 truncated from nucleotides 5669186 to 5712008). 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity. In case the sequence alignment for a target gene in a particular table is not shown, it is understood that none of the oligonucleotides presented in that table align with 100% complementarity with that target gene.

Table 64

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
472445	1000	1019	CTGCATTCTTGCCAGGCATG	70	38153	38172	4527
472446	1001	1020	ACTGCATTCTTGCCAGGCAT	76	38154	38173	4528
472447	1003	1022	TGACTGCATTCTTGCCAGGC	82	38156	38175	4529
472448	1004	1023	GTGACTGCATTCTTGCCAGG	76	38157	38176	4530
472449	1006	1025	GGGTGACTGCATTCTTGCCA	42	38159	38178	4531
472450	1007	1026	AGGGTGACTGCATTCTTGCC	81	38160	38179	4532
472451	1008	1027	CAGGGTGACTGCATTCTTGC	71	38161	38180	4533
472452	1010	1029	CGCAGGGTGACTGCATTCTT	69	38163	38182	4534

472453	1011	1030	CCGCAGGGTGACTGCATTCT	78	38164	38183	4535
472454	1013	1032	TTCCGCAGGGTGACTGCATT	53	38166	38185	4536
472455	1014	1033	GTTCCGCAGGGTGACTGCAT	76	38167	38186	4537
472456	1015	1034	GGTTCCGCAGGGTGACTGCA	86	38168	38187	4538
472457	1017	1036	GCGGTTCCGCAGGGTGACTG	77	38170	38189	4539
472458	1018	1037	TGCGGTTCCGCAGGGTGACT	81	38171	38190	4540
472459	1020	1039	CTTGCGGTTCCGCAGGGTGA	60	38173	38192	4541
472460	1021	1040	CCTTGCGGTTCCGCAGGGTG	55	38174	38193	4542
472461	1023	1042	GCCCTTGCGGTTCCGCAGGG	23	38176	38195	4543
472462	1024	1043	AGCCCTTGCGGTTCCGCAGG	61	38177	38196	4544
472463	1026	1045	AAAGCCCTTGCGGTTCCGCA	76	38179	38198	4545
472464	1027	1046	CAAAGCCCTTGCGGTTCCGC	74	38180	38199	4546
472465	1029	1048	CACAAAGCCCTTGCGGTTCC	53	38182	38201	4547
472466	1030	1049	TCACAAAGCCCTTGCGGTTC	23	38183	38202	4548
472467	1032	1051	TTTCACAAAGCCCTTGCGGT	0	38185	38204	4549
472468	1033	1052	GTTTCACAAAGCCCTTGCGG	46	38186	38205	4550
472469	1035	1054	CAGTTTCACAAAGCCCTTGC	51	38188	38207	4551
472470	1036	1055	CCAGTTTCACAAAGCCCTTG	55	38189	38208	4552
472471	1038	1057	GGCCAGTTTCACAAAGCCCT	37	38191	38210	4553
472472	1039	1058	GGGCCAGTTTCACAAAGCCC	0	38192	38211	4554
472473	1041	1060	CAGGGCCAGTTTCACAAAGC	34	38194	38213	4555
472474	1042	1061	GCAGGGCCAGTTTCACAAAG	63	38195	38214	4556
472475	1089	1108	TTCATTCTCTCCAAAGGAGT	66	39136	39155	4557
472476	1090	1109	CTTCATTCTCTCCAAAGGAG	75	39137	39156	4558
472477	1092	1111	CACTTCATTCTCTCCAAAGG	78	39139	39158	4559
472478	1093	1112	ACACTTCATTCTCTCCAAAG	84	39140	39159	4560
472479	1094	1113	TACACTTCATTCTCTCCAAA	62	39141	39160	4561
472480	1096	1115	TGTACACTTCATTCTCTCCA	95	39143	39162	4562
472481	1097	1116	TTGTACACTTCATTCTCTCC	89	39144	39163	4563
472482	1099	1118	GCTTGTACACTTCATTCTCT	91	39146	39165	4564
472483	1100	1119	TGCTTGTACACTTCATTCTC	75	39147	39166	4565
472484	1102	1121	CCTGCTTGTACACTTCATTC	90	39149	39168	4566
472485	1103	1122	ACCTGCTTGTACACTTCATT	86	39150	39169	4567
472486	1104	1123	CACCTGCTTGTACACTTCAT	95	39151	39170	4568
472487	1106	1125	ATCACCTGCTTGTACACTTC	90	39153	39172	4569
472488	1107	1126	GATCACCTGCTTGTACACTT	86	39154	39173	4570
472489	1109	1128	AAGATCACCTGCTTGTACAC	69	39156	39175	4571
472490	1110	1129	GAAGATCACCTGCTTGTACA	63	39157	39176	4572
472491	1112	1131	TCGAAGATCACCTGCTTGTA	72	39159	39178	4573
472492	1113	1132	CTCGAAGATCACCTGCTTGT	51	39160	39179	4574
472493	1115	1134	TCCTCGAAGATCACCTGCTT	71	39162	39181	4575
472494	1116	1135	CTCCTCGAAGATCACCTGCT	70	39163	39182	4576

472495	1118	1137	CCCTCCTCGAAGATCACCTG	69	39165	39184	4577
472496	1119	1138	GCCCTCCTCGAAGATCACCT	87	39166	39185	4578
472497	1121	1140	GAGCCCTCCTCGAAGATCAC	54	39168	39187	4579
472498	1122	1141	GGAGCCCTCCTCGAAGATCA	77	39169	39188	4580
472499	1124	1143	CAGGAGCCCTCCTCGAAGAT	65	39171	39190	4581
472500	1125	1144	CCAGGAGCCCTCCTCGAAGA	72	39172	39191	4582
472501	1127	1146	CCCCAGGAGCCCTCCTCGAA	60	39174	39193	4583
472502	1128	1147	GCCCCAGGAGCCCTCCTCGA	48	39175	39194	4584
472503	1130	1149	CGGCCCCAGGAGCCCTCCTC	21	39177	39196	4585
472504	1131	1150	TCGGCCCCAGGAGCCCTCCT	26	39178	39197	4586
472505	1132	1151	ATCGGCCCCAGGAGCCCTCC	1	39179	39198	4587
472506	1134	1153	CCATCGGCCCCAGGAGCCCT	70	39181	39200	4588
472507	1135	1154	CCCATCGGCCCCAGGAGCCC	74	39182	39201	4589
472508	1137	1156	GACCCATCGGCCCCAGGAGC	44	39184	39203	4590
472509	1138	1157	GGACCCATCGGCCCCAGGAG	45	39185	39204	4591
472510	1158	1177	GTATTTCTGGAACTTCTTCT	71	39205	39224	4592
472511	1159	1178	TGTATTTCTGGAACTTCTTC	63	39206	39225	4593
472512	1161	1180	AATGTATTTCTGGAACTTCT	60	39208	39227	4594
472513	1162	1181	CAATGTATTTCTGGAACTTC	36	39209	39228	4595
472514	1164	1183	ACCAATGTATTTCTGGAACT	72	39211	39230	4596
472515	1165	1184	AACCAATGTATTTCTGGAAC	68	39212	39231	4597
472516	1166	1185	AAACCAATGTATTTCTGGAA	50	39213	39232	4598
472517	1167	1186	GAAACCAATGTATTTCTGGA	65	39214	39233	4599
472518	1169	1188	GCGAAACCAATGTATTTCTG	76	39216	39235	4600
472519	1170	1189	GGCGAAACCAATGTATTTCT	75	39217	39236	4601
472520	1209	1228	GTCGGAGGAGAAGAGGCCTC	43	39256	39275	4602
472444	998	1017	GCATTCTTGCCAGGCATGGA	89	38151	38170	4526
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	87	32431	32450	425

Table 65

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
472588	1558	1577	TTCTTAAAAAAGACCTAACA	22	41529	41548	4603
472589	1560	1579	CCTTCTTAAAAAAGACCTAA	70	41531	41550	4604
472590	1561	1580	TCCTTCTTAAAAAAGACCTA	65	41532	41551	4605
472591	1562	1581	TTCCTTCTTAAAAAAGACCT	58	41533	41552	4606
472592	1564	1583	TTTTCCTTCTTAAAAAAGAC	14	41535	41554	4607
472593	1565	1584	TTTTTCCTTCTTAAAAAAGA	9	41536	41555	4608
472594	1566	1585	CTTTTTCCTTCTTAAAAAAG	15	41537	41556	4609

472595	1568	1587	GACTTTTTCCTTCTTAAAAA	36	41539	41558	4610
472596	1569	1588	TGACTTTTTCCTTCTTAAAA	36	41540	41559	4611
472597	1570	1589	CTGACTTTTTCCTTCTTAAA	75	41541	41560	4612
472598	1571	1590	ACTGACTTTTTCCTTCTTAA	77	41542	41561	4613
472599	1615	1634	CACCACCTAGAACAGGGCAA	70	41586	41605	4614
472600	1617	1636	GCCACCACCTAGAACAGGGC	44	41588	41607	4615
472601	1618	1637	AGCCACCACCTAGAACAGGG	70	41589	41608	4616
472602	1619	1638	TAGCCACCACCTAGAACAGG	46	41590	41609	4617
472603	1621	1640	TTTAGCCACCACCTAGAACA	51	41592	41611	4618
472604	1622	1641	ATTTAGCCACCACCTAGAAC	40	41593	41612	4619
472605	1623	1642	GATTTAGCCACCACCTAGAA	63	41594	41613	4620
472606	1624	1643	AGATTTAGCCACCACCTAGA	54	41595	41614	4621
472607	1626	1645	CCAGATTTAGCCACCACCTA	74	41597	41616	4622
472608	1627	1646	CCCAGATTTAGCCACCACCT	88	41598	41617	4623
472609	1628	1647	GCCCAGATTTAGCCACCACC	78	41599	41618	4624
472610	1629	1648	GGCCCAGATTTAGCCACCAC	83	41600	41619	4625
472611	1631	1650	TAGGCCCAGATTTAGCCACC	51	41602	41621	4626
472612	1632	1651	TTAGGCCCAGATTTAGCCAC	14	41603	41622	4627
472613	1633	1652	ATTAGGCCCAGATTTAGCCA	45	41604	41623	4628
472614	1634	1653	GATTAGGCCCAGATTTAGCC	44	41605	41624	4629
472615	1636	1655	CAGATTAGGCCCAGATTTAG	16	41607	41626	4630
472616	1637	1656	CCAGATTAGGCCCAGATTTA	40	41608	41627	4631
472617	1638	1657	CCCAGATTAGGCCCAGATTT	40	41609	41628	4632
472618	1639	1658	ACCCAGATTAGGCCCAGATT	50	41610	41629	4633
472619	1641	1660	CCACCCAGATTAGGCCCAGA	71	41612	41631	4634
472620	1642	1661	GCCACCCAGATTAGGCCCAG	73	41613	41632	4635
472621	1643	1662	AGCCACCCAGATTAGGCCCA	65	41614	41633	4636
472622	1644	1663	GAGCCACCCAGATTAGGCCC	26	41615	41634	4637
472623	1646	1665	CTGAGCCACCCAGATTAGGC	23	41617	41636	4638
472624	1647	1666	GCTGAGCCACCCAGATTAGG	24	41618	41637	4639
472625	1648	1667	AGCTGAGCCACCCAGATTAG	2	41619	41638	4640
472626	1649	1668	TAGCTGAGCCACCCAGATTA	31	41620	41639	4641
472627	1651	1670	GTTAGCTGAGCCACCCAGAT	48	41622	41641	4642
472628	1652	1671	GGTTAGCTGAGCCACCCAGA	57	41623	41642	4643
472629	1654	1673	GAGGTTAGCTGAGCCACCCA	66	41625	41644	4644
472630	1655	1674	AGAGGTTAGCTGAGCCACCC	51	41626	41645	4645
472631	1677	1696	GTCACTTCAGGAAGGGAAGA	54	41648	41667	4646
472632	1678	1697	TGTCACTTCAGGAAGGGAAG	58	41649	41668	4647
472633	1749	1768	AAAAGTGAATCATCTAACTG	23	41720	41739	4648
472634	1750	1769	AAAAAGTGAATCATCTAACT	0	41721	41740	4649
472635	1751	1770	CAAAAAGTGAATCATCTAAC	2	41722	41741	4650
472636	1752	1771	GCAAAAAGTGAATCATCTAA	55	41723	41742	4651

472637	1754	1773	GGGCAAAAAGTGAATCATCT	79	41725	41744	4652
472638	1790	1809	CTTGTATGAGAAGTGGCTTT	58	41761	41780	4653
472639	1791	1810	GCTTGTATGAGAAGTGGCTT	49	41762	41781	4654
472640	1793	1812	GGGCTTGTATGAGAAGTGGC	67	41764	41783	4655
472641	1838	1857	CCTGCAGTTTCAGGACTAGA	64	41809	41828	4656
472642	1839	1858	TCCTGCAGTTTCAGGACTAG	50	41810	41829	4657
472643	1841	1860	GGTCCTGCAGTTTCAGGACT	11	41812	41831	4658
472644	1842	1861	TGGTCCTGCAGTTTCAGGAC	20	41813	41832	4659
472645	1843	1862	CTGGTCCTGCAGTTTCAGGA	41	41814	41833	4660
472646	1845	1864	AACTGGTCCTGCAGTTTCAG	50	41816	41835	4661
472647	1846	1865	AAACTGGTCCTGCAGTTTCA	56	41817	41836	4662
472648	1848	1867	AGAAACTGGTCCTGCAGTTT	40	41819	41838	4663
472649	1849	1868	GAGAAACTGGTCCTGCAGTT	24	41820	41839	4664
472650	1850	1869	AGAGAAACTGGTCCTGCAGT	29	41821	41840	4665
472651	1851	1870	CAGAGAAACTGGTCCTGCAG	35	41822	41841	4666
472652	1853	1872	GGCAGAGAAACTGGTCCTGC	84	41824	41843	4667
472653	1854	1873	TGGCAGAGAAACTGGTCCTG	71	41825	41844	4668
472654	1855	1874	TTGGCAGAGAAACTGGTCCT	63	41826	41845	4669
472655	1856	1875	CTTGGCAGAGAAACTGGTCC	62	41827	41846	4670
472656	1858	1877	CCCTTGGCAGAGAAACTGGT	49	41829	41848	4671
472657	1859	1878	CCCCTTGGCAGAGAAACTGG	66	41830	41849	4672
472658	1861	1880	CTCCCCTTGGCAGAGAAACT	58	41832	41851	4673
472659	1862	1881	CCTCCCCTTGGCAGAGAAAC	54	41833	41852	4674
472660	1863	1882	TCCTCCCCTTGGCAGAGAAA	49	41834	41853	4675
472661	1865	1884	ACTCCTCCCCTTGGCAGAGA	47	41836	41855	4676
472662	1866	1885	AACTCCTCCCCTTGGCAGAG	39	41837	41856	4677
472663	1867	1886	CAACTCCTCCCCTTGGCAGA	0	41838	41857	4678
472664	1869	1888	TCCAACTCCTCCCCTTGGCA	29	41840	41859	4679
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	85	32431	32450	425

Table 66

Inhibition of DGAT2 mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence	% inhibition	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	SEQ ID NO
472445	1000	1019	CTGCATTCTTGCCAGGCATG	53	38153	38172	4527
472446	1001	1020	ACTGCATTCTTGCCAGGCAT	60	38154	38173	4528
472447	1003	1022	TGACTGCATTCTTGCCAGGC	52	38156	38175	4529
472448	1004	1023	GTGACTGCATTCTTGCCAGG	60	38157	38176	4530
472449	1006	1025	GGGTGACTGCATTCTTGCCA	0	38159	38178	4531
472450	1007	1026	AGGGTGACTGCATTCTTGCC	62	38160	38179	4532

472451	1008	1027	CAGGGTGACTGCATTCTTGC	43	38161	38180	4533
472452	1010	1029	CGCAGGGTGACTGCATTCTT	25	38163	38182	4534
472453	1011	1030	CCGCAGGGTGACTGCATTCT	45	38164	38183	4535
472454	1013	1032	TTCCGCAGGGTGACTGCATT	16	38166	38185	4536
472455	1014	1033	GTTCCGCAGGGTGACTGCAT	29	38167	38186	4537
472456	1015	1034	GGTTCCGCAGGGTGACTGCA	62	38168	38187	4538
472457	1017	1036	GCGGTTCCGCAGGGTGACTG	33	38170	38189	4539
472458	1018	1037	TGCGGTTCCGCAGGGTGACT	57	38171	38190	4540
472459	1020	1039	CTTGCGGTTCCGCAGGGTGA	39	38173	38192	4541
472460	1021	1040	CCTTGCGGTTCCGCAGGGTG	25	38174	38193	4542
472461	1023	1042	GCCCTTGCGGTTCCGCAGGG	9	38176	38195	4543
472462	1024	1043	AGCCCTTGCGGTTCCGCAGG	32	38177	38196	4544
472463	1026	1045	AAAGCCCTTGCGGTTCCGCA	46	38179	38198	4545
472464	1027	1046	CAAAGCCCTTGCGGTTCCGC	48	38180	38199	4546
472465	1029	1048	CACAAAGCCCTTGCGGTTCC	8	38182	38201	4547
472466	1030	1049	TCACAAAGCCCTTGCGGTTC	0	38183	38202	4548
472467	1032	1051	TTTCACAAAGCCCTTGCGGT	0	38185	38204	4549
472468	1033	1052	GTTTCACAAAGCCCTTGCGG	18	38186	38205	4550
472469	1035	1054	CAGTTTCACAAAGCCCTTGC	0	38188	38207	4551
472470	1036	1055	CCAGTTTCACAAAGCCCTTG	23	38189	38208	4552
472471	1038	1057	GGCCAGTTTCACAAAGCCCT	2	38191	38210	4553
472472	1039	1058	GGGCCAGTTTCACAAAGCCC	0	38192	38211	4554
472473	1041	1060	CAGGGCCAGTTTCACAAAGC	0	38194	38213	4555
472474	1042	1061	GCAGGGCCAGTTTCACAAAG	10	38195	38214	4556
472475	1089	1108	TTCATTCTCTCCAAAGGAGT	47	39136	39155	4557
472476	1090	1109	CTTCATTCTCTCCAAAGGAG	65	39137	39156	4558
472477	1092	1111	CACTTCATTCTCTCCAAAGG	51	39139	39158	4559
472478	1093	1112	ACACTTCATTCTCTCCAAAG	68	39140	39159	4560
472479	1094	1113	TACACTTCATTCTCTCCAAA	41	39141	39160	4561
472480	1096	1115	TGTACACTTCATTCTCTCCA	85	39143	39162	4562
472481	1097	1116	TTGTACACTTCATTCTCTCC	72	39144	39163	4563
472482	1099	1118	GCTTGTACACTTCATTCTCT	80	39146	39165	4564
472483	1100	1119	TGCTTGTACACTTCATTCTC	64	39147	39166	4565
472484	1102	1121	CCTGCTTGTACACTTCATTC	75	39149	39168	4566
472485	1103	1122	ACCTGCTTGTACACTTCATT	67	39150	39169	4567
472486	1104	1123	CACCTGCTTGTACACTTCAT	88	39151	39170	4568
472487	1106	1125	ATCACCTGCTTGTACACTTC	59	39153	39172	4569
472488	1107	1126	GATCACCTGCTTGTACACTT	70	39154	39173	4570
472489	1109	1128	AAGATCACCTGCTTGTACAC	28	39156	39175	4571
472490	1110	1129	GAAGATCACCTGCTTGTACA	53	39157	39176	4572
472491	1112	1131	TCGAAGATCACCTGCTTGTA	52	39159	39178	4573
472492	1113	1132	CTCGAAGATCACCTGCTTGT	49	39160	39179	4574

472493	1115	1134	TCCTCGAAGATCACCTGCTT	46	39162	39181	4575
472494	1116	1135	CTCCTCGAAGATCACCTGCT	55	39163	39182	4576
472495	1118	1137	CCCTCCTCGAAGATCACCTG	54	39165	39184	4577
472496	1119	1138	GCCCTCCTCGAAGATCACCT	74	39166	39185	4578
472497	1121	1140	GAGCCCTCCTCGAAGATCAC	54	39168	39187	4579
472498	1122	1141	GGAGCCCTCCTCGAAGATCA	68	39169	39188	4580
472499	1124	1143	CAGGAGCCCTCCTCGAAGAT	37	39171	39190	4581
472500	1125	1144	CCAGGAGCCCTCCTCGAAGA	41	39172	39191	4582
472501	1127	1146	CCCCAGGAGCCCTCCTCGAA	34	39174	39193	4583
472502	1128	1147	GCCCCAGGAGCCCTCCTCGA	17	39175	39194	4584
472503	1130	1149	CGGCCCCAGGAGCCCTCCTC	0	39177	39196	4585
472504	1131	1150	TCGGCCCCAGGAGCCCTCCT	16	39178	39197	4586
472505	1132	1151	ATCGGCCCCAGGAGCCCTCC	0	39179	39198	4587
472506	1134	1153	CCATCGGCCCCAGGAGCCCT	64	39181	39200	4588
472507	1135	1154	CCCATCGGCCCCAGGAGCCC	55	39182	39201	4589
472508	1137	1156	GACCCATCGGCCCCAGGAGC	34	39184	39203	4590
472509	1138	1157	GGACCCATCGGCCCCAGGAG	50	39185	39204	4591
472510	1158	1177	GTATTTCTGGAACTTCTTCT	64	39205	39224	4592
472511	1159	1178	TGTATTTCTGGAACTTCTTC	49	39206	39225	4593
472512	1161	1180	AATGTATTTCTGGAACTTCT	40	39208	39227	4594
472513	1162	1181	CAATGTATTTCTGGAACTTC	4	39209	39228	4595
472514	1164	1183	ACCAATGTATTTCTGGAACT	41	39211	39230	4596
472515	1165	1184	AACCAATGTATTTCTGGAAC	41	39212	39231	4597
472516	1166	1185	AAACCAATGTATTTCTGGAA	34	39213	39232	4598
472517	1167	1186	GAAACCAATGTATTTCTGGA	51	39214	39233	4599
472518	1169	1188	GCGAAACCAATGTATTTCTG	54	39216	39235	4600
472519	1170	1189	GGCGAAACCAATGTATTTCT	59	39217	39236	4601
472520	1209	1228	GTCGGAGGAGAAGAGGCCTC	17	39256	39275	4602
472444	998	1017	GCATTCTTGCCAGGCATGGA	77	38151	38170	4526
413433	n/a	n/a	GCCTGGACAAGTCCTGCCCA	76	32431	32450	425

Example 6: Dose-dependent antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Gapmers from the studies described in the Examples above exhibiting significant *in vitro* inhibition of DGAT2 mRNA were selected and tested at various doses in HepG2 cells. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. Previously disclosed oligonucleotides, ISIS 21316, ISIS 217317, ISIS 217328, ISIS 369185, ISIS 366714, ISIS 366730, ISIS 366746, and ISIS 369241 from earlier published application, WO 2005/019418, were included in the assay. The results for each experiment are presented in separate tables shown below. Cells were plated at a density of 10,000 cells per well and transfected using Lipofectin reagent with 6.25 nM, 12.5 nM, 25.0 nM, 50 nM, 100 nM, or 200.0 nM concentrations of antisense oligonucleotide, as specified in the Tables below. After a

treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2367 was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited. 'n.d.' indicates that the inhibition levels were not recorded.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells. The results also demonstrate that several newly designed oligonucleotides had greater efficacy than the previously disclosed oligonucleotides.

Table 67

ISIS No	6.25 nM	12.5 nM	25.0 nM	50.0 nM	100.0 nM	200.0 nM	IC_{50} (nM)
217316	7	7	27	47	68	63	55
217317	3	12	32	50	75	84	44
369185	17	12	34	63	78	81	42
381726	4	30	44	56	76	83	37
411874	15	31	27	54	66	66	40
411899	5	22	31	57	74	87	39
411901	0	6	24	46	66	65	58
411905	6	30	29	58	73	76	34
411912	8	24	31	56	79	89	35
411941	11	22	30	59	77	82	35

Table 68

ISIS No	6.25 nM	12.5 nM	25.0 nM	50.0 nM	100.0 nM	200.0 nM	IC_{50} (nM)
366714	7	8	42	67	79	82	33
366730	0	18	33	72	84	91	43
411944	2	14	46	65	82	93	30
411945	14	21	51	68	86	n.d.	24
411950	6	5	28	66	84	n.d.	29
413176	7	16	24	58	78	88	38
413192	0	6	30	62	80	80	57
413200	2	18	20	60	78	77	36

413213	9	12	34	55	84	90	45
413226	3	22	13	36	72	87	41

Table 69

ISIS No	6.25 nM	12.5 nM	25.0 nM	50.0 nM	100.0 nM	200.0 nM	IC_{50} (nM)
366746	5	7	21	32	62	77	66
369241	0	4	10	35	56	63	106
413198	10	16	24	53	72	73	51
413214	1	17	43	61	81	77	34
413232	8	23	33	60	78	82	35
413236	0	12	3	52	71	72	47
413253	6	7	27	59	72	75	64
413258	0	12	27	46	78	77	62
413266	0	0	21	48	76	75	52
413284	4	0	22	45	57	65	78

Table 70

ISIS No	6.25 nM	12.5 nM	25.0 nM	50.0 nM	100.0 nM	200.0 nM	IC_{50} (nM)
217328	4	15	31	50	64	72	62
413243	0	10	28	50	69	77	66
413351	4	16	16	39	56	69	51
413356	16	12	23	51	63	69	34
413364	0	0	21	41	58	53	52
413399	0	3	23	35	60	58	78
413413	1	0	30	50	71	77	64
413422	0	0	8	41	63	70	62
413433	5	5	20	55	77	82	47
413441	2	5	26	50	70	79	106
413446	0	0	10	41	63	78	35

Table 71

ISIS No	6.25 nM	12.5 nM	25.0 nM	50.0 nM	100.0 nM	200.0 nM	IC_{50} (nM)
217317	0	0	11	34	64	84	77
366730	0	15	33	61	87	91	45
381726	1	11	31	51	71	83	48

411899	6	0	25	39	70	89	55
411912	0	0	13	58	77	87	40
411944	7	21	32	67	76	87	42
413176	0	12	20	54	89	88	46
413232	16	10	30	60	79	90	31
413433	15	17	37	71	84	87	24
413446	0	0	44	73	77	86	47

Example 7: Dose-dependent antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Gapmers from the studies described in the Examples above exhibiting significant *in vitro* inhibition of DGAT2 mRNA were selected and tested at various doses in HepG2 cells. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. Previously disclosed oligonucleotides from earlier published application, WO 2005/019418, were included in the assay. The results for each experiment are presented in separate tables shown below.

Study 1

Cells were plated at a density of 10,000 cells per well and transfected using Lipofectin reagent with 18.75 nM, 37.5 nM, 75.0 nM, or 150.0 nM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 72

ISIS No	Motif	18.75 nM	37.5 nM	75.0 nM	150.0 nM	IC_{50} (nM)
217328	5-10-5	27	44	62	73	47
366730	5-10-5	27	36	61	77	48
411944	5-10-5	19	38	48	69	67
411945	5-10-5	14	26	45	61	93

413253	5-10-5	24	34	50	68	73
413433	5-10-5	28	39	56	68	58
423440	5-10-5	18	39	53	70	67
423441	5-10-5	23	36	54	66	63
423444	5-10-5	15	32	53	69	71
423447	5-10-5	24	36	55	71	60
423463	5-10-5	23	39	59	73	56
423489	3-14-3	21	32	55	73	60
423490	3-14-3	27	32	51	60	76
423498	3-14-3	19	38	56	77	59
423499	5-10-5	23	37	59	77	53
423523	3-14-3	25	41	60	73	56
423524	3-14-3	24	37	62	75	54
423601	2-13-5	28	38	58	75	51

Table 73

ISIS No	Motif	18.75 nM	37.5 nM	75.0 nM	150.0 nM	IC_{50} (nM)
217317	5-10-5	4	23	39	61	104
217328	5-10-5	20	33	54	67	73
411899	5-10-5	11	34	51	66	74
413214	5-10-5	8	32	52	68	73
413232	5-10-5	17	26	50	70	71
423452	5-10-5	12	26	45	65	88
423453	5-10-5	15	33	46	67	76
423458	5-10-5	14	31	49	70	74
423459	5-10-5	17	29	61	73	64
423464	5-10-5	19	33	52	64	74
423507	3-14-3	15	32	52	68	73
423508	3-14-3	14	37	48	69	73
423526	3-14-3	13	23	41	58	109
423527	3-14-3	13	28	51	58	102
423565	2-13-5	17	27	48	69	80
423567	2-13-5	0	29	53	74	79
423585	2-13-5	12	25	42	64	94
423595	2-13-5	12	26	47	69	81
423606	2-13-5	13	27	55	71	68

The same gapmers were also tested at various doses in HepG2 cells using electroporation. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 2.5 μM, 5.0 μM, 10.0 μM, or 20.0 μM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 74

ISIS No	Motif	2.5 μM	5.0 μM	10.0 μM	20.0 μM	IC_{50} (μM)
217328	5-10-5	55	70	85	94	2
366730	5-10-5	38	51	78	89	5
411944	5-10-5	30	32	48	73	10
411945	5-10-5	31	26	48	69	11
413253	5-10-5	39	51	77	84	4
413433	5-10-5	72	81	82	85	<2.5
423440	5-10-5	30	54	65	91	5
423441	5-10-5	41	47	60	90	6
423444	5-10-5	19	46	70	81	6
423447	5-10-5	25	49	76	79	5
423463	5-10-5	59	79	85	86	2
423489	3-14-3	33	56	72	92	5
423490	3-14-3	17	25	53	82	9
423498	3-14-3	30	41	59	88	7
423499	5-10-5	27	26	63	78	10
423523	3-14-3	45	48	81	89	5
423524	3-14-3	35	59	84	92	4
423601	2-13-5	44	55	87	90	4

Table 75

ISIS No	Motif	18.75 nM	37.5 nM	75.0 nM	150.0 nM	IC_{50} (nM)
217317	5-10-5	16	33	63	65	7
217328	5-10-5	32	56	79	91	4
411899	5-10-5	28	38	74	87	5
413214	5-10-5	37	46	65	91	6
413232	5-10-5	18	20	43	78	11
423452	5-10-5	14	47	73	85	6
423453	5-10-5	52	70	83	93	2
423458	5-10-5	28	31	65	87	8
423459	5-10-5	24	33	57	88	8
423464	5-10-5	68	81	86	88	1
423507	3-14-3	29	42	71	89	5
423508	3-14-3	16	38	53	83	7
423526	3-14-3	48	73	81	90	3
423527	3-14-3	27	51	68	85	6
423565	2-13-5	13	35	66	84	7
423567	2-13-5	27	42	61	91	7
423585	2-13-5	24	28	67	91	7
423595	2-13-5	12	25	50	78	10
423606	2-13-5	42	59	74	85	3

Study 2

Cells were plated at a density of 35,000 cells per well and transfected using electroporation with 0.22 μM, 0.67 μM , 2.0 μM, 6.0 μM, or 18.0 μM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2977_MGB (forward sequence ACTGGGCGGGCTTCATATT, designated herein as SEQ ID NO: 10; reverse sequence CCCGGAGTAGGCGGCTAT, designated herein as SEQ ID NO: 11; probe sequence AGCCATGAAGACCC, designated herein as SEQ ID NO: 12) was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 76

ISIS No	Motif	0.22 μM	0.67 μM	2.0 μM	6.0 μM	18.0 μM	IC_{50} (μM)
217328	5-10-5	0	17	52	83	96	2.1
366730	5-10-5	0	0	27	72	93	3.9
413433	5-10-5	0	10	58	84	93	2.2
423453	5-10-5	14	21	53	86	94	1.9
423459	5-10-5	0	18	36	68	92	3.0
423463	5-10-5	16	15	50	76	80	2.7
423464	5-10-5	0	29	56	86	92	1.6
423489	3-14-3	0	0	37	63	91	3.8
423498	3-14-3	0	0	21	56	82	5.3
423499	3-14-3	0	6	26	62	88	4.1
423523	3-14-3	0	0	34	69	95	4.2
423524	3-14-3	0	6	15	62	90	4.4
423526	3-14-3	5	7	45	87	94	2.6
423601	2-13-5	0	0	31	65	89	4.3
423606	2-13-5	58	19	43	72	94	2.6

Study 3

Cells were plated at a density of 10,000 cells per well and transfected using Lipofectin reagent with 12.5 nM, 25.0 nM, 50.0 nM, 100.0 nM, or 200.0 nM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 77

ISIS No	Motif	0.22 μM	0.67 μM	2.0 μM	6.0 μM	18.0 μM	IC_{50} (μM)
217328	5-10-5	25	31	58	71	85	38
366730	5-10-5	21	34	53	74	90	44
413433	5-10-5	23	40	63	75	86	37
423453	5-10-5	0	2	33	61	72	90
423459	5-10-5	16	22	44	65	79	64
423463	5-10-5	6	24	46	63	82	62
423464	5-10-5	20	28	45	64	79	60
423489	3-14-3	15	28	57	75	84	42
423498	3-14-3	8	21	52	71	85	49
423499	3-14-3	13	23	43	65	84	62
423523	3-14-3	25	38	58	72	86	38
423524	3-14-3	16	32	56	66	83	52
423526	3-14-3	28	33	51	54	68	71
423601	2-13-5	13	30	54	71	84	49
423606	2-13-5	12	36	52	69	80	47

Study 4

Cells were plated at a density of 10,000 cells per well and transfected using Lipofectin reagent with 12.5 nM, 25.0 nM, 50.0 nM, 100.0 nM, or 200.0 nM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 78

ISIS No	Motif	0.22 μM	0.67 μM	2.0 μM	6.0 μM	18.0 μM	IC_{50} (μM)
217328	5-10-5	42	54	60	88	95	2
366730	5-10-5	26	44	61	85	95	3
413433	5-10-5	55	69	76	83	87	<1.25

423453	5-10-5	40	62	78	91	95	2
423459	5-10-5	19	25	47	79	92	5
423463	5-10-5	51	52	83	86	90	<1.25
423464	5-10-5	42	67	82	90	89	2
423489	3-14-3	8	19	40	77	96	5
423498	3-14-3	5	1	20	51	89	9
423499	3-14-3	23	24	35	71	95	5
423523	3-14-3	19	42	67	87	93	3
423524	3-14-3	38	53	71	90	95	2
423526	3-14-3	33	59	78	91	93	2
423601	2-13-5	22	45	72	88	93	3
423606	2-13-5	30	46	64	83	86	3

Study 5

Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 12.5 μM, 25.0 μM , 50.0 μM, 100.0 μM, or 200.0 μM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB (forward sequence AACTGGCCCTGCGTCATG, designated herein as SEQ ID NO: 7; reverse sequence CTTGTACACTTCATTCTCTCCAAAGG; designated herein as SEQ ID NO: 8; probe sequence CTGACCTGGTTCCC, designated herein as SEQ ID NO: 9) was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 79

ISIS No	Motif	12.5 μM	25 μM	50 μM	100 μM	200 μM	IC_{50} (μM)
217316	5-10-5	0	0	17	43	76	10.9
217318	5-10-5	0	0	10	48	45	18.4
217328	5-10-5	12	22	40	69	82	6.0
217376	5-10-5	0	0	51	50	70	9.8
381728	5-10-5	0	3	17	37	58	15.8

411896	5-10-5	5	16	52	73	87	5.5
411899	5-10-5	0	0	15	42	54	15.7
411900	5-10-5	0	0	18	38	76	11.5
411950	5-10-5	5	13	21	49	70	10.7
411951	5-10-5	0	10	31	52	76	8.9
413433	5-10-5	0	37	58	75	82	5.6
423453	5-10-5	16	21	41	73	86	5.5
423463	5-10-5	26	33	62	81	85	3.5
423464	5-10-5	21	43	58	82	84	3.4
423606	2-13-5	30	43	53	76	80	3.6

Study 6

Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.625 μM, 1.25 μM, 2.5 μM, 5.0 μM, 10 μM, or 20 μM, concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 80

ISIS No	Motif	0.625 μM	1.25 μM	2.5 μM	5.0 μM	10.0 μM	20.0 μM	IC_{50} (μM)
217317	5-10-5	11	18	39	59	79	94	3.5
217328	5-10-5	13	45	58	87	84	95	1.9
217376	5-10-5	10	9	4	28	12	11	>20
217376	5-10-5	18	15	12	23	9	0	>20
366730	5-10-5	14	23	55	74	86	97	2.6
411897	5-10-5	30	28	28	57	73	94	3.3
411901	5-10-5	19	22	30	58	76	93	4.0
411902	5-10-5	11	6	19	42	72	83	5.6
411947	5-10-5	14	14	10	35	66	87	7.1
411948	5-10-5	25	21	34	50	57	80	5.4
411950	5-10-5	7	24	41	56	74	83	3.9

411950	5-10-5	13	14	34	46	79	88	4.6
411951	5-10-5	28	18	22	43	83	92	5.4
411955	5-10-5	11	26	52	71	96	97	2.5
411958	5-10-5	19	17	21	60	81	92	4.7
413433	5-10-5	39	62	82	87	88	89	0.9
423463	5-10-5	15	36	76	87	92	90	1.7
423463	5-10-5	31	64	85	90	91	89	1.0
423489	3-14-3	21	17	39	73	89	98	3.2
423606	2-13-5	18	36	50	85	87	92	2.2

Example 8: Dose-dependent antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Gapmers from the studies described in the Examples above exhibiting significant *in vitro* inhibition of DGAT2 mRNA were selected and tested at various doses in HepG2 cells. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.625 μM, 1.25 μM, 2.50 μM, 5.00 μM, or 10.00 μM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 81

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
483817	47	71	82	89	90	<0.6
483825	40	56	78	85	85	0.8
483828	45	69	75	70	76	<0.6
483832	42	59	67	78	72	0.8
483834	26	38	64	86	90	1.6

483852	47	60	69	81	85	0.7
483866	76	77	82	86	86	<0.6
483869	39	69	74	72	80	0.6
483873	46	71	78	82	87	<0.6

Table 82

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
483811	29	34	58	87	87	1.7
483816	21	14	34	71	87	3.0
483831	34	37	55	81	83	1.7
483835	28	47	56	82	89	1.6
483840	4	17	49	75	81	2.9
483870	13	31	52	84	88	2.2
483889	21	0	56	81	85	2.7
483895	43	21	74	88	92	2.0
483898	46	47	81	89	86	0.8
483908	29	16	73	84	88	1.9
483910	31	39	73	79	76	1.5
483923	24	0	62	81	89	3.4
483952	63	67	86	91	89	<0.6

Table 83

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
483968	39	55	76	89	88	0.9
483969	29	57	70	82	89	1.2
483970	16	48	62	71	85	1.9
483972	17	52	69	78	78	1.7
483984	53	74	85	83	78	<0.6
483986	15	37	59	71	83	2.2
483987	9	0	76	78	91	1.5
483993	42	58	69	69	78	0.8
483996	20	46	53	63	74	2.3
483997	20	61	72	82	82	1.3
484004	27	57	65	74	83	1.4
484006	22	47	65	72	86	1.7

484010	27	0	51	78	86	2.0
484017	28	51	66	79	88	1.4

Table 84

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	11	53	74	85	83	1.6
484012	19	36	49	76	88	2.2
484020	26	49	66	70	78	1.6
484041	12	45	51	68	80	2.4
484049	35	62	68	82	81	0.9
484094	20	37	52	62	74	2.7
484099	32	44	77	84	89	1.3
484111	22	50	65	54	80	2.0
484114	29	47	69	68	72	1.6
484118	10	42	60	74	84	2.1
484182	0	57	59	79	74	2.3

Table 85

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	33	46	65	81	87	1.4
484109	17	1	46	65	83	3.3
484138	9	15	17	28	53	>10
484139	14	21	60	75	90	2.3
484152	25	46	75	89	91	1.4
484175	10	15	21	35	43	>10
484183	3	15	20	34	55	>10
484203	23	35	54	70	75	2.3
484209	21	36	50	74	88	2.2
484215	42	45	59	84	91	1.2
484217	23	36	56	82	93	1.9
484231	34	0	72	79	82	1
423463	35	53	73	86	87	1.1

Table 86

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	37	55	72	84	88	1
423464	41	62	79	92	90	0.7
484268	34	57	73	81	84	1
484269	24	47	64	67	75	1.8
484270	29	50	65	88	91	1.3
484271	43	66	81	88	84	0.6
484273	42	62	73	79	78	0.7
484283	26	0	61	85	93	1.6
484284	27	38	54	76	81	1.9
484292	31	31	53	81	91	1.8
484293	26	36	61	78	87	1.8
484327	24	48	48	67	79	2.1
484342	21	34	48	67	88	2.4
484387	21	0	21	40	58	9.6
484396	15	13	18	24	44	>10

Table 87

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	30	57	80	81	86	1.1
484345	17	28	68	60	79	2.4
484354	20	28	75	60	79	2.2
484366	25	33	37	62	82	2.8
484368	16	39	57	73	89	2.1
484369	22	18	57	27	35	>10
484372	3	28	37	69	76	3.3
484376	12	0	52	64	67	3.1
484379	0	19	21	37	75	5.6
484380	0	26	34	47	71	4.7
484395	7	41	61	29	46	>10
484397	0	7	52	16	34	>10
484406	17	6	53	39	53	7.5
484408	4	0	16	24	38	>10
484409	0	6	0	41	59	9.0

Table 88

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	22	51	68	72	88	1.6
472316	15	45	45	82	89	2.1
472317	34	30	43	77	91	2.0
472318	22	38	52	68	85	2.2
472444	22	27	41	39	74	4.4
472447	0	18	16	18	69	9.0
472456	10	10	48	51	68	4.3
472480	7	0	41	59	87	3.0
472481	29	29	37	62	84	2.7
472482	16	29	42	67	85	2.7
472484	23	19	51	72	87	2.4
472486	28	40	59	83	90	1.7
472488	27	31	36	53	64	4.4
472496	0	0	37	51	76	3.8
484410	0	40	19	24	39	>10

Table 89

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	37	51	70	84	88	1.1
472548	15	30	25	54	78	3.9
472552	15	28	33	51	66	4.7
472570	29	46	56	83	90	1.6
472571	29	34	53	70	86	2
411955	0	41	46	68	85	2.2
472608	28	26	56	59	72	2.7
472610	18	0	51	70	79	2.6
472637	24	37	39	53	72	3.4
472652	18	43	55	71	81	2.1
472725	35	46	61	77	86	1.4
472733	39	34	41	63	74	2.5
472738	38	53	65	81	85	1.1

472793	0	0	51	67	75	2
472811	0	44	65	78	77	1.4

Table 90

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	47	72	84	88	2
472316	21	42	69	86	94	2
484152	20	57	79	90	93	1
484215	33	39	70	91	95	1
484217	19	18	49	89	94	2
484231	4	52	76	83	91	2
423463	33	54	79	91	91	1
423464	0	48	78	83	88	3
484268	0	3	0	13	50	>10
484270	7	36	49	80	83	2
484271	16	59	76	86	91	1
484283	10	35	56	87	92	2
484369	25	1	0	5	33	>10

Table 91

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	28	60	69	84	92	1
483811	0	19	53	77	85	3
483817	47	69	85	88	94	<0.6
483825	18	50	80	82	87	1
483834	16	37	72	89	87	2
483835	1	29	56	80	85	2
483866	55	79	88	83	90	<0.6
483873	27	75	87	86	91	1
483898	49	72	82	89	89	<0.6
483908	35	45	76	89	88	1
483913	0	42	76	86	89	2

Table 92

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	47	68	84	90	88	<0.6
423453	36	66	81	95	96	0.8
472158	56	51	75	91	96	0.6
472725	43	59	63	78	80	0.8
472738	38	58	65	77	81	1
483895	35	53	76	92	93	1.0
483923	26	46	76	88	92	1.3
483952	60	82	88	93	92	<0.6
483968	46	70	82	91	93	<0.6
483984	39	67	87	88	88	0.6
483987	40	60	75	90	95	0.9
483997	50	63	73	90	92	0.6
484099	56	75	88	93	95	<0.6

Table 93

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	26	53	75	86	91	1.3
495429	8	42	68	86	92	1.9
495449	19	53	74	87	86	1.4
495450	30	58	74	87	93	1.1
495470	0	36	59	82	92	2.2
495481	15	39	75	84	86	1.7
495484	19	50	73	87	87	1.5
495488	5	32	45	67	86	2.8
495489	13	36	54	81	91	2.1
495490	20	42	66	83	88	1.7
495492	5	38	64	81	90	2.1
495495	29	32	62	78	90	1.8
495496	21	44	62	79	92	1.7
495497	20	42	59	69	88	2.0
495498	21	54	68	81	90	1.5

Table 94

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	35	42	73	86	90	1.3
495442	6	29	43	68	80	3.0
495451	21	31	51	76	87	2.2
495453	21	34	64	80	84	1.9
495454	23	33	53	80	86	2.1
495463	4	28	53	74	85	2.6
495464	21	41	65	84	84	1.7
495466	12	35	57	76	84	2.2
495467	17	28	44	69	89	2.6
495469	17	24	53	81	83	2.4
495471	29	43	58	83	84	1.6
495472	4	38	63	78	80	2.3
495482	7	32	52	76	91	2.4
495485	8	29	55	76	76	2.6
495491	25	42	64	85	92	1.6

Table 95

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	40	48	75	86	86	1
495430	0	5	11	47	67	6.2
495441	17	17	55	77	87	2.5
495443	28	51	59	74	84	1.6
495448	13	28	32	61	79	3.4
495452	13	51	47	71	78	2.3
495462	46	47	51	76	84	1.2
495465	2	20	35	68	78	3.5
495468	22	20	46	56	84	3
495473	11	24	48	69	75	3
495479	19	29	54	76	85	2.2
495483	15	9	47	77	88	2.7
495516	49	76	89	90	93	<0.6
495562	20	55	70	88	92	1.4
495576	51	69	88	93	94	<0.6

Table 96

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	34	51	71	86	89	1.1
495505	34	58	80	87	91	1.0
495517	19	55	78	85	91	1.3
495518	24	51	72	87	90	1.4
495519	33	46	70	86	90	1.3
495520	63	84	89	90	91	<0.6
495522	45	32	54	82	89	1.5
495523	14	46	66	86	91	1.7
495524	12	39	60	84	93	1.9
495554	35	64	75	89	90	0.9
495555	42	49	72	87	91	1
495563	35	41	66	84	91	1.4
495571	21	41	67	87	93	1.6
495575	33	43	62	82	84	1.5
495577	33	56	71	85	91	1.1

Table 97

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	39	52	66	81	87	1.1
495570	27	50	55	78	89	1.6
495650	0	38	58	65	85	2.7
495561	24	54	71	87	92	1.3
495618	0	35	50	79	87	2.5
495540	11	35	48	74	88	2.4
495649	0	24	43	76	82	3.1
495515	22	45	69	83	91	1.6
495599	25	23	42	73	86	2.5
495620	27	54	63	85	91	1.4
495606	16	27	56	80	90	2.2
495604	31	48	77	83	90	1.2
495609	52	66	80	84	90	<0.6
495619	29	42	63	73	90	1.6
495621	0	28	31	69	84	3.3

Table 98

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	19	24	66	81	88	2.1
495591	7	24	43	66	82	3.0
495744	25	41	51	73	84	2.0
495685	34	58	73	84	83	1.0
495738	26	41	61	81	83	1.7
495707	33	46	61	76	72	1.5
495837	30	33	67	90	94	1.6
495752	14	30	68	86	91	1.9
495839	15	67	83	90	91	1.2
495736	28	41	65	83	85	1.6
495840	39	59	78	92	93	0.8
495753	43	48	69	87	97	1.0
495878	34	62	78	92	96	0.9
495749	21	23	52	84	89	2.2
495756	24	29	58	80	89	2.0

Table 99

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	28	60	70	83	84	1.1
495853	39	51	78	92	96	1
495857	41	49	67	87	91	1.1
495829	41	68	81	90	90	0.6
495818	12	38	57	77	93	2.1
495842	40	67	80	88	91	0.7
495849	37	53	66	79	82	1.1
495836	16	54	63	80	88	1.6
495875	22	58	63	80	93	1.4
495841	43	66	76	87	90	0.6
495819	13	38	54	74	90	2.2
495825	36	52	69	88	93	1.1
495832	20	50	65	78	85	1.6
495809	16	37	46	78	85	2.3

495876	19	39	65	86	95	1.7

Table 100

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	46	61	82	86	86	0.6
496037	23	38	57	74	93	1.9
496038	10	31	42	67	93	2.6
496039	9	19	35	67	88	3.1
496040	4	38	45	70	88	2.6
496041	21	30	50	84	95	2.1
496043	2	26	58	80	87	2.4
495826	7	44	72	82	85	1.9
495868	27	38	75	83	85	1.5
495901	18	46	69	79	83	1.7
495902	20	48	66	82	85	1.6
495955	3	3	54	66	75	3.5
495992	26	43	74	86	92	1.4
496100	20	30	56	71	85	2.3
496104	37	35	48	72	81	1.9

Table 101

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	33	49	70	75	90	1.3
501838	32	52	67	73	71	1.3
501849	39	63	76	85	93	0.8
501850	29	59	72	88	92	1.1
501852	43	63	75	80	87	0.7
501855	57	70	87	90	92	<0.6
501861	39	63	80	90	93	0.8
501871	28	53	76	84	93	1.2
501883	33	45	62	73	82	1.5
501884	41	59	75	86	92	0.8
501886	42	63	71	78	84	0.7
501890	32	49	61	72	79	1.5
501932	38	49	68	80	85	1.1

501944	30	43	69	80	87	1.4
501950	32	49	70	72	91	1.3

Table 102

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	35	53	69	86	91	1.1
501903	32	39	62	80	90	1.6
501916	29	42	61	78	88	1.6
501933	37	51	66	75	77	1.2
501934	26	41	52	69	82	2
501946	15	34	57	76	90	2.1
501947	35	54	74	87	93	1.1
501951	36	54	75	85	93	1
501957	27	41	67	76	86	1.7
501959	40	52	72	81	87	1
501960	35	52	67	82	90	1.2
501966	34	42	64	75	84	1.5
501968	29	49	73	84	91	1.3
501977	19	28	49	74	88	2.3
502040	24	38	54	73	88	2

Table 103

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	37	53	72	83	39	1.1
501981	21	43	62	79	90	1.7
501982	28	53	64	70	82	1.5
501983	29	41	57	75	84	1.8
502013	24	42	60	74	80	1.9
502015	19	39	57	63	71	2.5
502025	22	48	59	78	89	1.7
502026	21	39	56	77	86	2
502037	15	13	38	56	87	3.4
502038	3	14	52	55	77	3.5
502045	45	47	63	75	85	1.1
502046	21	37	50	71	81	2.3

502056	44	67	82	86	41	0.6
502083	37	55	76	89	93	1
502119	37	60	77	88	92	0.9

Table 104

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	40	58	77	88	91	0.8
502075	30	47	69	82	91	1.4
502098	37	59	74	88	94	0.9
502099	43	59	76	88	94	0.8
502154	64	72	84	88	90	<0.6
502155	34	54	72	82	87	1.1
502156	17	38	57	83	87	2
502163	41	60	82	92	93	0.7
502164	41	73	78	89	90	0.6
502175	33	58	74	87	90	1
502179	61	74	81	87	87	<0.6
502189	33	52	79	91	94	1.1
502191	53	67	84	92	92	<0.6
502194	48	64	83	87	92	<0.6
502228	34	47	67	80	89	1.3

Table 105

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	24	28	51	68	83	2.4
495756	49	71	87	88	94	<0.6
507692	48	70	83	88	93	<0.6
507693	48	68	86	91	93	<0.6
507694	41	61	81	88	93	0.7
507695	36	53	72	84	93	1.1
507696	51	74	83	89	94	<0.6
507710	48	72	71	90	91	<0.6
507716	42	54	83	91	95	0.8
507717	44	65	79	86	90	0.6
502314	25	38	61	79	93	1.7

502319	47	66	80	92	94	0.6
502322	45	69	81	89	86	<0.6
502331	34	45	53	71	89	1.6
502334	52	68	77	89	93	<0.6

Table 106

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	30	49	73	87	90	1.2
522366	32	53	68	80	84	1.2
522373	39	62	81	87	91	0.8
522374	39	50	71	85	91	1.1
522375	23	49	73	87	91	1.4
522383	46	64	79	83	85	<0.6
522435	39	62	76	86	88	0.8
522437	33	62	78	87	90	0.9
522444	37	69	81	88	92	0.7
522445	62	54	68	85	91	<0.6
522450	29	46	69	86	86	1.4
522473	19	33	66	78	86	2
522484	63	72	81	80	81	<0.6
522485	37	43	70	82	90	1.3
522501	38	66	79	84	86	0.7

Table 107

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	20	48	75	84	89	1.5
522440	31	51	69	79	85	1.3
522465	26	45	68	81	89	1.5
522474	17	40	65	78	87	1.9
522495	15	28	69	82	85	2
522509	24	38	61	88	87	1.7
522529	21	38	68	58	87	2
522553	15	29	61	81	90	2.1
522579	23	43	58	83	89	1.7

522580	50	36	68	84	93	1.1
522581	16	21	59	82	92	2.2
522582	23	48	59	86	91	1.6
522587	21	52	69	90	95	1.4
522588	19	41	65	88	94	1.7
522589	38	57	80	96	92	0.9

Table 108

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	34	49	77	79	91	1.2
522550	16	45	58	80	89	1.9
522554	26	39	60	71	87	1.9
522555	38	50	66	74	81	1.2
522556	33	39	59	76	85	1.7
522609	41	67	87	92	84	0.6
522610	21	41	65	71	93	1.8
522621	35	54	71	85	94	1.1
522627	18	9	57	81	95	2.3
522631	26	34	70	81	93	1.7
522632	40	55	82	91	95	0.8
522638	8	33	63	74	91	2.2
522643	64	53	69	82	93	<0.6
522667	23	55	75	86	91	1.3
522688	45	57	80	88	94	0.7

Table 109

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	33	51	73	80	86	1.2
522672	20	20	57	89	93	2.1
522675	20	29	63	78	94	2
522676	6	43	62	88	93	1.9
522677	6	39	63	83	96	2
522679	17	35	62	82	92	1.9
522682	61	57	69	86	90	<0.6
522689	29	57	78	87	93	1.1

522694	28	33	57	76	92	1.8
522697	19	31	68	86	95	1.8
522698	20	54	72	85	93	1.4
522715	12	48	68	80	88	1.8
522716	25	35	67	84	90	1.7
522717	27	56	74	90	88	1.2
522745	42	62	85	90	92	0.7

Table 110

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	34	52	78	84	91	1.1
522671	36	43	72	85	92	1.2
522678	35	43	65	83	92	1.3
522680	25	50	63	82	86	1.5
522681	26	57	69	86	90	1.3
522683	24	33	65	77	88	1.8
522687	36	41	68	82	93	1.3
522690	23	51	67	84	93	1.5
522692	33	38	59	77	92	1.6
522705	35	48	66	73	86	1.3
522719	29	38	62	80	92	1.7
522757	29	41	60	79	93	1.6
522770	33	47	78	91	94	1.1
522784	20	33	54	71	90	2.2
522807	20	35	61	78	92	1.9

Table 111

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	32	54	75	84	89	1.1
522758	26	49	66	87	94	1.4
522783	32	33	59	77	89	1.8
522838	16	39	64	75	82	2.0
522865	16	34	58	80	92	2.0
522866	16	25	45	66	83	2.8
522870	18	38	46	79	95	2.1

522871	13	35	57	80	91	2.1
522888	27	52	71	85	89	1.3
522889	36	59	75	81	80	0.9
522894	31	42	54	80	92	1.6
522897	29	53	76	88	92	1.2
522898	18	34	63	77	87	2.0
522913	40	54	79	90	90	0.9
522942	27	57	77	85	88	1.1

Table 112

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	20	46	71	82	89	1.6
334177	9	30	60	74	92	2.3
522905	9	24	50	76	94	2.5
522917	17	35	58	82	93	2.0
522924	7	36	59	79	95	2.1
522925	15	36	64	85	95	1.8
522932	9	29	53	80	92	2.3
522941	23	44	65	85	91	1.6
522943	13	44	75	81	88	1.7
522947	45	30	62	78	94	1.4
522964	27	48	71	85	95	1.4
495876	24	33	58	86	94	1.8
495877	16	25	52	77	87	2.4
495878	37	69	86	91	96	0.7
523002	34	54	80	89	93	1.0

Example 9: Dose-dependent antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Gapmers from the studies described in the Examples above exhibiting significant *in vitro* inhibition of DGAT2 mRNA were selected and tested at various doses in HepG2 cells. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.3125 μM, 0.625 μM, 1.25 μM, 2.50 μM, 5.00 μM, or 10.00 μM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels.

DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 113

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	41	65	75	81	87	1.3
484157	24	52	78	87	95	94	0.6
484127	10	39	71	86	93	94	0.9
484181	49	57	76	79	89	90	0.3
484137	29	41	62	79	89	91	0.8
484148	0	30	72	77	91	93	1.2
484169	18	31	48	68	87	88	1.3
484170	0	51	58	75	94	90	1.3
484133	36	63	50	58	85	91	1.0
484140	31	60	65	73	87	92	0.6
484129	48	62	73	87	91	93	0.3
484141	40	33	55	64	85	96	0.9

Table 114

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	36	38	57	64	83	87	0.9
484158	8	6	39	61	86	91	1.9
484377	0	2	15	33	78	94	2.8
484130	18	41	51	79	91	96	1.0
484336	26	24	45	67	90	92	1.3
484167	0	0	33	72	89	96	2.3
484344	17	18	29	48	75	83	2.2
484156	0	5	29	47	76	81	2.9
484391	0	0	42	66	84	96	2.0
484353	0	16	48	72	91	99	1.6

484350	0	37	49	79	89	87	1.5
484357	15	23	39	69	91	94	1.5
484343	25	28	58	80	90	93	1.0

Table 115

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	34	34	65	83	86	85	0.8
472155	21	14	20	35	54	73	4.1
472156	11	23	41	42	66	84	2.3
472158	27	36	62	77	87	95	0.9
472175	4	25	30	60	69	89	2.1
472178	0	0	6	30	54	82	4.2
423453	32	31	57	77	90	94	0.9
380132	17	9	0	30	21	54	>10
472433	0	0	0	0	18	62	>10
217328	29	28	45	65	76	83	1.4

Table 116

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	36	55	70	81	92	93	<0.6
501094	43	60	76	85	90	90	<0.6
501097	23	39	56	74	81	82	1.1
501098	56	70	83	92	90	91	<0.6
501100	51	62	82	91	92	90	<0.6
501103	58	65	77	86	93	92	<0.6
501118	26	50	54	72	85	88	0.9
501122	28	40	59	69	85	84	1.0
501127	38	61	75	81	89	88	<0.6
501165	34	24	59	70	85	82	1.1
501171	38	57	64	80	88	89	<0.6
501214	36	50	68	84	83	85	<0.6

Table 117

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	17	38	61	84	88	91	1.0

500998	37	57	74	84	90	92	0.4
501020	29	53	73	83	89	92	0.6
501033	9	27	45	66	76	80	1.7
501034	14	42	56	75	83	90	1.1
501035	39	61	77	86	86	86	0.3
501040	17	25	40	71	86	91	1.4
501041	49	66	80	81	85	83	<0.3
501062	24	29	50	66	81	88	1.3
501064	45	51	73	84	85	85	0.4
501093	12	34	55	72	76	78	1.4
501111	14	26	43	65	69	78	1.9

Table 118

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	41	47	65	81	91	94	0.6
500841	32	38	67	75	83	84	0.8
500844	35	51	77	74	77	63	0.4
500852	35	38	63	79	88	89	0.8
500859	58	39	52	85	91	96	0.5
500867	21	54	46	88	90	93	0.8
500913	42	65	58	89	91	90	0.4
500942	32	31	50	86	92	95	0.9
500966	53	75	78	84	88	89	<0.3
500989	32	69	74	90	87	86	0.3
501018	13	58	72	86	87	82	0.7
501067	7	63	45	77	88	94	1.0

Table 119

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	39	44	70	77	92	1.7
501385	0	9	30	25	37	63	7.0
501387	0	0	0	14	27	75	6.8
501404	28	37	48	59	61	83	1.5
501412	0	23	24	16	51	75	4.6
501427	3	18	50	41	68	92	2.1

501430	21	7	47	53	74	90	1.9
501442	35	39	65	72	92	94	0.8
501443	36	50	34	48	62	75	1.6
501447	21	9	49	56	74	90	1.8
501448	23	25	48	60	69	88	1.6
501450	27	36	28	31	52	77	3.4

Table 120

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	13	31	51	80	86	2.1
501391	0	9	15	7	46	67	8.6
501393	0	0	0	50	64	81	3.1
501398	0	5	0	0	41	58	>10
501405	0	31	33	57	73	80	2.0
501429	5	10	0	2	40	62	>10
501435	20	15	34	50	79	89	1.9
501438	12	39	30	64	83	89	1.6
501440	42	21	41	57	81	92	1.3
501451	0	0	19	39	67	84	3.5
501452	0	7	14	38	54	85	3.6
501454	12	4	1	19	65	82	4.2

Table 121

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	26	56	75	82	92	1.2
501388	0	15	28	63	86	88	1.8
501389	0	0	0	58	69	84	2.1
501390	0	33	0	0	73	86	2.0
501392	0	19	57	60	75	81	2.2
501396	0	13	0	53	81	83	2.3
501411	0	0	0	31	45	78	5.5
501428	14	0	14	38	74	81	3.2
501436	0	0	41	61	80	78	2.2
501449	0	0	35	56	71	82	2.7
501455	0	0	19	30	61	75	4.1

501457	18	0	23	39	63	87	3.1

Table 122

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	19	33	46	69	80	91	1.3
501154	24	22	33	42	74	81	2.2
501183	18	42	54	71	71	80	1.2
501199	23	22	44	68	80	79	1.5
501200	8	13	40	65	78	87	1.9
501212	39	32	24	52	65	70	2.3
501213	12	34	40	69	75	79	1.6
501224	36	33	53	65	74	81	1.1
501270	12	9	42	59	67	76	2.3
501287	2	24	33	46	71	80	2.5
501322	8	9	6	31	54	77	4.4
501345	10	17	21	50	55	81	3.0

Table 123

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	11	17	33	60	69	4.2
525395	18	18	15	47	49	69	4.4
525401	10	28	33	58	68	68	2.5
525402	0	9	23	43	62	73	3.5
525414	2	11	29	36	56	56	5.2
525415	22	0	21	39	49	73	4.7
525431	6	19	36	49	67	66	2.9
525442	13	0	23	44	56	81	3.4
525443	4	6	24	61	65	78	2.7
525469	28	38	50	69	79	85	1.1
525470	3	17	23	41	70	82	2.8
525501	0	5	34	31	58	79	3.5

Table 124

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	22	35	48	62	76	86	1.4
525468	11	30	21	61	72	83	2.1
525471	29	47	62	70	77	84	0.8
525472	23	35	54	70	81	81	1.2
525474	22	38	54	69	79	78	1.2
525479	25	26	35	63	75	84	1.6
525480	0	21	29	50	75	75	2.7
525500	4	23	39	60	80	87	1.8
525513	32	21	45	55	77	86	1.6
525551	15	31	38	8	84	90	2.3
525552	11	29	49	56	78	87	1.6
525554	16	7	31	62	68	79	2.3

Table 125

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	28	21	44	50	68	79	1.9
525544	0	3	22	41	52	63	4.8
525612	26	36	56	72	76	79	1.1
525631	0	8	26	54	77	82	2.7
525649	0	0	10	46	64	76	3.7
496041	14	9	8	31	53	65	5.7
525688	5	25	43	68	82	89	1.6
525705	27	30	48	69	82	90	1.2
525708	5	26	54	69	84	89	1.5
525711	14	28	49	67	81	88	1.4
525733	21	42	60	76	82	93	1.0
525754	0	17	34	55	79	85	2.2

Example 10: Final confirmation of antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Gapmers from the studies described in the Examples above exhibiting significant *in vitro* inhibition of DGAT2 mRNA were selected and tested at various doses in HepG2 cells. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.3125 μM, 0.625 μM, 1.25 μM, 2.50 μM,

5.00 μM, or 10.00 μM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 126

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	19	26	52	72	86	92	1.3
483817	18	31	60	74	86	90	1.1
483898	40	41	68	77	89	90	0.6
483908	21	47	63	83	89	92	0.8
484152	18	25	47	63	84	91	1.4
484181	42	45	73	81	87	86	0.5
484215	27	37	47	69	80	93	1.1
484231	16	33	58	71	83	89	1.2
472316	0	5	40	50	84	92	2.3
423463	17	34	55	80	90	93	1.1
484271	26	29	62	83	89	92	1.0
484283	7	12	30	50	79	90	2.2

Table 127

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	3	25	51	69	89	92	1.5
472158	18	25	26	44	71	80	2.4
483874	30	42	62	82	90	93	0.8
483910	20	30	49	74	85	90	1.2
483952	36	62	80	88	92	93	0.4
483968	8	35	57	73	86	91	1.2
483984	32	34	62	78	88	91	0.9

483987	12	10	36	61	80	92	1.9
483997	0	7	33	57	77	89	2.4
484085	25	24	53	72	87	89	1.2
484099	29	44	67	82	91	94	0.7
423453	19	24	46	62	88	95	1.4

Table 128

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	22	19	46	61	83	90	1.5
484127	16	18	54	74	90	95	1.3
484129	33	39	64	79	90	89	0.8
484130	30	29	52	66	85	92	1.1
484140	0	16	37	63	86	87	1.9
484133	1	2	44	71	83	93	1.8
484137	0	27	64	81	92	92	1.3
484148	16	37	67	79	91	94	1.0
484157	0	31	70	86	92	93	0.9
484170	23	40	57	77	90	94	1.0
484181	9	18	63	83	76	88	1.4
484343	18	21	40	72	88	91	1.4

Table 129

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	23	30	57	71	83	2.4
501849	22	33	46	65	79	87	1.4
501850	12	19	40	52	76	83	2.0
501852	17	25	47	63	68	77	1.8
501855	24	37	59	78	82	84	1.0
501861	15	23	45	61	77	84	1.7
501871	14	19	39	57	71	85	2.0
501884	14	25	42	57	74	83	1.9
501886	30	40	47	58	70	73	1.4
501932	8	24	28	55	68	78	2.4
501944	6	31	0	44	67	82	3.3
501950	0	14	19	55	79	85	2.4

Table 130

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	31	43	53	74	80	84	0.9
502154	29	46	68	81	86	91	0.7
502163	22	33	55	71	89	97	1.1
502164	20	32	71	72	85	91	1.0
502179	28	50	67	84	81	90	0.7
502191	29	47	64	74	94	97	0.7
502194	24	23	62	78	90	90	1.1
502314	25	14	21	44	66	85	2.6
502319	20	32	56	78	86	92	1.1
502322	17	35	49	68	79	83	1.4
502331	11	22	11	45	60	82	3.1
502334	35	40	59	69	82	92	0.8

Table 131

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	13	16	25	38	59	75	3.5
495702	29	37	49	65	78	80	1.2
495718	21	34	28	56	71	77	2.0
495756	23	40	56	76	87	95	1.0
507692	20	33	56	68	89	91	1.1
507693	28	38	56	79	89	94	0.9
507694	19	30	45	72	87	94	1.3
507695	28	32	44	70	84	92	1.2
507696	18	37	59	78	88	90	1.0
507710	27	39	52	73	91	92	1.0
507716	32	51	52	68	88	93	0.8
507717	31	49	44	66	84	90	1.0

Table 132

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	43	64	80	84	90	1.2
501947	7	23	42	65	79	89	1.7

501951	13	25	45	68	85	92	1.5
501959	8	29	38	66	74	90	1.7
501960	14	22	41	68	75	88	1.7
501968	17	33	44	59	88	87	1.4
502038	0	7	8	36	58	84	3.7
502045	13	38	53	67	81	88	1.3
502056	0	31	66	83	88	91	1.2
502098	9	35	48	72	86	93	1.3
502099	9	31	52	74	82	92	1.3
502119	1	45	61	79	89	95	1.1

Table 133

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	0	43	59	69	84	90	1.1
495697	15	32	50	66	78	79	1.5
495705	25	37	53	59	76	79	1.3
495719	21	30	44	64	76	84	1.5
501388	13	34	44	62	71	87	1.6
501389	11	44	47	54	80	91	1.4
501392	0	25	42	51	75	87	1.9
501396	19	31	52	66	76	87	1.4
501428	0	0	33	46	63	85	2.8
501436	4	28	23	57	76	88	2.1
501449	19	21	42	59	75	92	1.7
501457	7	29	35	50	75	92	1.9

Table 134

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	13	35	53	73	83	87	1.3
522373	19	34	54	72	83	84	1.2
522374	13	31	54	65	79	85	1.4
522383	23	44	62	72	76	81	1.0
522435	25	39	55	73	81	80	1.1
522437	26	35	56	70	81	85	1.1
522440	14	33	50	67	77	82	1.5

522444	24	35	57	78	83	89	1.0
522445	25	45	57	69	83	86	1.0
522465	14	15	40	55	75	82	2.0
522484	37	0	72	75	76	74	1.3
522501	25	45	55	72	78	76	1.0

Table 135

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	25	36	50	79	83	87	1.1
522580	27	34	55	62	86	85	1.1
522587	35	40	56	73	88	92	0.8
522589	27	40	56	71	82	91	1.0
522609	37	48	70	82	94	93	0.5
522621	20	35	55	74	86	91	1.1
522632	31	52	66	80	90	93	0.6
522643	16	28	48	67	78	87	1.5
522688	16	38	57	75	76	89	1.2
522689	29	34	58	78	84	91	0.9
522717	18	24	50	72	82	88	1.4
522745	22	35	57	75	89	92	1.0

Table 136

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	23	32	45	74	78	88	1.3
522682	26	34	63	68	74	81	1.1
522770	8	26	50	65	83	91	1.5
522889	25	40	59	70	77	78	1.1
522897	14	22	45	69	83	89	1.5
522913	19	30	57	73	86	90	1.2
522941	8	18	41	56	73	82	2.1
522942	20	30	49	67	83	86	1.3
522947	14	0	40	58	80	91	2.0
522964	9	20	51	63	78	89	1.7
495878	16	36	62	80	90	93	1.0
523002	21	32	51	67	73	84	1.4

Table 137

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	40	35	66	81	87	89	0.7
525401	17	58	64	79	85	86	0.8
525402	30	41	49	74	87	90	0.9
525431	31	29	64	82	86	84	0.9
525442	35	39	59	76	90	87	0.8
525443	39	53	64	76	88	89	0.5
525469	32	68	85	93	92	93	0.3
525470	39	34	59	74	91	89	0.8
525471	27	34	59	84	86	0	0.9
525474	32	47	69	80	93	87	0.6
525479	25	33	51	60	75	75	1.5
525501	31	29	56	82	91	88	1.0

Table 138

ISIS No	0.3125 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	22	41	54	69	81	88	1.1
525472	26	31	50	69	84	82	1.2
525500	11	33	52	68	83	83	1.4
525513	16	20	48	64	79	87	1.6
525552	27	30	57	70	83	90	1.1
525612	0	44	65	76	83	82	0.3
525688	11	40	60	75	88	97	1.1
525705	25	41	65	76	90	95	0.8
525708	36	38	64	75	93	96	0.7
525711	24	53	67	80	90	94	0.7
525733	27	70	73	86	91	95	0.4
525754	23	23	48	70	85	89	1.3

Example 11: Final confirmation of antisense inhibition of human DGAT2 in HepG2 cells by MOE gapmers

Gapmers from the studies described in the Examples above exhibiting significant *in vitro* inhibition of DGAT2 mRNA were selected and tested at various doses in HepG2 cells. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.625 μM, 1.25 μM, 2.50 μM, 5.00 μM, or 10.00 μM concentrations of antisense oligonucleotide, as specified in the Tables below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and DGAT2 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2988_MGB was used to measure mRNA levels. DGAT2 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of DGAT2, relative to untreated control cells. '0' indicates that the mRNA levels were not inhibited.

The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. DGAT2 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

Table 139

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	48	60	77	85	86	0.6
495450	42	50	73	83	83	1.0
495516	64	78	87	84	84	<0.6
495520	70	76	87	83	82	<0.6
495554	26	61	75	76	85	1.1
495555	30	72	80	87	84	0.8
495576	61	73	86	88	88	<0.6
495577	44	64	75	85	80	0.6
495609	64	69	83	86	89	<0.6
495685	0	53	75	82	85	2.0
495707	9	41	72	75	66	2.2
495736	16	61	80	85	81	1.3
495749	16	33	76	90	93	1.7
495752	0	66	75	74	93	1.7
495753	0	59	79	91	92	1.8

Table 140

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	54	70	87	91	93	<0.6
495738	55	57	81	92	92	<0.6
495744	37	59	78	88	90	0.9
495756	52	61	80	90	94	<0.6
495825	34	69	89	94	97	0.7
495829	38	79	88	90	91	<0.6
495837	52	67	93	93	96	<0.6
495839	66	89	91	93	93	<0.6
495840	64	84	94	96	94	<0.6
495841	51	82	90	92	93	<0.6
495842	54	73	88	90	92	<0.6
495849	63	69	82	85	91	<0.6
495853	72	77	91	96	94	<0.6
495857	52	61	88	91	92	<0.6
495878	54	77	93	97	96	<0.6

Table 141

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	38	63	73	85	88	0.8
501171	38	53	69	83	84	1.0
501183	51	70	79	87	89	<0.6
501199	44	68	88	91	87	<0.6
501213	25	57	82	93	96	1.1
501214	35	56	72	88	92	1.0
501224	48	68	83	90	90	<0.6
501405	27	51	72	90	96	1.3
501430	10	26	65	90	94	2.0
501435	35	41	71	92	94	1.3
501438	27	71	83	92	92	0.9
501440	24	40	66	90	97	1.6
501442	58	79	91	96	94	<0.6
501443	32	29	57	89	96	1.7
501448	27	46	72	91	93	1.4

Table 142

ISIS No	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
413433	43	58	82	91	94	0.8
501127	46	68	81	91	92	<0.6
501103	34	70	85	93	91	0.7
501100	54	75	88	93	94	<0.6
501098	55	81	91	91	89	<0.6
501094	62	70	87	90	92	<0.6
501064	52	67	81	88	89	<0.6
501041	53	71	82	86	85	<0.6
501035	57	77	87	88	90	<0.6
501020	47	63	86	94	94	0.6
500998	47	61	86	91	95	0.6
500989	55	75	83	86	85	<0.6
500966	71	82	85	87	87	<0.6
500913	29	46	74	85	88	1.3
500859	6	44	75	87	90	1.8

Example 12: Tolerability of antisense oligonucleotides targeting human DGAT2 in CD1 mice

CD1® mice (Charles River, MA) are a multipurpose mice model, frequently utilized for safety and efficacy testing. The mice were treated with ISIS antisense oligonucleotides selected from studies described above and evaluated for changes in the levels of various plasma chemistry markers. Liver and kidney tissue from the treated mice were microscopically reviewed; no toxicity or tissue injury was seen in any treated animal.

Treatment

Groups of five male CD1 mice each were injected subcutaneously twice a week for 6 weeks with 100 mg/kg (200 mg/kg/week) of ISIS oligonucleotide. One group of ten male CD1 mice was injected subcutaneously twice a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma chemistry markers

To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, bilirubin, albumin, and BUN were measured on day 27 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). The results are presented in the Table below. ISIS

oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

Table 143
Plasma chemistry markers in CD1 mice

	ALT (IU/L)	AST (IU/L)	BUN (mg/dL)	Bilirubin (mg/dL)
PBS	33	50	30	0.3
ISIS 483984	193	177	30	0.3
ISIS 484099	69	77	23	0.2
ISIS 484129	43	46	24	0.2
ISIS 484157	136	105	26	0.2
ISIS 495576	36	53	30	0.3
ISIS 495609	102	112	28	0.3
ISIS 495753	68	76	28	0.2
ISIS 495756	154	123	26	0.3
ISIS 501849	45	58	26	0.2
ISIS 501850	294	306	26	0.3
ISIS 501855	62	56	28	0.2
ISIS 501861	100	97	30	0.3
ISIS 502322	42	46	28	0.2
ISIS 507696	99	132	30	0.2
ISIS 507710	50	68	27	0.3
ISIS 507716	3112	3302	19	7.8

Body and organ weights

Body weights of the mice were measured on day 35 and are presented in the Table below. Liver, spleen and kidney weights were measured at the end of the study (day 41), and are also presented in the Table below. ISIS oligonucleotides that caused any changes in body or organ weights outside the expected range for antisense oligonucleotides were excluded from further studies. ‘n/a’ indicates that the particular endpoint was not measured in that group of mice.

Table 144
Body and organ weights of CD1 mice (g)

	Body weight	Kidney	Liver	Spleen
PBS	41.2	0.7	2.0	0.1
ISIS 483984	41.0	n/a	n/a	n/a

ISIS 484129	41.0	0.6	2.1	0.2
ISIS 484157	38.8	n/a	n/a	n/a
ISIS 495576	41.4	0.6	2.1	0.2
ISIS 495609	42.5	0.6	2.1	0.2
ISIS 495753	40.0	0.5	2.2	0.2
ISIS 495756	42.0	0.7	2.6	0.2
ISIS 501849	42.3	0.6	2.4	0.2
ISIS 501850	41.7	0.7	2.5	0.2
ISIS 501855	39.9	n/a	n/a	n/a
ISIS 501861	40.3	0.6	2.3	0.2
ISIS 502322	41.1	0.7	2.2	0.2
ISIS 507696	38.9	0.6	2.3	0.2
ISIS 507710	42.7	0.6	2.5	0.2

Example 13: Tolerability of antisense oligonucleotides targeting human DGAT2 in CD1 mice

CD1® mice were treated with ISIS antisense oligonucleotides selected from studies described above and evaluated for changes in the levels of various plasma chemistry markers.

Treatment

Groups of five male CD1 mice each were injected subcutaneously twice a week for 6 weeks with 50 mg/kg of ISIS 483817, ISIS 483910, ISIS 484085, ISIS 484127, ISIS 484130, ISIS 484137, ISIS 484215, ISIS 484231, ISIS 484271, ISIS 501871, ISIS 502098, ISIS 502119, ISIS 502154, ISIS 502163, ISIS 502164, ISIS 502194, ISIS 525443, ISIS 525474, ISIS 525552, ISIS 525612, ISIS 525688, ISIS 525705, ISIS 525708, ISIS 525711, and ISIS 525733. One group of ten male CD1 mice was injected subcutaneously twice a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma chemistry markers

To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, bilirubin, albumin, and BUN were measured on day 26 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

Table 145
Plasma chemistry markers in CD1 mice

	ALT (IU/L)	AST (IU/L)	BUN (mg/dL)	Bilirubin (mg/dL)
PBS	26	55	29	0.6
ISIS 483817	40	54	27	0.3
ISIS 483910	244	155	28	0.6
ISIS 484085	46	58	27	0.4
ISIS 484127	100	147	25	0.4
ISIS 484130	151	91	29	0.3
ISIS 484137	31	49	26	0.3
ISIS 484215	42	49	25	0.2
ISIS 484231	31	45	26	0.2
ISIS 484271	2847	3267	26	2.9
ISIS 501871	108	96	23	0.2
ISIS 502098	60	62	24	0.3
ISIS 502119	402	370	26	0.3
ISIS 502154	293	294	28	0.3
ISIS 502163	45	60	23	0.4
ISIS 502164	81	75	25	0.4
ISIS 502194	32	43	24	0.4
ISIS 525443	93	101	24	0.3
ISIS 525474	49	94	24	0.6
ISIS 525552	1374	874	25	0.3
ISIS 525612	78	54	27	0.4
ISIS 525705	76	117	31	0.3
ISIS 525708	59	79	29	0.3
ISIS 525711	1670	787	26	0.3

Body and organ weights

Body weights of the mice were measured on day 36 and are presented in the Table below. Liver, spleen and kidney weights were measured at the end of the study, and are also presented in the Table below. ISIS oligonucleotides that caused any changes in body or organ weights outside the expected range for antisense oligonucleotides were excluded from further studies. 'n/a' indicates that the particular endpoint was not measured in that group of mice.

Table 146
Body and organ weights of CD1 mice (g)

	Body weight	Kidney	Liver	Spleen
PBS	39.4	0.7	2.0	0.1
ISIS 483817	38.8	0.6	2.3	0.2
ISIS 483910	39.2	0.6	2.3	0.2
ISIS 484085	37.9	0.6	2.3	0.1
ISIS 484127	35.3	n/a	n/a	n/a
ISIS 484130	41.5	n/a	n/a	n/a
ISIS 484137	39.6	0.7	2.3	0.1
ISIS 484215	38.5	0.6	2.4	0.2
ISIS 484231	38.3	0.6	2.1	0.1
ISIS 501871	38.7	0.6	2.3	0.2
ISIS 502098	38.8	0.6	2.5	0.2
ISIS 502163	39.1	0.6	2.0	0.2
ISIS 502164	37.7	0.6	2.1	0.2
ISIS 502194	40.5	0.6	1.9	0.1
ISIS 525443	39.5	0.6	2.0	0.2
ISIS 525474	37.0	0.6	1.8	0.1
ISIS 525612	37.8	0.6	2.0	0.1
ISIS 525705	36.5	0.7	2.0	0.4
ISIS 525708	38.7	0.7	2.0	0.3

Example 14: Tolerability of antisense oligonucleotides targeting human DGAT2 in Sprague-Dawley rats

Sprague-Dawley rats are a multipurpose model used for safety and efficacy evaluations. The rats were treated with ISIS antisense oligonucleotides from the study described above and evaluated for changes in the levels of various plasma chemistry markers.

Treatment

Male Sprague-Dawley rats were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 Sprague-Dawley rats each were injected subcutaneously twice a week for 8 weeks with 50 mg/kg of ISIS 484129, ISIS 495576, ISIS 495609, ISIS 495753, ISIS 495756, ISIS 501849, ISIS 501850, ISIS 501861, ISIS 502322, ISIS 507696, and ISIS 507710. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver function

To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured on day 56 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). Plasma levels of ALT and AST were measured and the results are presented in the Table below expressed in IU/L. Plasma levels of Bilirubin were also measured using the same clinical chemistry analyzer and the results are also presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any markers of liver function outside the expected range for antisense oligonucleotides were excluded in further studies.

Table 147
Liver function markers in Sprague-Dawley rats

	ALT (IU/L)	AST (IU/L)	Bilirubin (mg/dL)
PBS	49	70	0.16
ISIS 484129	133	130	0.18
ISIS 495576	99	148	0.17
ISIS 495609	406	269	0.32
ISIS 495753	968	1258	1.83
ISIS 495756	165	206	0.24
ISIS 501849	57	103	0.16
ISIS 501850	1218	1916	6.55
ISIS 501861	61	113	0.14
ISIS 502322	79	84	0.14

Kidney function

To evaluate the effect of ISIS oligonucleotides on kidney function, urine levels of creatinine and total protein were measured on day 56 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). Results are presented in the Table below, expressed in mg/dL.

Table 148
Kidney function markers (mg/dL) in Sprague-Dawley rats

	Creatinine	Total protein
PBS	146	114
ISIS 495756	63	978
ISIS 501849	82	445
ISIS 501861	67	309
ISIS 501850	52	268
ISIS 502322	84	507
ISIS 495576	108	587
ISIS 495609	38	264
ISIS 495753	73	411
ISIS 484129	66	312

Body and organ weights

Body weights of the rat were measured on day 50 and are presented in the Table below. Liver, heart, spleen and kidney weights were measured at the end of the study, and are also presented in the Table below. ISIS oligonucleotides that caused any changes in body or organ weights outside the expected range for antisense oligonucleotides were excluded from further studies. 'n/a' indicates that the particular endpoint was not measured in that group of mice.

Table 149
Body and organ weights of Sprague-Dawley rats (g)

	Body weight	Heart	Kidney	Liver	Spleen
PBS	486	1.7	3.5	14.2	0.7
ISIS 495756	374	1.1	3.5	15.5	2.2
ISIS 501849	404	1.2	3.3	13.7	1.9
ISIS 501861	390	1.1	3.6	16.0	2.7

ISIS 501850	329	1.3	4.1	16.3	4.5
ISIS 502322	424	1.3	3.4	15.6	1.7
ISIS 495576	461	1.3	3.5	17.3	2.1
ISIS 495609	383	1.4	3.8	18.9	3.8
ISIS 495753	384	1.2	3.4	16.3	3.6
ISIS 484129	415	1.3	3.1	14.9	1.5

Example 15: Tolerability of antisense oligonucleotides targeting human DGAT2 in Sprague-Dawley rats

Sprague-Dawley rats were treated with ISIS antisense oligonucleotides from the studies described above and evaluated for changes in the levels of various plasma chemistry markers.

Treatment

Male Sprague-Dawley rats were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 Sprague-Dawley rats each were injected subcutaneously twice a week for 8 weeks with 50 mg/kg of ISIS 483817, ISIS 483910, ISIS 484085, ISIS 484137, ISIS 484215, ISIS 484231, ISIS 501871, ISIS 502098, ISIS 502163, ISIS 502164, ISIS 502194, ISIS 525443, ISIS 525474, ISIS 525612, and ISIS 525708. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver function

To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured on day 53 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). Plasma levels of ALT and AST were measured and the results are presented in the Table below expressed in IU/L. Plasma levels of Bilirubin were also measured using the same clinical chemistry analyzer and the results are also presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any markers of liver function outside the expected range for antisense oligonucleotides were excluded in further studies.

Table 150
Liver function markers in Sprague-Dawley rats

	ALT (IU/L)	AST (IU/L)	Bilirubin (mg/dL)
PBS	53	83	0.21
ISIS 483817	81	127	0.13
ISIS 483910	283	428	3.38

ISIS 484085	131	208	0.27
ISIS 484137	63	98	0.16
ISIS 484215	50	86	0.13
ISIS 484231	75	106	0.17
ISIS 501871	45	73	0.10
ISIS 502098	57	156	0.12
ISIS 502163	85	177	0.21
ISIS 502164	67	94	0.15
ISIS 502194	54	82	0.15
ISIS 525443	50	82	0.13
ISIS 525474	118	136	0.22
ISIS 525612	313	314	0.18
ISIS 525708	65	117	0.16

Kidney function

To evaluate the effect of ISIS oligonucleotides on kidney function, plasma levels of creatinine and total protein were measured on day 53 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). Results are presented in the Table below, expressed in mg/dL. Urine levels of creatinine and total protein were also measured on day 53 using the same automated clinical chemistry analyzer. Results are presented in the Table below, expressed in mg/dL.

Table 151

Kidney function markers in the plasma (mg/dL) in Sprague-Dawley rats

	BUN	Creatinine
PBS	20	0.44
ISIS 483817	22	0.40
ISIS 483910	24	0.42
ISIS 484085	19	0.37
ISIS 484137	22	0.43
ISIS 484215	19	0.36
ISIS 484231	21	0.39
ISIS 501871	23	0.31
ISIS 502098	25	0.42
ISIS 502163	21	0.37

ISIS 502164	23	0.43
ISIS 502194	21	0.44
ISIS 525443	24	0.51
ISIS 525474	22	0.39
ISIS 525612	18	0.38
ISIS 525708	31	0.53

Table 152
Kidney function markers in the urine (mg/dL) in Sprague-Dawley rats

	Creatinine	Total protein
PBS	227	193
ISIS 483817	95	2129
ISIS 483910	60	1030
ISIS 484085	87	868
ISIS 484137	84	517
ISIS 484215	146	1115
ISIS 484231	89	652
ISIS 501871	52	3426
ISIS 502098	64	550
ISIS 502163	73	522
ISIS 502164	100	554
ISIS 502194	95	410
ISIS 525443	73	595
ISIS 525474	79	1547
ISIS 525612	94	453
ISIS 525708	41	2043

Body and organ weights

Body weights of the rat were measured on day 49 and are presented in the Table below. Liver, heart, spleen and kidney weights were measured at the end of the study, and are also presented in the Table below. ISIS oligonucleotides that caused any changes in body or organ weights outside the expected range for antisense oligonucleotides were excluded from further studies. ‘n/a’ indicates that the particular endpoint was not measured in that group of mice.

Table 153
Body and organ weights of Sprague-Dawley rats (g)

	Body weight	Heart	Kidney	Liver	Spleen
PBS	485	1.6	3.5	14.5	0.9
ISIS 483817	362	1.2	4.2	17.0	2.3
ISIS 483910	358	1.0	3.2	19.0	3.0
ISIS 484085	348	1.1	2.9	15.3	1.6
ISIS 484137	353	1.1	3.0	14.2	1.6
ISIS 484215	391	1.2	3.7	16.6	2.0
ISIS 484231	386	1.1	3.2	16.6	2.5
ISIS 501871	322	1.1	3.5	17.4	1.8
ISIS 502098	315	1.2	2.9	15.8	2.3
ISIS 502163	326	1.0	3.5	14.5	3.4
ISIS 502164	381	1.2	2.8	15.4	2.2
ISIS 502194	439	1.3	3.4	18.6	2.0
ISIS 525443	469	1.5	3.7	22.1	1.7
ISIS 525474	445	1.7	3.8	19.2	2.2
ISIS 525612	427	1.5	3.1	13.1	1.4
ISIS 525708	338	1.0	3.6	15.9	2.3

Example 16: Effect of ISIS antisense oligonucleotides targeting human DGAT2 in cynomolgus monkeys

Cynomolgus monkeys were treated with ISIS antisense oligonucleotides selected from studies described above. Antisense oligonucleotide efficacy and tolerability were evaluated.

At the time this study was undertaken, the cynomolgus monkey genomic sequence was not available in the National Center for Biotechnology Information (NCBI) database; therefore, cross-reactivity with the cynomolgus monkey gene sequence could not be confirmed. Instead, the sequences of the ISIS antisense oligonucleotides used in the cynomolgus monkeys was compared to a rhesus monkey sequence for homology. It is expected that ISIS oligonucleotides with homology to the rhesus monkey sequence are fully cross-reactive with the cynomolgus monkey sequence as well. The human antisense oligonucleotides tested are cross-reactive with the rhesus genomic sequence (RefSeq No. NW_001100387.1 truncated from nucleotides 1232000 to 1268000, designated herein as SEQ ID NO: 3). The greater the complementarity between the human oligonucleotide and the rhesus monkey sequence, the more likely the human

oligonucleotide can cross-react with the rhesus monkey sequence. The start and stop sites of each oligonucleotide to SEQ ID NO: 3 is presented in the Table below. "Start site" indicates the 5'-most nucleotide to which the gapmer is targeted in the rhesus monkey gene sequence.

Table 154
Antisense oligonucleotides complementary to SEQ ID NO: **3**

ISIS No	Start Site	Stop Site	Sequence	Motif	SEQ ID NO
484085	14986	15005	GTCTGGGAACAGCAGCATCA	5-10-5	1371
484129	18207	18226	GCACTGACATGGTAAGTCCT	5-10-5	1415
484137	18355	18374	TGCCATTTAATGAGCTTCAC	5-10-5	1423
495576	7054	7073	CACCATAATCTGCACAGGTT	5-10-5	1849
501861	19517	19536	TCACAGAATTATCAGCAGTA	5-10-5	2959
502194	27298	27317	CCTCTTAGAAGTAATGCTTC	5-10-5	3292
525443	2716	2732	TCCATGTCAGAGAGGCT	3-10-4	4198
525612	14990	15006	GGTCTGGGAACAGCAGC	3-10-4	4373

Treatment

Prior to the study, the monkeys were kept in quarantine for a 30-week period, during which the animals were observed daily for general health. The monkeys were 2-4 years old and weighed between 2 and 4 kg. Eight groups of 5 randomly assigned male cynomolgus monkeys each were injected subcutaneously with ISIS oligonucleotide or PBS using a stainless steel dosing needle and syringe of appropriate size into the intracapsular region and outer thigh of the monkeys. The monkeys were dosed 3 times a week for the first week (days 1, 3, and 5) as loading doses, and subsequently twice a week for weeks 2-13, with 20 mg/kg of ISIS oligonucleotide. A control group of 6 cynomolgus monkeys was injected with 0.9% sterile saline subcutaneously three times a week for the first week (days 1, 3, and 5), and subsequently once a week for weeks 2-13.

During the study period, the monkeys were observed for signs of mortality, clinical observations, and body weight, qualitative food consumption, ophthalmoscopic and electrocardiographic examination, clinical and anatomic pathology. Scheduled euthanasia of the animals was conducted on day 93 for animals assigned to terminal necroscopy and on Day 182 for animals assigned to the recovery necroscopy. A full panel of tissues were taken, processed to slides and examined microscopically for histopathology. The protocols described in the Example were approved by the Institutional Animal Care and Use Committee (IACUC).

<u>Hepatic Target Reduction</u>

Target gene RNA analysis

On day 93, RNA was extracted from liver tissue for real-time PCR analysis of DGAT2 using primer probe set mkDGAT2 (forward sequence CCGCAAGGGCTTTGTGAA, designated herein as SEQ ID NO: 13, reverse sequence TTCTCTCCAAAGGAGTACATGGG, designated herein as SEQ ID NO: 14, probe sequence CCTGCGCCATGGAGCCGAC, designated herein as SEQ ID NO: 15). Results are presented as percent inhibition of DGAT2 mRNA, relative to PBS control, normalized to the house keeping gene CyclophilinA. Similar results were obtained on normalization with RIBOGREEN®. As shown in the Table below, treatment with ISIS antisense oligonucleotides resulted in significant reduction of DGAT2 mRNA in comparison to the sterile saline control. Specifically, treatment with ISIS 484137 and ISIS 501861 resulted in the significant reduction of DGAT2 mRNA expression.

Inhibition levels with select oligonucleotides were also measured with the human primer probe set RTS2977_MGB. As presented in the Table below, treatment with ISIS oligonucleotides significantly reduced DGAT2 levels. Specifically, treatment with ISIS 484137 and ISIS 501861 resulted in the significant reduction of DGAT2 mRNA expression.

Table 155
Percent Inhibition of DGAT2 mRNA in the cynomolgus monkey liver relative to the saline control (mkDGAT2 primer probe set)

ISIS No	RIBOGREEN	CyclophilinA
484085	20	21
484129	54	52
484137	71	69
495576	70	66
501861	89	88
502194	26	29
525443	49	48
525612	35	43

Table 156
Percent Inhibition of DGAT2 mRNA in the cynomolgus monkey liver relative to the saline control (RTS2977_MGB primer probe set)

ISIS No	RIBOGREEN	CyclophilinA
501861	82	79
484137	63	58
525443	22	17

Secondary lipid gene RNA analysis

Gene expression analysis of secondary lipid genes, DGAT1, ACC1, ACC2, FAS, and SCD1 2 was also performed . The results are presented in the Table below, expressed as % expression of each gene compared to the PBS control. As presented in the Table below, treatment with ISIS oligonucleotides significantly reduced lipogenic gene levels. Specifically, treatment with ISIS 484137 resulted in the significant reduction of mRNA expression.

Table 157
% lipid gene expression

	DGAT1	ACC1	ACC2	FAS	SCD-1
sterile saline	100	100	100	100	100
ISIS 484129	85	95	95	122	64
ISIS 495576	82	66	59	65	40
ISIS 501861	140	69	67	51	22
ISIS 484085	118	122	86	281	123
ISIS 484137	81	99	77	115	51
ISIS 502194	103	91	81	114	63
ISIS 525443	118	87	75	57	25
ISIS 525612	170	106	96	83	42

Tolerability studies

Body weight measurements

To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were measured at regularly and are presented in the Table below. The results indicate that effect of treatment with antisense oligonucleotides on body weights was within the expected range for antisense oligonucleotides. Specifically, treatment with ISIS 484137 was well tolerated in terms of the body weights of the monkeys.

Table 158
Body weights in the cynomolgus monkey

	Day 1	Day 15	Day 29	Day 36	Day 50	Day 64	Day 78	Day 85
sterile saline	2734	2795	2775	2719	2743	2739	2807	2779
ISIS 484085	2759	2785	2822	2762	2815	2812	2910	2911
ISIS 484129	2780	2889	2906	2852	2918	2937	3043	3029
ISIS 484137	2756	2793	2847	2763	2850	2823	2906	2900
ISIS 495576	2748	2865	2905	2823	2869	2908	2996	2979
ISIS 501861	2702	2775	2797	2750	2775	2828	2893	2860
ISIS 502194	2817	2886	2902	2840	2926	2929	3038	3045

ISIS 525443	2790	2835	2814	2767	2790	2772	2843	2859
ISIS 525612	2921	2962	2995	2937	3006	3020	3093	3166

Liver function

To evaluate the effect of ISIS oligonucleotides on hepatic function, blood samples were collected from all the study groups. The blood samples were collected via femoral venipuncture on day 93, 48 hrs post-dosing. The monkeys were fasted overnight prior to blood collection. Blood was collected in tubes without any anticoagulant, and kept at room temperature for a minimum of 30 min for serum separation. The tubes were then centrifuged to obtain serum. Levels of various liver function markers were measured using a Toshiba 200FR NEO chemistry analyzer (Toshiba Co., Japan). Serum levels of ALT and AST were measured and the results are presented in the Table below, expressed in IU/L. Bilirubin, a liver function marker, was similarly measured and is presented in the Table below, expressed in mg/dL. The results indicate that antisense oligonucleotides had no effect on liver function outside the expected range for antisense oligonucleotides. Specifically, treatment with ISIS 484137 was well tolerated in terms of the liver function in monkeys.

Table 159
Liver function markers in cynomolgus monkey serum

	ALT (IU/L)	AST (IU/L)	Bilirubin (mg/dL)
sterile saline	40	42	0.20
ISIS 484085	57	52	0.15
ISIS 484129	43	43	0.16
ISIS 484137	52	57	0.16
ISIS 495576	56	45	0.15
ISIS 501861	70	67	0.16
ISIS 502194	88	54	0.16
ISIS 525443	56	45	0.23
ISIS 525612	38	37	0.23

Kidney function

To evaluate the effect of ISIS oligonucleotides on kidney function, blood samples were collected from all the study groups. The blood samples were collected via femoral venipuncture on day 93, 48 hrs post-dosing. The monkeys were fasted overnight prior to blood collection. Blood was collected in tubes without any anticoagulant, and kept at room temperature for a minimum of 30 min for serum separation. The tubes

were then centrifuged to obtain serum. Levels of BUN and creatinine were measured using a Toshiba 200FR NEO chemistry analyzer (Toshiba Co., Japan). Results are presented in the Table below, expressed in mg/dL.

The plasma chemistry data indicate that most of the ISIS oligonucleotides did not have any effect on the kidney function outside the expected range for antisense oligonucleotides. Specifically, treatment with ISIS 484137 was well tolerated in terms of the kidney function of the monkeys.

Table 160
BUN and creatinine levels (mg/dL) in cynomolgus monkeys

	BUN	Creatinine
sterile saline	25	0.87
ISIS 484085	26	0.94
ISIS 484129	21	0.81
ISIS 484137	24	0.94
ISIS 495576	22	0.92
ISIS 501861	25	0.90
ISIS 502194	27	0.86
ISIS 525443	26	1.08
ISIS 525612	23	0.98

Example 17: Effect of ISIS 484137 targeting human DGAT2 in cynomolgus monkeys

Cynomolgus monkeys were treated with ISIS 484137 to evaluate the safety of this antisense oligonucleotide over a 13-week dosing period followed by a 13 week recovery period. The protocols described in the Example were approved by the Testing Facility's Institutional Animal Care and Use Committee (IACUC).

Treatment

The monkeys were 2-4 years old and weighed between 2.3 and 3.7 kg. Five groups of 6-10 randomly assigned cynomolgus monkeys each were injected subcutaneously with ISIS oligonucleotide or 0.9% sterile saline using a stainless steel dosing needle and syringe of appropriate size into one of four delineated sites on the backs of the monkeys. The monkeys were dosed on Days 1, 3, 5, and 7, and then once weekly thereafter for a total of 13 weeks at dose levels of 4 mg/kg, 8 mg/kg, 12 mg/kg, or 40 mg/kg of ISIS 484137. A control group of 10 cynomolgus monkeys was injected with 0.9% sterile saline subcutaneously using the same regimen. Toxicokinetics were assessed in a sixth group of 14 animals (7 of each sex) at the 8 mg/kg dose level. Recovery was assessed in the controls and at the 12 mg/kg and 40 mg/kg dose levels of ISIS 484137 (2 per sex).

During the study period, the monkeys were observed for signs of mortality, clinical observations, and body weight, qualitative food consumption, ophthalmoscopic and electrocardiographic examination, clinical and anatomic pathology. Scheduled euthanasia of the animals was conducted on day 93 for animals assigned to terminal necroscopy and on Day 182 for animals assigned to the recovery necroscopy. A full panel of tissues were taken, processed to slides and examined microscopically for histopathology.

Body and organ weight measurements

To evaluate the effect of ISIS 484137 on the overall health of the animals, body weights were measured at regularly and are presented in the Table below. Organ weights were measured after euthanisia. 'n.d.' indicates that there is no data for that timepoint. The results indicate that effect of treatment with ISIS 484137 on body and organ weights was within the expected range for antisense oligonucleotides. Specifically, treatment with ISIS 484137 was well tolerated in terms of the body and organ weights of the monkeys.

Table 161
Body weights (g) of cynomolgus monkeys

	Dose (mg/kg)	Day 93	Day 182
sterile saline	-	3035	3075
ISIS 484137	4	2848	n.d.
	8	2850	n.d.
	12	3125	3325
	40	3027	2875

Table 162
Organ weights (g) of cynomolgus monkeys on day 93

	Dose (mg/kg)	Brain	Adrenal gland	Heart	Kidney	Liver	Spleen	Thyroid
sterile saline	-	67	0.46	10.8	12.6	60.0	4.1	0.4
ISIS 484137	4	67	0.52	9.7	13.2	60.8	3.9	0.3
	8	67	0.51	10.9	14.2	73.7	3.6	0.4
	12	69	0.56	10.1	14.0	65.1	3.2	0.3
	40	69	0.59	10.2	15.8	79.2	6.2	0.4

Plasma Homeostasis

To evaluate the potential for ISIS 484137 to produce complement activation, plasma samples were obtained once prior to treatment initiation on Day -7, then following the first dose on Day 1 at 4, 8 and 24 hours, and finally following the last dose on Day 91 predose and at 4 hours for determination of complement

split product Bb using ELISA. Serum samples were also obtained for measurement of Complement C5 on Day -7, on Day 1 (at 24 hours post dose), on Day 91 (predose and at 24 hours post dose) and for recovery animals on Days 121 and 182 using an automated clinical chemistry analyzer. Additionally, blood for coagulation analyses was taken on Day 1 (4 hours post dose) and on Day 91 (predose, 1, 4, 8, and 24 hours post dose) and evaluated using an automated coagulation analyzer.

At the 40 mg/kg dose level, indications of alternative pathway activation were observed as acute, transient increases in Complement Bb (up to 7-fold over baseline) at 4 hours post dose on Days 1 and 91. Complement Bb then returned to baseline levels at 24 hours on Day 1 or to near baseline levels on Day 91. There were no significant changes in Complement C5 observed during the study. Mild, transient prolongations of APTT (up to 29%), relative to controls were observed at 4 to 8 hours post dose and then diminished by 24 or 48 hours post dose. The acute transient increases in Complement Bb and APTT observed following treatment with ISIS 484137 were typical of those commonly seen oligonucleotide-treated monkeys.

Liver function

To evaluate the effect of ISIS 484137 on hepatic function, blood samples were collected from all the study groups on Days 44, 93, 121, and 182 for determination of liver transaminases and liver functions. Serum levels of ALT and AST were measured and the results are presented in the Table below, expressed in IU/L. Bilirubin, a liver function marker, was similarly measured and the results are presented in the Table below, expressed in mg/dL. ISIS 484137 had no adverse effect on liver function outside the expected range for antisense oligonucleotides. 'n.d.' indicates that there is no data for that timepoint. The results indicate that treatment with ISIS 484137 was well tolerated in terms of the liver function in monkeys.

Table 163
ALT levels (IU/L) in cynomolgus monkey serum

	Dose (mg/kg)	Day 44	Day 93	Day 182
sterile saline	-	43	36	36
ISIS 484137	4	31	38	n.d.
	8	33	31	n.d.
	12	32	40	27
	40	41	62	42

Table 164
AST levels (IU/L) in cynomolgus monkey serum

	Dose (mg/kg)	Day 44	Day 93	Day 121
sterile saline	-	54	65	41
ISIS 484137	4	33	53	n.d.
	8	50	53	n.d.
	12	29	71	31
	40	49	90	44

Table 165
Total bilirubin levels (mg/dL) in cynomolgus monkey serum

	Dose (mg/kg)	Day 44	Day 93	Day 121	Day 182
sterile saline	-	0.20	0.25	0.23	0.20
ISIS 484137	4	0.17	0.20	n.d.	n.d.
	8	0.20	0.20	n.d.	n.d.
	12	0.20	0.35	0.20	0.20
	40	0.20	0.20	0.18	0.23

Kidney function

To evaluate the effect of ISIS 484137 on kidney function, blood samples were collected from all the study groups on days 44, 93, 121, and 182. Results are presented in the Table below, expressed in mg/dL.

The serum chemistry data indicate that ISIS 484137 did not have any effect on the kidney function outside the expected range for antisense oligonucleotides. Similar results were found with urine samples of the monkeys. Treatment with ISIS 484137 was therefore well tolerated in terms of the kidney function of the monkeys.

Table 166
Albumin levels (g/dL) in cynomolgus monkey serum

	Dose (mg/kg)	Day 44	Day 93
sterile saline	-	4.2	4.1
ISIS 484137	4	4.2	4.1
	8	4.3	3.9
	12	3.8	4.0
	40	3.8	3.8

Table 167
BUN levels (mg/dL) in cynomolgus monkey serum

	Dose (mg/kg)	Day 44	Day 93	Day 121
sterile saline	-	23.7	22.5	23.0
ISIS 484137	4	18.0	17.7	n.d.
	8	20.0	21.0	n.d.
	12	22.0	22.0	21.0
	40	21.3	20.0	24.0

Table 168
Creatinine levels (mg/dL) in cynomolgus monkey serum

	Dose (mg/kg)	Day 44	Day 93	Day 121	Day 182
sterile saline	-	128	81	120	93
ISIS 484137	4	129	138	n.d.	n.d.
	8	69	79	n.d.	n.d.
	12	183	153	79	84
	40	129	85	74	72

Plasma toxicokinetics

Following subcutaneous injection in monkeys, ISIS 484137 was quickly absorbed into the systemic circulation with a median T_{max} (time to reach plasma C_{max}) ranging from 1 to 4 hours. Peak exposure (C_{max}) and total exposure ($AUC_{0\text{-}48hr}$) were dose-dependent on Day 1, Day 7, and Day 91. Similar AUC (area under the curve) values were observed between Day 1 (after a single dose) and Day 91 (after 16 doses). These results indicate a lack of plasma accumulation of ISIS 484137 following multiple doses. Mean clearance values ($CL/F_{0\text{-}48hr}$) following subcutaneous administration at all dose levels following single or multiple administrations ranged from 31.3 to 75.8 mL/hr/kg and appeared to decrease with increasing dose. The post-distribution plasma elimination half-life ($t_{1/2\lambda z}$) ranged from 9.42 days to 20.2 days following the 13 weeks of treatment. A review of ISIS 484137 plasma toxicokinetic parameters revealed no gender difference. The Table below presents the results. ‘n.d.’ means ‘not determined’.

Table 169
Plasma toxicokinetic summary in monkeys for ISIS 484137

Dose (mg/kg)	Day	Number of animals	C_{max} (μg/mL)	T_{max} (hr)	AUC_{0-48hr} (hr* μg/mL)	$t_{1/2\lambda z}$ (days)
4	1	6	15	1.5	59	n.d.
	91	6	7	3.0	53	n.d.
8	1	6	30	1.5	138	n.d.
	7	12	28	2.0	137	9.42
	91	6	19	2.0	127	n.d.
12	1	10	43	1.0	263	n.d.
	91	10	24	4.0	261	15.1
40	1	10	113	1.0	1030	n.d.
	91	10	92	1.0	1300	20.2

Tissue toxicokinetics

There was a dose-dependent increase in kidney cortex and liver concentrations over the 10-fold increase in dose of ISIS 484137. Based on the mean tissue ISIS 484137 concentrations at the end of treatment and after recovery, the estimated tissue half-lives were 16.4 to 21.3 days and 17.8 to 22.8 days in kidney and liver, respectively, similar to the tissue half-lives determined following 8 mg/kg ISIS 484137. These findings are also consistent with the estimated terminal elimination half-life values in plasma. The Table below presents the results. 'n.d.' means 'not determined'.

The tissue half-life (approximately 2-3 weeks) observed supports an infrequent clinical dosing regimen.

Table 170
Tissue toxicokinetic summary in monkeys for ISIS 484137

Dose (mg/kg)	Intact ISIS 484137 (μg/g)					
	Day 3 (2 days after 1st dose)		Day 93 (2 days after last dose)		Day 182 (91 days after last dose)	
	Kidney	Liver	Kidney	Liver	Kidney	Liver
4	n.d.	n.d.	610	221	n.d.	n.d.
8	594	84	889	406	n.d.	n.d.
12	n.d.	n.d.	1320	586	30	18
40	n.d.	n.d.	4220	993	233	66

Pro-inflammatory effects

None of the inflammatory marker levels were changed beyong the expected range for antisense oligonucleotides. Therefore, treatment with ISIS 484137 did not cause any adverse inflammation and was well tolerated in the monkeys.

In summary, 13 weeks treatment with ISIS 484137 was clinically well tolerated at doses up to 40 mg/kg/week. There was no mortality during the study and there were no treatment-related effects in clinical findings, body weights, food consumption/appetence, ophthalomoscopic and electrocardiographic examinations, hematology, urinalysis, or complement C3 levels during the study. Overall, the results of the study indicate that ISIS 484137 is the most potent and well tolerated compound of those tested for inhibiting DGAT2 and is an important candidate for the treatment of metabolic diseases, such as NAFLD and NASH.

Example 18: Double-blind, placebo-controlled, dose-escalation Phase I Study

A double-blind, placebo-controlled, dose-escalation Phase I study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple doses of ISIS 484137 administered subcutaneously to healthy overweight volunteers is conducted in a Study Center.

Treatment protocol

Approximately 48 subjects are planned to be enrolled in the study: 16 subjects in the single-dose cohorts and 32 subjects in the multiple-dose cohorts. Subjects are healthy males or females aged 18-65, inclusive, who have given written consent and are able to comply with all the study requirements. BMI of the volunteers is 29.0-38.0 kg/m^2 inclusive. Any volunteers with clinically significant abnormalities in medical history are excluded from the study. ISIS 484137 solution or placebo (0.9% sterile saline) is prepared by an unblinded pharmacist or qualified delegate shortly before use, using aseptic technique. Study staff, who are blinded to the identity of the drug, administer the drug to the subjects.

There are 4 single-dose cohorts (Cohort A-D) with 4 subjects per cohort randomized 3:1 of ISIS 484137: placebo. The length of each subject's participation is approximately 8 weeks, which includes a 4-week screening period, a single dose, and a 4-week post-treatment evaluation period. Subjects receive a single dose of ISIS 484137 by subcutaneous administration. The dose of the antisense oligonucleotide to each cohort is presented in the Table below.

Table 171
Single-dose cohort dosing regimen of ISIS 484137

Cohort	Total dose (mg)
A	50
B	100
C	200
D	400

There are 4 multiple-dose cohorts (Cohort AA-DD) with 8 subjects per cohort randomized 3:1 of ISIS 484137: placebo. The length of each subject's participation is approximately 23 weeks, which includes a

4-week screening period, a 6-week treatment period, and a 13-week post-treatment evaluation period. Subjects receive 3 doses of ISIS 484137 by subcutaneous administration during the first week (Days 1, 3, and 5) and subsequently receive one subcutaneous dose once a week for the next 5 weeks (Days 8, 15, 22, 29, and 36) for a total of 8 doses. Subjects have follow-up visits at the Study Center on Days 37, 43, 50, 64, 78, 92, 106, and 127.

Table 172
Multiple-dose cohort dosing regimen of ISIS 484137

Cohort	Dose per administration (mg)	Total dose (mg)
AA	100	800
BB	200	1600
CC	300	2400
DD	400	3200

Blood and urine samples are collected regularly throughout the study for safety, pharmacokinetic, and pharmacodynamics analysis. The safety and tolerability of ISIS 484137 is assessed by determining the incidence, severity, and dose-relationship of adverse events, vital signs, physical examination, ECG findings, and clinical laboratory parameters. Safety results in subjects dosed with ISIS 484137 are compared with those in subjects dosed with placebo.

WHAT IS CLAIMED:

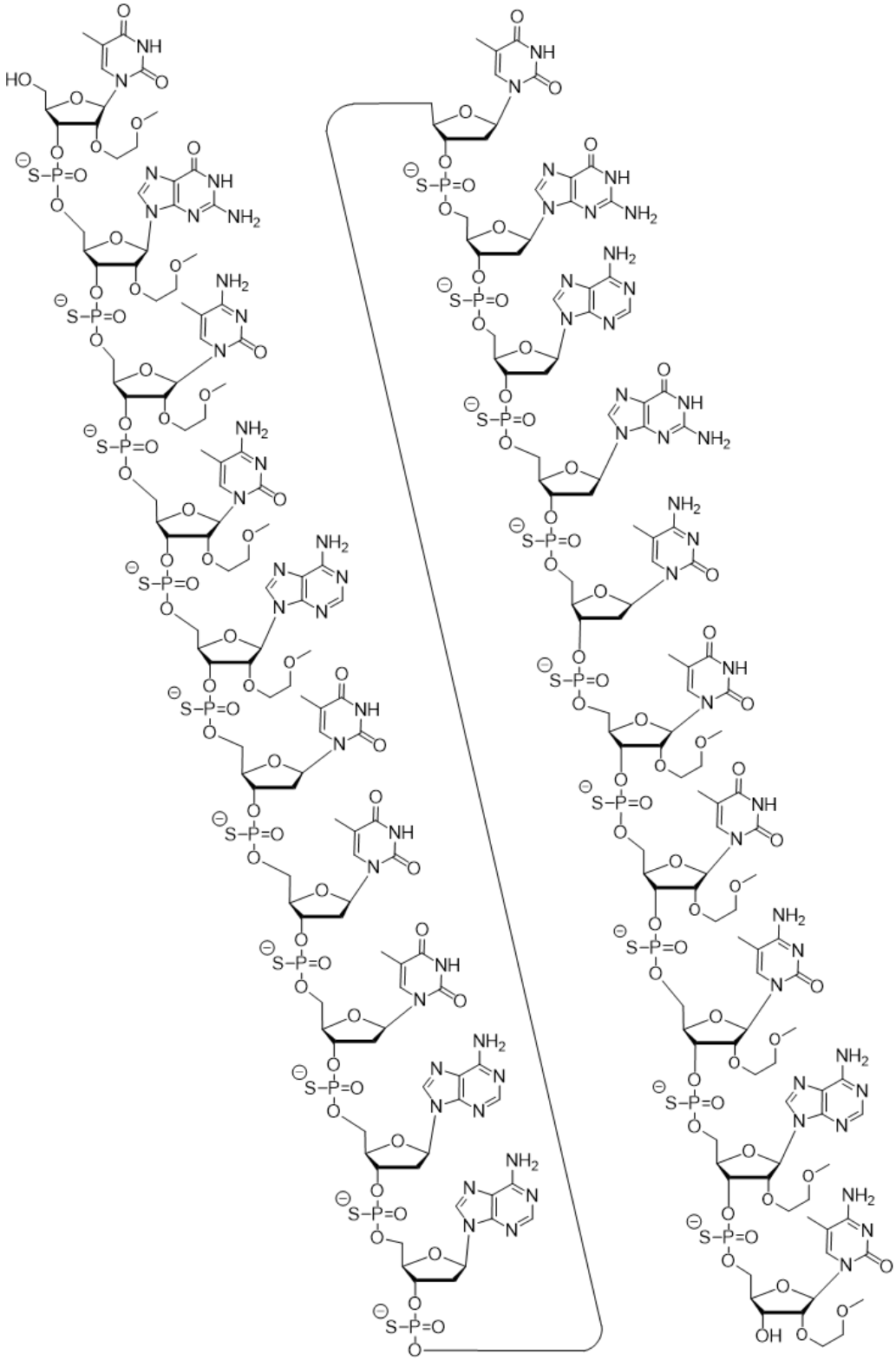
1. An oligomeric compound comprising or consisting of a modified oligonucleotide according to the following formula: Tes Ges mCes mCes Aes Tds Tds Tds Ads Ads Tds Gds Ads Gds mCds Tes Tes mCes Aes mCe (SEQ ID NO: 1423); wherein,

A = an adenine nucleobase,
mC = a 5-methylcytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-O$(CH_2)_2$-OCH_3 furanosyl modified sugar moiety,
d = a 2'-deoxyfuranosyl sugar moiety, and
s = a phosphorothioate internucleoside linkage.

2. The oligomeric compound of claim 1, further comprising a conjugate group.

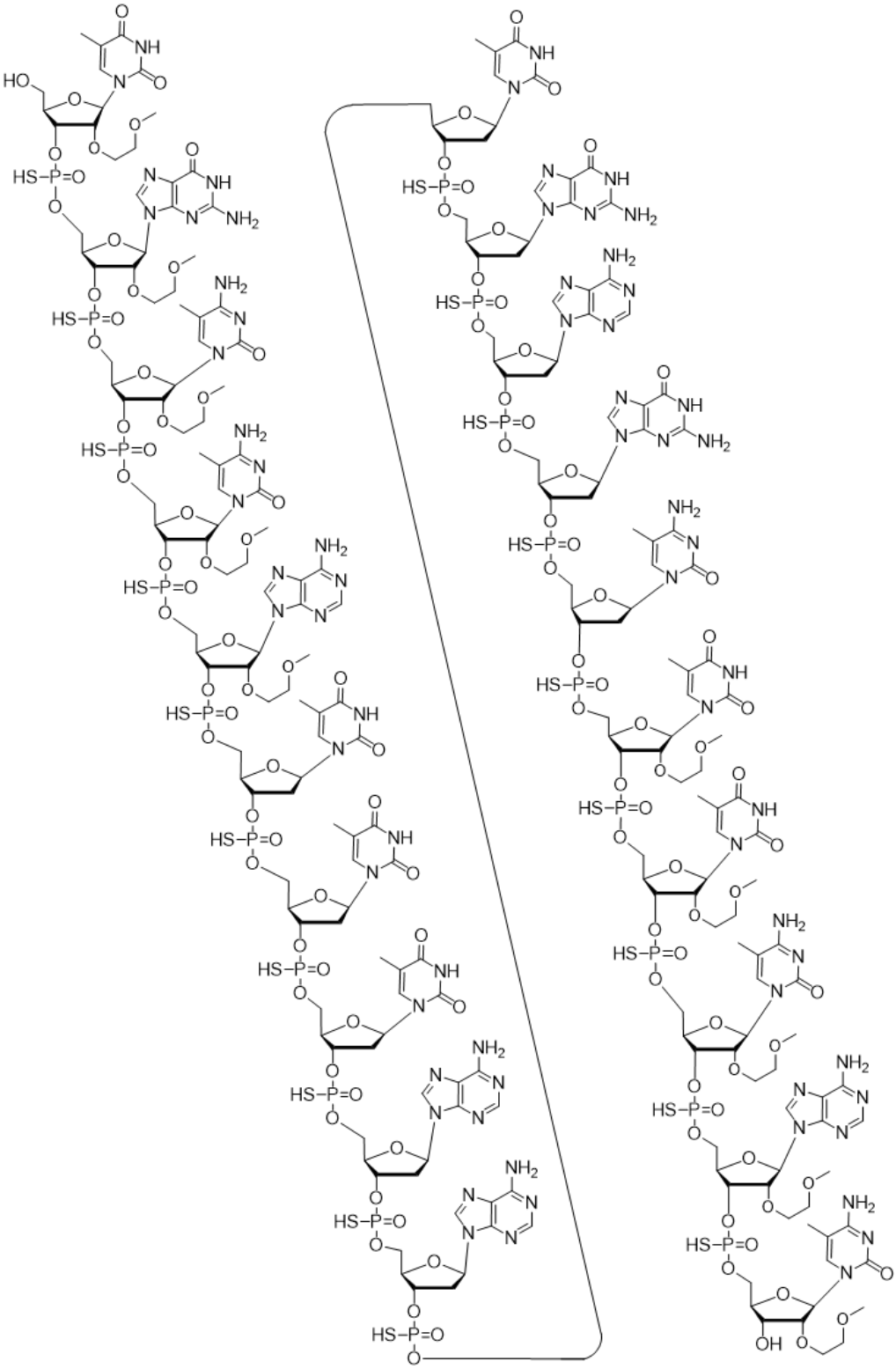
3. The oligomeric compound of claim 2, wherein the conjugate group is a GalNAc moiety.

4. A modified oligonucleotide, wherein the anion form of the modified oligonucleotide has the following chemical structure:



(SEQ ID NO: 1423).

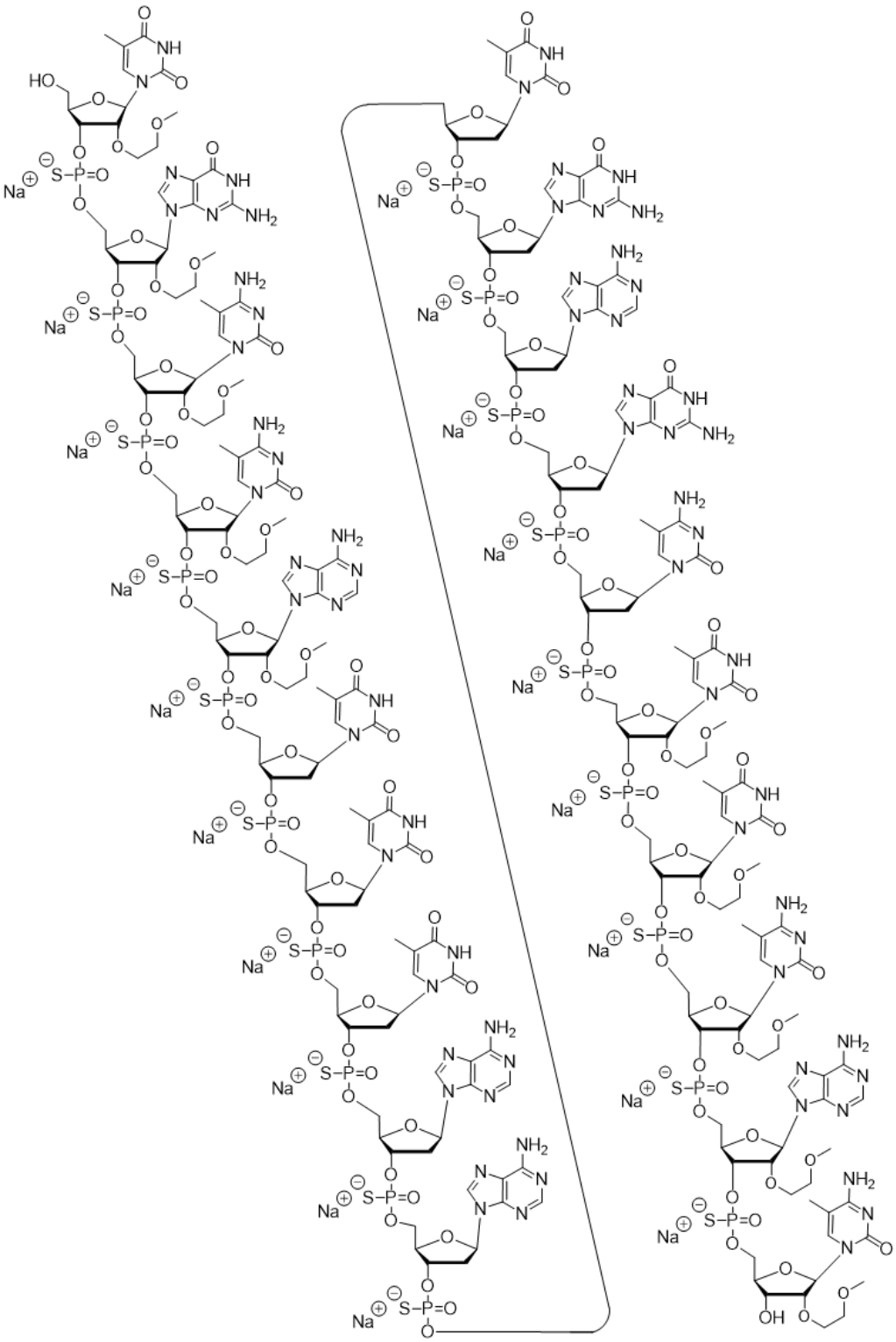
5. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1423), or a salt thereof.

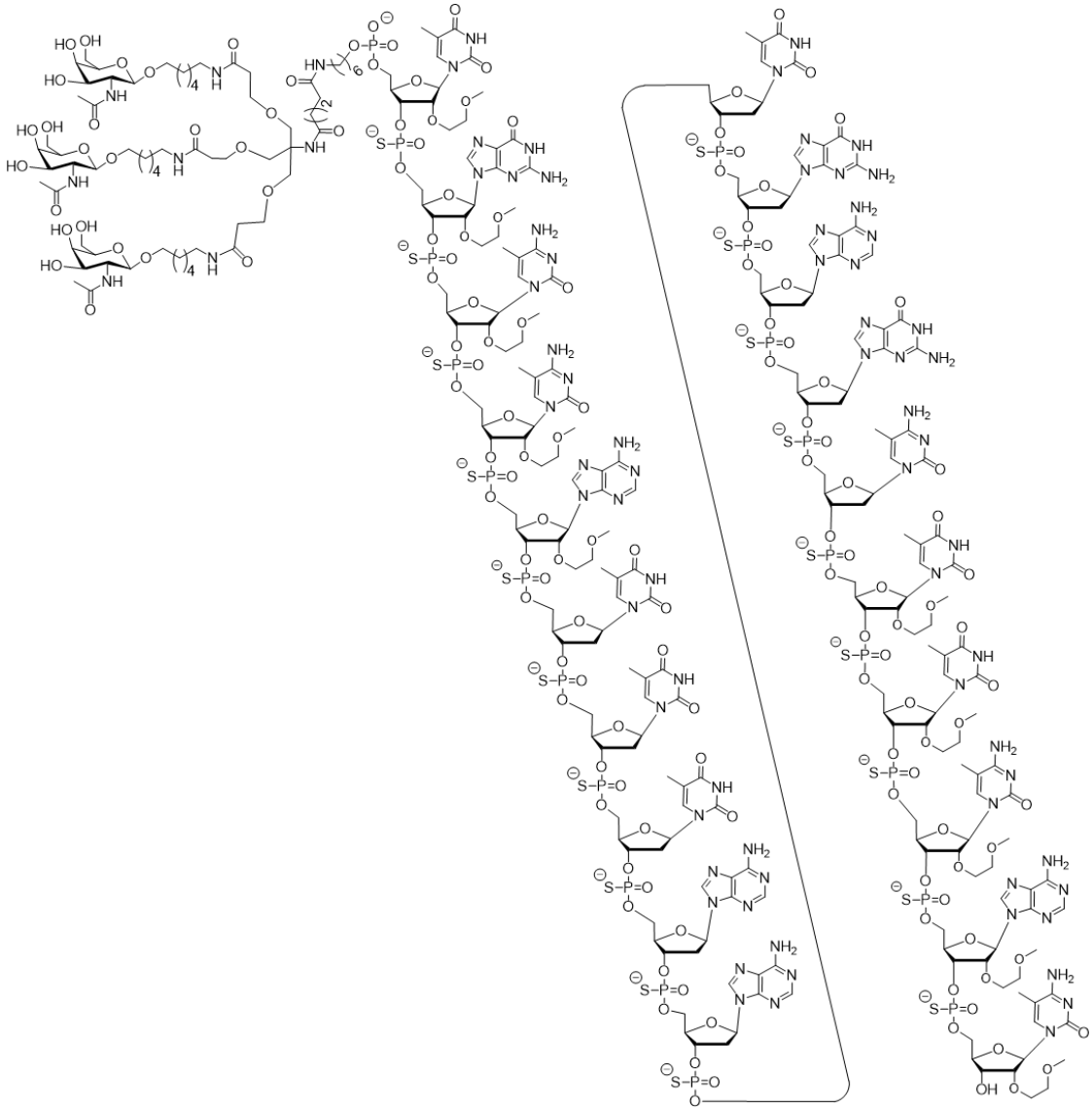
6. The modified oligonucleotide of claim 5, which is the sodium salt or the potassium salt.

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



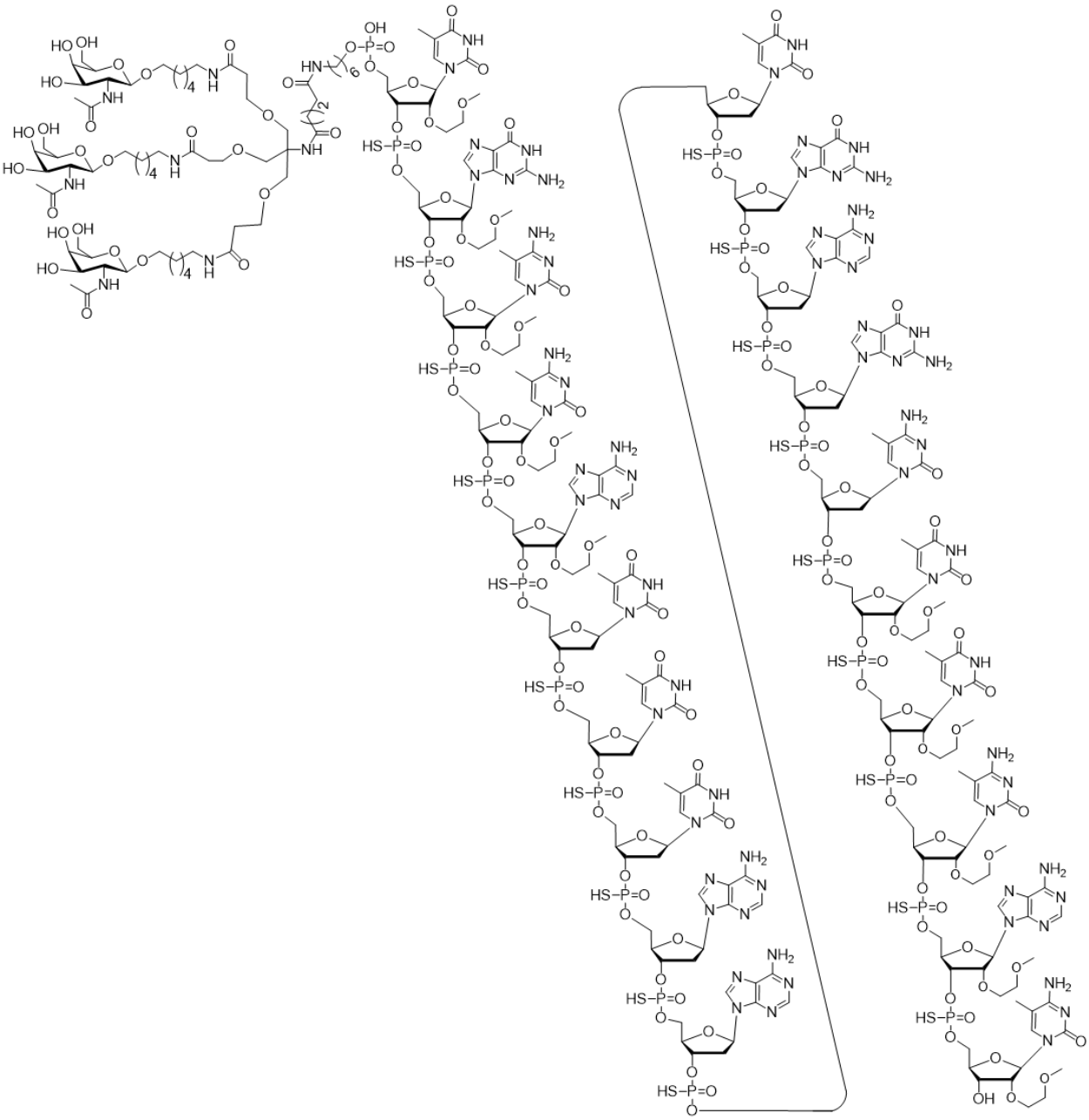
(SEQ ID NO: 1423).

8. An oligomeric compound, wherein the anion form of the oligomeric compound has the following chemical structure:



(SEQ ID NO: 1423).

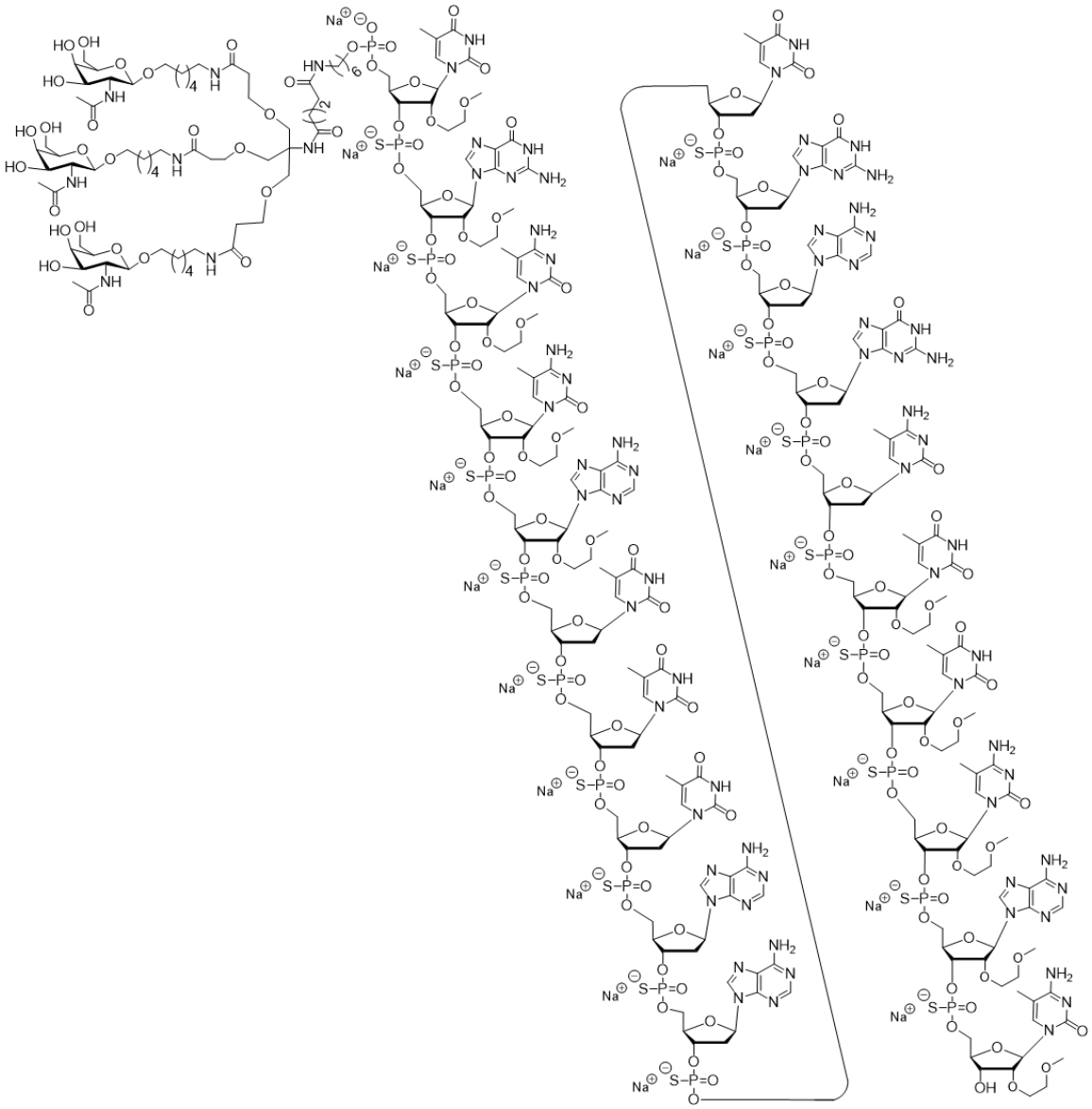
9. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 1423), or a salt thereof.

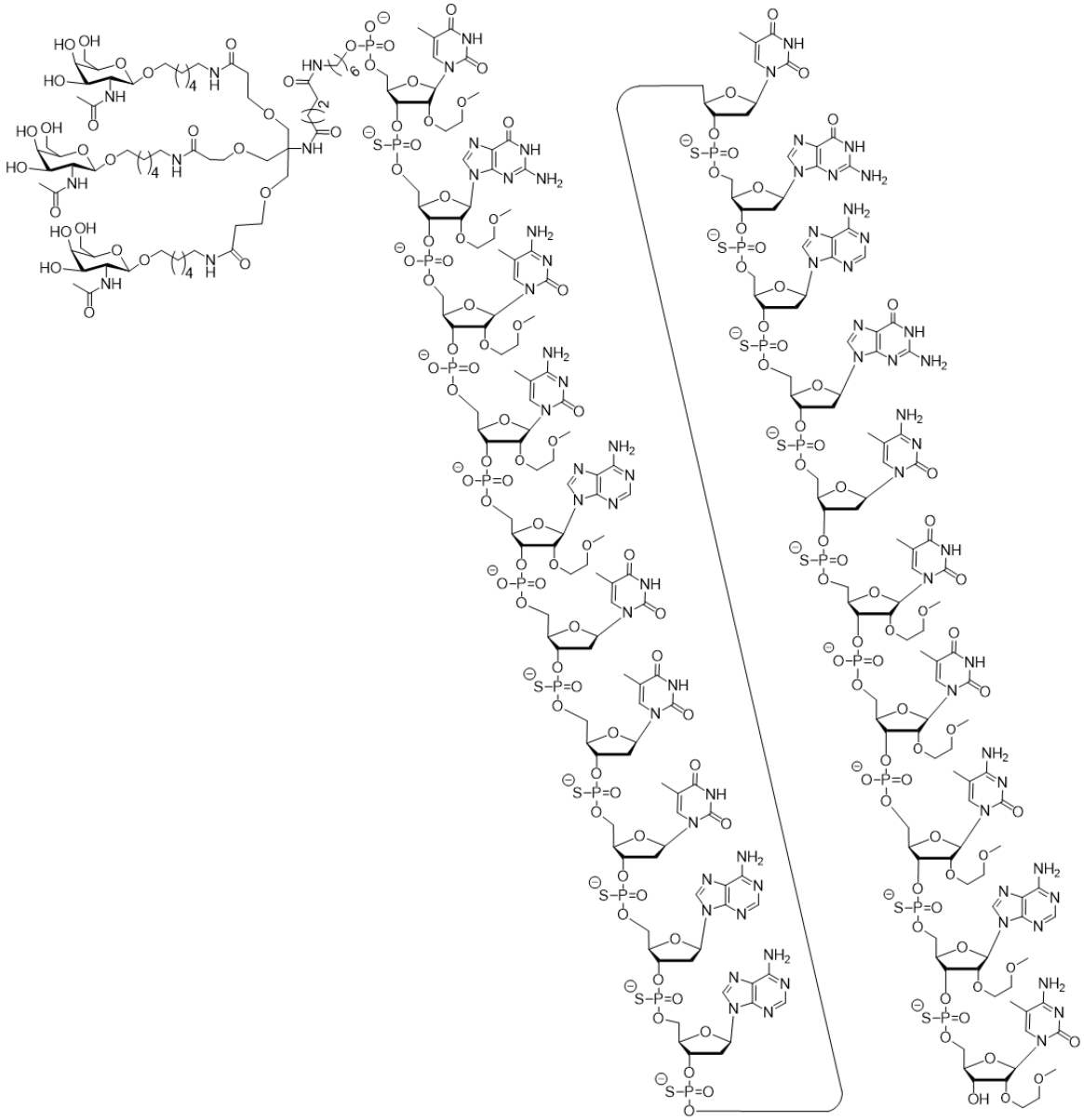
10. The oligomeric compound of claim 9, which is the sodium salt or the potassium salt.

11. An oligomeric compound according to the following chemical structure:



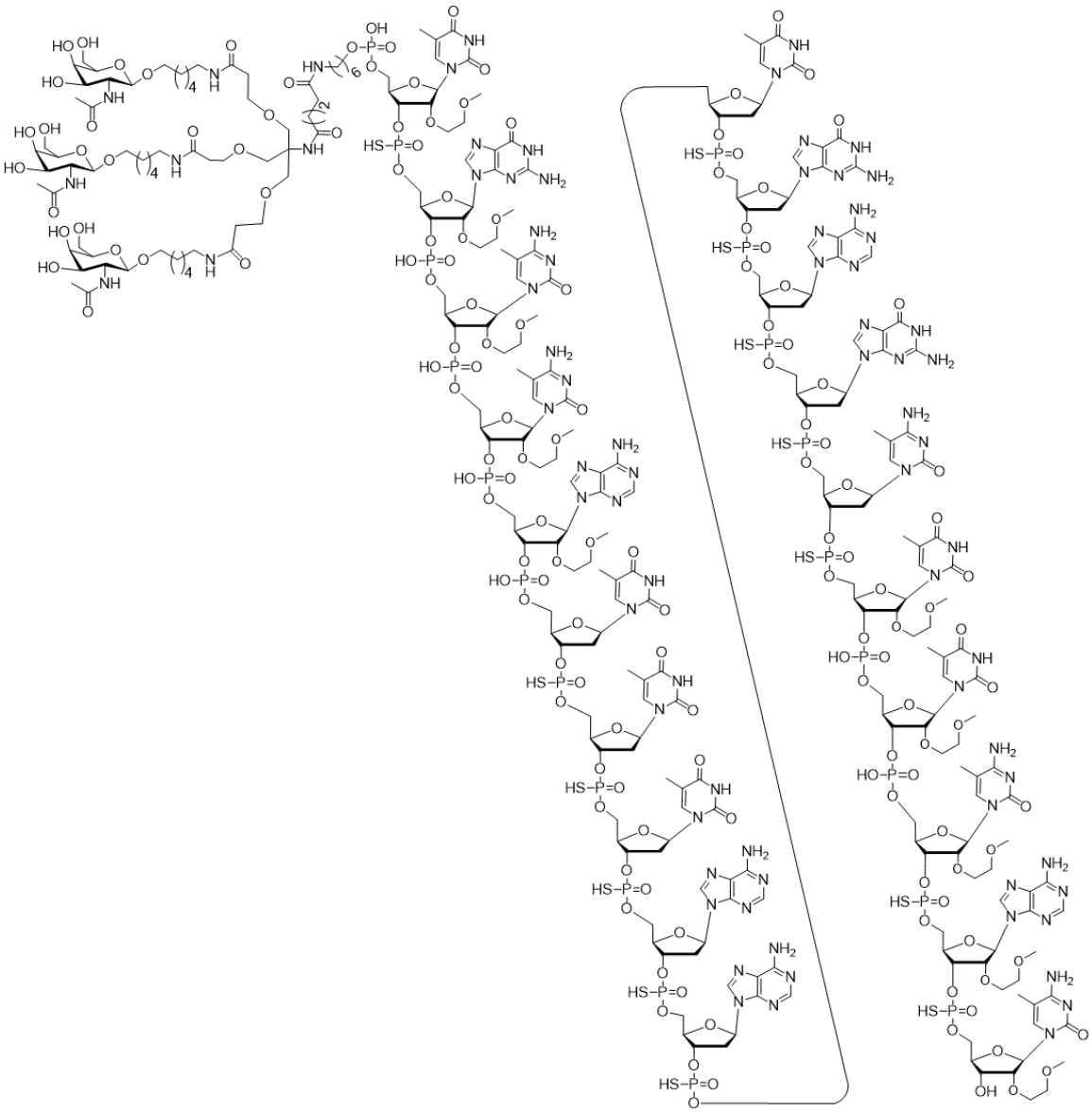
(SEQ ID NO: 1423).

12. An oligomeric compound, wherein the anion form of the oligomeric compound has the following chemical structure:



(SEQ ID NO: 1423).

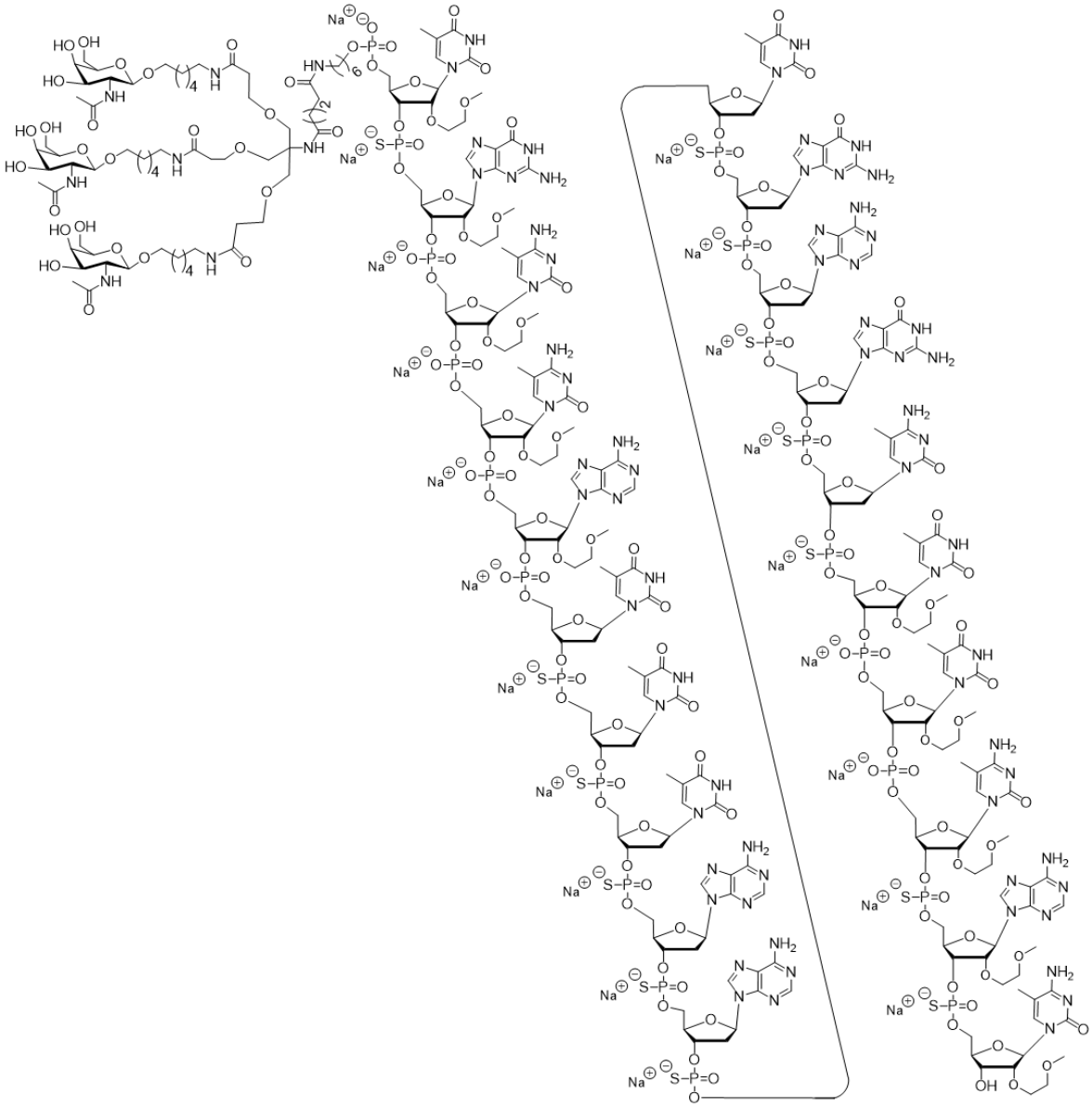
13. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 1423), or a salt thereof.

14. The oligomeric compound of claim 13, which is the sodium salt or the potassium salt.

15. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 1423).

16. A composition comprising the oligomeric compound or modified oligonucleotide of any one of the preceding claims and a pharmaceutically acceptable carrier or diluent.

17. The composition of claim 16, wherein the pharmaceutically acceptable carrier or diluent is phosphate-buffered saline (PBS) or water.

18. A composition comprising the oligomeric compound or modified oligonucleotide of any one of claims 1-15, or the composition of claim 16 or claim 17, for use in therapy.

19. The oligomeric compound or modified oligonucleotide of any one of claims 1-15, or the composition of claim 16 or claim 17, for use as a medicament.

20. Use of the oligomeric compound or modified oligonucleotide of any one of claims 1-15, or the composition of claim 16 or claim 17, in the manufacture of a medicament for treating NAFLD, NASH, lipodystrophy, or partial lipodystrophy.

21. Use of the oligomeric compound or modified oligonucleotide of any one of claims 1-15, or the composition of claim 16 or claim 17, in the manufacture of a medicament for treating NASH.