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(54) Benævnelse: **MODULERING AF EKSPRESSION AF SIGNALTRANSDUCER OG AKTIVATOR AF TRANSKRIPTION 3 (STAT3)**

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**DATABASE NCBI [Online] 27 March 2011 'Homo sapiens signal transducer and activator of transcription 3 (acute-phase response factor) (STAT3), transcript variant 1, mRNA.', XP003030266 Database accession no. NM_139276**
**DATABASE GENBANK [Online] 31 December 1994 'Homo sapiens DNA-binding protein (APRF) mRNA, complete cds.', XP003030211 Database accession no. L29277.1**

# DESCRIPTION

**Sequence Listing**

**[0001]** The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled BIOL0142WOSEQ.txt created March 29, 2012 which is 672 Kb in size.

**Field**

**[0002]** In certain embodiments provided are methods, compounds, and compositions for inhibiting expression of STAT3 mRNA and protein in an animal. Such methods, compounds, and compositions are useful to treat, prevent, or ameliorate hyperproliferative diseases.

**Background**

**[0003]** The STAT (signal transducers and activators of transcription) family of proteins are DNA-binding proteins that play a dual role in signal transduction and activation of transcription. Presently, there are six distinct members of the STAT family (STAT1, STAT2, STAT3, STAT4, STAT5, and STAT6) and several isoforms (STAT1α, STAT1β, STAT3 α and STAT3β). The activities of the STATs are modulated by various cytokines and mitogenic stimuli. Binding of a cytokine to its receptor results in the activation of Janus protein tyrosine kinases (JAKs) associated with these receptors. This phosphorylates STAT, resulting in translocation to the nucleus and transcriptional activation of STAT responsive genes. Phosphorylation on a specific tyrosine residue on the STATs results in their activation, resulting in the formation of homodimers and/or heterodimers of STAT which bind to specific gene promoter sequences. Events mediated by cytokines through STAT activation include cell proliferation and differentiation and prevention of apoptosis.

**[0004]** The specificity of STAT activation is due to specific cytokines, i.e., each STAT is responsive to a small number of specific cytokines. Other non-cytokine signaling molecules, such as growth factors, have also been found to activate STATs. Binding of these factors to a cell surface receptor associated with protein tyrosine kinase also results in phosphorylation of STAT.

**[0005]** STAT3 (also acute phase response factor (APRF)), in particular, has been found to be responsive to interleukin-6 (IL-6) as well as epidermal growth factor (EGF) (Darnell, Jr., J.E., et al., Science, 1994, 264, 1415-1421). In addition, STAT3 has been found to have an important role in signal transduction by interferons (Yang, C.-H., et al., Proc. Natl. Acad. Sci. USA, 1998, 95, 5568-5572). Evidence exists suggesting that STAT3 may be regulated by the MAPK pathway. ERK2 induces serine phosphorylation and also associates with STAT3 (Jain, N., et al., Oncogene, 1998, 17, 3157-3167).

**[0006]** STAT3 is expressed in most cell types (Zhong, Z., et al., Proc. Natl. Acad. Sci. USA, 1994, 91, 4806-4810). It induces the expression of genes involved in response to tissue injury and inflammation. STAT3 has also been shown to prevent apoptosis through the expression of bcl-2 (Fukada, T., et al., Immunity, 1996, 5, 449-460).

**[0007]** Recently, STAT3 was detected in the mitochondria of transformed cells, and was shown to facilitate glycolytic and oxidative phosphorylation activities similar to that of cancer cells (Gough, D.J., et al., Science, 2009, 324, 1713-1716). The inhibition of STAT3 in the mitochondria impaired malignant transformation by activated Ras. The data confirms a Ras-mediated transformation function for STAT3 in the mitochondria in

addition to its nuclear roles.

**[0008]** Aberrant expression of or constitutive expression of STAT3 is associated with a number of disease processes.

**[0009]** U.S. Patent Application Publication No. 2005/0196781 teaches small nucleic acid molecules, such as double-stranded SiRNA molecules, that modulate STAT3 gene expression. WO 2005/083124 teaches antisense oligonucleotides that modulate STAT3 gene expression.

**Summary**

**[0010]** Provided herein are methods, compounds, and compositions for modulating expression of STAT3 mRNA and protein. In certain embodiments, compounds useful for modulating expression of STAT3 mRNA and protein are antisense compounds. In certain embodiments, the antisense compounds are antisense oligonucleotides.

**[0011]** In certain embodiments, modulation can occur in a cell or tissue. In certain embodiments, the cell or tissue is in an animal. In certain embodiments, the animal is a human. In certain embodiments, STAT3 mRNA levels are reduced. In certain embodiments, STAT3 protein levels are reduced. Such reduction can occur in a time-dependent manner or in a dose-dependent manner.

**[0012]** Also provided are methods, compounds, and compositions useful for preventing, treating, and ameliorating diseases, disorders, and conditions. In certain embodiments, such diseases, disorders, and conditions are hyperproliferative diseases, disorders, and conditions. In certain embodiments such hyperproliferative diseases, disorders, and conditions include cancer as well as associated malignancies and metastases. In certain embodiments, such cancers include lung cancer, including non small cell lung cancer (NSCLC), pancreatic cancer, colorectal cancer, multiple myeloma, hepatocellular carcinoma (HCC), glioblastoma, ovarian cancer, osteosarcoma, head and neck cancer, breast cancer, epidermoid carcinomas, intestinal adenomas, prostate cancer, and gastric cancer.

**[0013]** Such diseases, disorders, and conditions can have one or more risk factors, causes, or outcomes in common. Certain risk factors and causes for development of a hyperproliferative disease include growing older; tobacco use; exposure to sunlight and ionizing radiation; contact with certain chemicals; infection with certain viruses and bacteria; certain hormone therapies; family history of cancer; alcohol use; and certain lifestyle choices including poor diet, lack of physical activity, and/or being overweight. Certain symptoms and outcomes associated with development of a hyperproliferative disease include a thickening or lump in the breast or any other part of the body; a new mole or a change in an existing mole; a sore that does not heal; hoarseness or a cough that does not go away; changes in bowel or bladder habits; discomfort after eating; difficulty in swallowing; unexplained weight gain or loss; unusual bleeding or discharge; fatigue; metastasis of one or more tumors throughout the body; cardiovascular complications, including, cardiac arrest and stroke; and death.

**[0014]** In certain embodiments, methods of treatment include administering a STAT3 antisense compound to an individual in need thereof. In certain embodiments, methods of treatment include administering a STAT3 antisense oligonucleotide to an individual in need thereof.

**Detailed Description**

**[0015]** 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.

**[0016]** The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

***Definitions***

**[0017]** Unless specific definitions are provided, the nomenclature utilized in connection with, and the procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well known and commonly used in the art. Standard techniques may be used for chemical synthesis, and chemical analysis.

**[0018]** Unless otherwise indicated, the following terms have the following meanings:
"2'-deoxynucleoside" means a nucleoside comprising 2'-H furanosyl sugar moiety, as found naturally occurring in deoxyribonucleosides (DNA). In certain embodiments, a 2'-deoxynucleoside may comprise a modified nucleobase or may comprise an RNA nucleobase (e.g., uracil).

**[0019]** "2'-O-methoxyethyl" (also 2'-MOE and 2'-O$(CH_2)_2$-$OCH_3$) refers to an O-methoxy-ethyl modification of the 2' position of a furosyl ring. A 2'-O-methoxyethyl modified sugar is a modified sugar.

**[0020]** "2'-MOE nucleoside" (also 2'-O-methoxyethyl nucleoside) means a nucleoside comprising a 2'-MOE modified sugar moiety.

**[0021]** "2'-substituted nucleoside" means a nucleoside comprising a substituent at the 2'-position other than H or OH. Unless otherwise indicated, a 2'-substituted nucleoside is not a bicyclic nucleoside.

**[0022]** "5-methylcytosine" means a cytosine modified with a methyl group attached to the 5' position. A 5-methylcytosine is a modified nucleobase.

**[0023]** "About" means within ±10% of a value. For example, if it is stated, "the compounds affected at least about 70% inhibition of STAT3", it is implied that the STAT3 levels are inhibited within a range of 63% and 77%.

**[0024]** "Active pharmaceutical agent" means the substance or substances in a pharmaceutical composition that provide a therapeutic benefit when administered to an individual. For example, in certain embodiments an antisense oligonucleotide targeted to STAT3 is an active pharmaceutical agent.

**[0025]** "Active target region" or "target region" means a region to which one or more active antisense compounds is targeted. "Active antisense compounds" means antisense compounds that reduce target nucleic acid levels or protein levels.

**[0026]** "Administered concomitantly" refers to the co-administration of two agents in any manner in which the pharmacological effects of both are manifest in the patient at the same time. Concomitant administration does not require that both agents be administered in a single pharmaceutical composition, in the same dosage form, or by the same route of administration. 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.

**[0027]** "Administering" means providing a pharmaceutical agent to an individual, and includes, but is not limited to administering by a medical professional and self-administering.

**[0028]** "Amelioration" refers to a lessening of at least one indicator, sign, or symptom of an associated disease, disorder, or condition. The severity of indicators may be determined by subjective or objective measures, which are known to those skilled in the art.

**[0029]** "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.

**[0030]** "Antibody" refers to a molecule characterized by reacting specifically with an antigen in some way, where the antibody and the antigen are each defined in terms of the other. Antibody may refer to a complete antibody molecule or any fragment or region thereof, such as the heavy chain, the light chain, Fab region, and Fc region.

**[0031]** "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.

**[0032]** "Antisense compound" means an oligomeric compound that is is capable of undergoing hybridization to a target nucleic acid through hydrogen bonding. Examples of antisense compounds include single-stranded and double-stranded compounds, such as, antisense oligonucleotides, siRNAs, shRNAs, snoRNAs, miRNAs, and satellite repeats.

**[0033]** "Antisense inhibition" means reduction of target nucleic acid levels or target protein levels in the presence of an antisense compound complementary to a target nucleic acid as compared to target nucleic acid levels or target protein levels in the absence of the antisense compound.

**[0034]** "Antisense oligonucleotide" means a single-stranded oligonucleotide having a nucleobase sequence that permits hybridization to a corresponding region or segment of a target nucleic acid.

**[0035]** "Bicyclic sugar" means a furosyl ring modified by the bridging of two atoms. A bicyclic sugar is a modified sugar.

**[0036]** "Bicyclic nucleoside" (also BNA) means a nucleoside having a sugar moiety comprising a bridge connecting two carbon atoms of the sugar ring, thereby forming a bicyclic ring system. In certain embodiments, the bridge connects the 4'-carbon and the 2'-carbon of the sugar ring.

**[0037]** "Cap structure" or "terminal cap moiety" means chemical modifications, which have been incorporated at either terminus of an antisense compound.

**[0038]** "cEt" or "constrained ethyl" means a bicyclic nucleoside having a 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'.

**[0039]** "Constrained ethyl nucleoside" (also cEt nucleoside) means a nucleoside comprising a bicyclic sugar moiety comprising a 4'-$CH(CH_3)$-O-2' bridge.

**[0040]** "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.

**[0041]** "Chimeric antisense compound" means an antisense compound that has at least two chemically distinct regions.

**[0042]** "Co-administration" means administration of two or more pharmaceutical agents to an individual. The two or more pharmaceutical agents may be in a single pharmaceutical composition, or may be in separate pharmaceutical compositions. Each of the two or more pharmaceutical agents may be administered through the same or different routes of administration. Co-administration encompasses parallel or sequential administration.

**[0043]** "Complementarity" means the capacity for pairing between nucleobases of a first nucleic acid and a second nucleic acid.

**[0044]** "Contiguous nucleobases" means nucleobases immediately adjacent to each other.

**[0045]** "Diluent" means an ingredient in a composition that lacks pharmacological activity, but is pharmaceutically necessary or desirable. For example, the diluent in an injected composition may be a liquid, e.g. saline solution.

**[0046]** "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 one, two, or more boluses, tablets, or injections. For example, in certain embodiments where subcutaneous administration is desired, the desired dose requires a volume not easily accommodated by a single injection, therefore, two or more injections may be used to achieve the desired dose. In certain 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.

**[0047]** "Effective amount" means the amount of active pharmaceutical agent 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.

**[0048]** "Fully complementary" or "100% complementary" means each nucleobase of a first nucleic acid has a complementary nucleobase in a second nucleic acid. In certain embodiments, a first nucleic acid is an antisense compound and a target nucleic acid is a second nucleic acid.

**[0049]** "Gapmer" means a chimeric antisense compound in which an internal region having a plurality of nucleosides that support RNase H cleavage 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."

**[0050]** "Gap-widened" means a chimeric antisense compound having a gap segment of 12 or more contiguous 2'-deoxyribonucleosides positioned between and immediately adjacent to 5' and 3' wing segments having from one to six nucleosides.

**[0051]** "Hybridization" means the annealing of complementary nucleic acid molecules. In certain embodiments, complementary nucleic acid molecules include an antisense compound and a target nucleic acid.

**[0052]** "Hyperproliferative disease" means a disease characterized by rapid or excessive growth and reproduction of cells. Examples of hyperproliferative diseases include cancer, *e.g.*, carcinomas, sarcomas, lymphomas, and leukemias as well as associated malignancies and metastases.

**[0053]** "Identifying an animal at risk for hyperproliferative disease" means identifying an animal having been diagnosed with a hyperproliferative disease or identifying an animal predisposed to develop a hyperproliferative disease. Individuals predisposed to develop a hyperproliferative disease include those having one or more risk factors for hyperproliferative disease including older age; history of other hyperproliferative diseases; history of tobacco use; history of exposure to sunlight and/or ionizing radiation; prior contact with certain chemicals, especially continuous contact; past or current infection with certain viruses and bacteria; prior or current use of certain hormone therapies; genetic predisposition; alcohol use; and certain lifestyle choices including poor diet, lack of physical activity, and/or being overweight. Such identification may be accomplished by any method including evaluating an individual's medical history and standard clinical tests or assessments.

**[0054]** "Immediately adjacent" means there are no intervening elements between the immediately adjacent elements.

**[0055]** "Inhibiting STAT3" means reducing expression of STAT3 mRNA and/or protein levels in the presence of a STAT3 antisense compound, including a STAT3 antisense oligonucleotide, as compared to expression of STAT3 mRNA and/or protein levels in the absence of a STAT3 antisense compound, such as an antisense oligonucleotide.

**[0056]** "Individual" means a human or non-human animal selected for treatment or therapy.

**[0057]** "Internucleoside linkage" refers to the chemical bond between nucleosides.

**[0058]** "Linked nucleosides" means adjacent nucleosides which are bonded together.

**[0059]** "Mismatch" or "non-complementary nucleobase" refers to the case when a nucleobase of a first nucleic acid is not capable of pairing with the corresponding nucleobase of a second or target nucleic acid.

**[0060]** "Modified internucleoside linkage" refers to a substitution or any change from a naturally occurring internucleoside bond (i.e. a phosphodiester internucleoside bond).

**[0061]** "Modified nucleobase" refers to 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).

**[0062]** "Modified nucleotide" means a nucleotide having, independently, a modified sugar moiety, modified internucleoside linkage, or modified nucleobase. A "modified nucleoside" means a nucleoside having, independently, a modified sugar moiety or modified nucleobase.

**[0063]** "Modified oligonucleotide" means an oligonucleotide comprising a modified internucleoside linkage, a modified sugar, and/or a modified nucleobase.

**[0064]** "Modified sugar" refers to a substitution or change from a natural sugar.

**[0065]** "Motif" means the pattern of chemically distinct regions in an antisense compound.

**[0066]** "Naturally occurring internucleoside linkage" means a 3' to 5' phosphodiester linkage.

**[0067]** "Natural sugar moiety" means a sugar found in DNA (2'-H) or RNA (2'-OH).

**[0068]** "Nucleic acid" refers to molecules composed of monomeric nucleotides. A nucleic acid includes ribonucleic acids (RNA), deoxyribonucleic acids (DNA), single-stranded nucleic acids, double-stranded nucleic acids, small interfering ribonucleic acids (siRNA), and microRNAs (miRNA).

**[0069]** "Nucleobase" means a heterocyclic moiety capable of pairing with a base of another nucleic acid.

**[0070]** "Nucleobase sequence" means the order of contiguous nucleobases independent of any sugar, linkage, or nucleobase modification.

**[0071]** "Nucleoside" means a nucleobase linked to a sugar.

**[0072]** "Nucleoside mimetic" includes those structures used to replace the sugar or the sugar and the base and not necessarily the linkage at one or more positions of an oligomeric compound such as for example nucleoside mimetics having morpholino, cyclohexenyl, cyclohexyl, tetrahydropyranyl, bicyclo or tricyclo sugar mimetics, *e.g.*, non furanose sugar units. Nucleotide mimetic includes those structures used to replace the nucleoside and the linkage at one or more positions of an oligomeric compound such as for example peptide nucleic acids or morpholinos (morpholinos linked by -N(H)-C(=O)-O- or other non-phosphodiester linkage). Sugar surrogate overlaps with the slightly broader term nucleoside mimetic but is intended to indicate replacement of the sugar unit (furanose ring) only. The tetrahydropyranyl rings provided herein are illustrative of an example of a sugar surrogate wherein the furanose sugar group has been replaced with a tetrahydropyranyl ring system.

**[0073]** "Nucleotide" means a nucleoside having a phosphate group covalently linked to the sugar portion of the nucleoside.

**[0074]** "Off-target effect" refers to an unwanted or deleterious biological effect associated with modulation of RNA or protein expression of a gene other than the intended target nucleic acid.

**[0075]** "Oligomeric compound" or "oligomer" means a polymer of linked monomeric subunits which is capable of hybridizing to at least a region of a nucleic acid molecule.

**[0076]** "Oligonucleotide" means a polymer of linked nucleosides each of which can be modified or unmodified, independent one from another.

**[0077]** "Parenteral administration" means administration through injection (e.g., bolus 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.

**[0078]** "Peptide" means a molecule formed by linking at least two amino acids by amide bonds. Peptide refers to polypeptides and proteins.

**[0079]** "Pharmaceutical composition" means a mixture of substances suitable for administering to an individual. For example, a pharmaceutical composition may comprise one or more active pharmaceutical agents and a sterile aqueous solution. In certain embodiments, a pharmaceutical composition shows activity in free uptake assay in certain cell lines.

**[0080]** "Pharmaceutically acceptable derivative" encompasses pharmaceutically acceptable salts, conjugates, prodrugs or isomers of the compounds described herein.

**[0081]** "Pharmaceutically acceptable salts" means physiologically and pharmaceutically acceptable salts of antisense compounds, i.e., salts that retain the desired biological activity of the parent oligonucleotide and do not impart undesired toxicological effects thereto.

**[0082]** "Phosphorothioate linkage" means a linkage between nucleosides where the phosphodiester bond is modified by replacing one of the non-bridging oxygen atoms with a sulfur atom. A phosphorothioate linkage (P=S) is a modified internucleoside linkage.

**[0083]** "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 antisense compound.

**[0084]** "Prevent" refers to delaying or forestalling the onset or development of a disease, disorder, or condition for a period of time from minutes to indefinitely. Prevent also means reducing risk of developing a disease, disorder, or condition.

**[0085]** "Prodrug" means a therapeutic agent that is prepared in an inactive form that is converted to an active form within the body or cells thereof by the action of endogenous enzymes or other chemicals or conditions.

**[0086]** "Side effects" means physiological responses 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.

**[0087]** "Signal Transducer and Activator of Transcription 3 nucleic acid" or "STAT3 nucleic acid" means any nucleic acid encoding STAT3. For example, in certain embodiments, a STAT3 nucleic acid includes a DNA sequence encoding STAT3, an RNA sequence transcribed from DNA encoding STAT3 (including genomic DNA comprising introns and exons), and an mRNA sequence encoding STAT3. "STAT3 mRNA" means an mRNA encoding a STAT3 protein.

**[0088]** "Single-stranded oligonucleotide" means an oligonucleotide which is not hybridized to a complementary strand.

**[0089]** "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 under conditions in which specific binding is desired, i.e., under physiological conditions in the case of *in vivo* assays and therapeutic treatments.

**[0090]** "Targeting" or "targeted" 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.

**[0091]** "Target nucleic acid," "target RNA," "target mRNA," and "target RNA transcript" all refer to a nucleic acid capable of being targeted by antisense compounds.

**[0092]** "Target segment" means the sequence of nucleotides of a target nucleic acid to which an antisense 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.

**[0093]** "Therapeutically effective amount" means an amount of a pharmaceutical agent that provides a therapeutic benefit to an individual.

**[0094]** "Treat" refers to administering a pharmaceutical composition to effect an alteration or improvement of a disease, disorder, or condition.

**[0095]** "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-ribonucleosides) or a DNA nucleotide (i.e. β-D-deoxyribonucleoside).

***Certain Embodiments***

**[0096]** In certain embodiments provided are methods, compounds, and compositions for inhibiting STAT3 mRNA or protein expression.

**[0097]** In certain embodiments provided are methods for preventing tumor growth and tumor volume. In certain embodiments provided are methods for reducing tumor growth and tumor volume.

**[0098]** In certain embodiments provided are methods, compounds, and compositions for the treatment, prevention, or amelioration of diseases, disorders, and conditions associated with STAT3 in an individual in need thereof. Also contemplated are methods and compounds for the preparation of a medicament for the treatment, prevention, or amelioration of a disease, disorder, or condition associated with STAT3. STAT3 associated diseases, disorders, and conditions include hyperproliferative diseases, *e.g.*, cancer, carcinomas, sarcomas, lymphomas, and leukemias as well as associated malignancies and metastases.

**[0099]** In certain embodiments provided are STAT3 antisense compounds for use in treating, preventing, or ameliorating a STAT3 associated disease. In certain embodiments, STAT3 antisense compounds are STAT3 antisense oligonucleotides, which are capable of inhibiting the expression of STAT3 mRNA and/or STAT3 protein in a cell, tissue, or animal.

**[0100]** In certain embodiments provided are a STAT3 antisense compound as described herein for use in treating or preventing lung cancer, including non small cell lung cancer (NSCLC), pancreatic cancer, colorectal cancer, multiple myeloma, hepatocellular carcinoma (HCC), glioblastoma, ovarian cancer, osteosarcoma, head and neck cancer, breast cancer, epidermoid carcinomas, intestinal adenomas, prostate cancer, and gastric cancer.

**[0101]** In certain embodiments provided are a STAT3 antisense compound as described herein for use in treating or preventing cancer from metastasizing.

**[0102]** In certain embodiments provided are a STAT3 antisense compound, as described herein, for use in treating, preventing, or ameliorating hyperproliferative diseases, *e.g.*, cancer, carcinomas, sarcomas, lymphomas, and leukemias as well as associated malignancies and metastases.

**[0103]** Disclosed herein are antisense compounds targeted to a STAT3 nucleic acid. As disclosed herein, the STAT3 nucleic acid is any of the sequences set forth in GENBANK Accession No. NM_139276.2 (incorporated herein as SEQ ID NO: 1) or the complement of GENBANK Accession No. NT_010755.14 truncated from nucleotides 4185000 to 4264000 (incorporated herein as SEQ ID NO: 2).

**[0104]** Disclosed herein are compounds comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides having a nucleobase sequence comprising a portion of at least 12 contiguous nucleobases complementary to an equal length portion of nucleobases 3016 to 3031 of SEQ ID NO: 1, wherein the nucleobase sequence is complementary to SEQ ID NO: 1.

**[0105]** In certain embodiments there is provided a single-stranded compound comprising a modified single-stranded oligonucleotide consisting of 16 linked nucleosides having a nucleobase sequence consisting of SEQ ID NO: 245, or a pharmaceutically acceptable salt thereof, wherein the modified oligonucleotide comprises:

a 5'-wing consisting of 3 linked nucleosides;

a 3'-wing consisting of 3 linked nucleosides;

a gap between the 5'-wing and the 3'-wing consisting of 10 linked 2'-deoxynucleosides; wherein each nucleoside of each of the 5'-wing and the 3'-wing comprises a constrained ethyl nucleoside; wherein each internucleoside linkage is a phosphorothioate linkage; and

wherein each cytosine is a 5-methylcytosine.

**[0106]** In certain embodiments, the nucleobase sequence of the modified oligonucleotide consists of the sequence of SEQ ID NO: 245.

**[0107]** As disclosed herein, the modified oligonucleotide is 100% complementary to SEQ ID NO: 1 or 2.

**[0108]** In certain embodiments, the modified oligonucleotide consists of a single-stranded modified oligonucleotide.

**[0109]** In certain embodiments, the modified oligonucleotide has at least one modified internucleoside linkage.

**[0110]** In certain embodiments, each internucleoside linkage is a phosphorothioate internucleoside linkage.

**[0111]** In certain embodiments, at least one nucleoside comprises a modified sugar.

**[0112]** In certain embodiments, at least one modified sugar is a bicyclic sugar.

**[0113]** In certain embodiments, the bicyclic sugar comprises a 4'-$CH_2$-O-2' bridge.

**[0114]** In certain embodiments, the bicyclic sugar comprises a 4'-$CH(CH_3)$-O-2' bridge.

**[0115]** In certain embodiments, the modified sugar comprises a 2'-$O(CH_2)_2$-$OCH_3$ group.

**[0116]** In certain embodiments, the modified sugar comprises a 2'-O-$CH_3$ group.

**[0117]** In certain embodiments, at least one nucleoside of the modified oligonucleotide comprises a modified nucleobase.

**[0118]** In certain embodiments, the modified nucleobase is a 5-methylcytosine.

**[0119]** In certain embodiments, the modified oligonucleotide comprises:

a 5'-wing consisting of 3 linked nucleosides;

a 3'-wing consisting of 3 linked nucleosides;

a gap between the 5'-wing and the 3'-wing consisting of 10 linked 2'-deoxynucleosides;

wherein each nucleoside of each of the 5'-wing and the 3'-wing comprises a constrained ethyl nucleoside;

wherein each internucleoside linkage is a phosphorothioate linkage; and

wherein each cytosine is a 5-methylcytosine.

**[0120]** Disclosed herein are methods of treating a hyperproliferative disease in an animal, comprising administering to an animal in need thereof a compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 12 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 9-426, 430-442, 445-464, 471-498, 500-1034, 1036-1512, and 1541-2757.

**[0121]** Certain embodiments provide methods of treating a hyperproliferative disease in an animal, comprising administering to an animal in need thereof a compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 12 contiguous nucleobases of SEQ ID NO: 245.

**[0122]** In certain embodiments, the administering reduces tumor size in the animal.

**[0123]** In certain embodiments, the administering reduces tumor volume in the animal.

**[0124]** In certain embodiments, the administering prevents metastasis in the animal.

**[0125]** In certain embodiments, the administering prolongs survival of the animal.

**[0126]** In certain embodiments, the administering reduces cachaxia in the animal.

**[0127]** Certain embodiments provide a single-stranded compound comprising a modified single-stranded oligonucleotide consisting of 16 linked nucleosides having a nucleobase sequence consisting of SEQ ID NO: 245, or a pharmaceutically acceptable salt thereof, wherein the modified oligonucleotide comprises:

a 5'-wing consisting of 3 linked nucleosides;

a 3'-wing consisting of 3 linked nucleosides;

a gap between the 5'-wing and the 3'-wing consisting of 10 linked 2'-deoxynucleosides;

wherein each nucleoside of each of the 5'-wing and the 3'-wing comprises a constrained ethyl nucleoside;

wherein each internucleoside linkage is a phosphorothioate linkage; and

wherein each cytosine is a 5-methylcytosine for use in a method of treating a hyperproliferative disease in an animal.

***Antisense compounds***

**[0128]** Oligomeric compounds include, but are not limited to, oligonucleotides, oligonucleosides, oligonucleotide analogs, oligonucleotide mimetics, 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.

**[0129]** 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 such embodiments, an antisense oligonucleotide 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.

**[0130]** Disclosed herein, an antisense compound targeted to a STAT3 nucleic acid is 12 to 30 subunits in length. Disclosed herein, an antisense compound targeted to a STAT3 nucleic acid is 14 to 30 subunits in length. Disclosed herein, an antisense compound targeted to a STAT3 nucleic acid is 12 to 22 subunits in length. In other words, such antisense compounds are from 12 to 30 linked subunits, 14 to 30 linked subunits, or 12 to 22 linked subunits, respectively. Disclosed herein, 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. Disclosed herein, 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. Disclosed herein, the antisense compound is an antisense oligonucleotide, and the linked subunits are nucleotides.

**[0131]** In certain embodiments antisense oligonucleotides targeted to a STAT3 nucleic acid may be shortened or truncated. For example, a single subunit 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 a STAT3 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.

**[0132]** 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.

**[0133]** 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. For example, in Woolf et al. (Proc. Natl. Acad. Sci. USA 89:7305-7309, 1992), a series of antisense oligonucleotides 13-25 nucleobases in length were tested for their ability to induce cleavage of a target RNA in an oocyte injection model. Antisense oligonucleotides 25 nucleobases in length with 8 or 11 mismatch bases near the ends of the antisense oligonucleotides were able to direct specific cleavage of the target mRNA, albeit to a lesser extent than the antisense oligonucleotides that contained no mismatches. Similarly, target specific cleavage was achieved using 13 nucleobase antisense oligonucleotides, including those with 1 or 3 mismatches.

**[0134]** Gautschi et al. (J. Natl. Cancer Inst. 93:463-471, March 2001) demonstrated the ability of an oligonucleotide having 100% complementarity to the bcl-2 mRNA and having 3 mismatches to the bcl-xL mRNA to reduce the expression of both bcl-2 and bcl-xL *in vitro* and *in vivo*. Furthermore, this oligonucleotide demonstrated potent anti-tumor activity *in vivo*.

**[0135]** Maher and Dolnick (Nuc. Acid. Res. 16:3341-3358,1988) tested a series of tandem 14 nucleobase antisense oligonucleotides, and a 28 and 42 nucleobase antisense oligonucleotides comprised of the sequence of two or three of the tandem antisense oligonucleotides, respectively, for their ability to arrest translation of human DHFR in a rabbit reticulocyte assay. Each of the three 14 nucleobase antisense oligonucleotides alone was able to inhibit translation, albeit at a more modest level than the 28 or 42 nucleobase antisense oligonucleotides.

**[0136]** In certain embodiments, the compounds as described herein are efficacious by virtue of having at least one of an *in vitro* $IC_{50}$ of less than 20uM, less than 19uM, less than 18uM, less than 17uM, less than 16uM, less than 15uM, less than 14uM, less than 13uM, less than 12uM, less than 11uM, less than 10uM, less than 9uM, less than 8uM, less than 7uM, less than 6uM, less than 5uM, less than 4uM, less than 3uM, less than 2uM, less than 1uM when delivered to HuVEC cells as described herein.

**[0137]** In certain embodiments, the compounds as described herein are efficacious by virtue of having at least one of an *in vitro* $IC_{50}$ of less than 1.0uM, less than 0.9uM, less than 0.8uM, less than 0.7uM, less than 0.6uM, less than 0.5uM, less than 0.4uM, less than 0.3uM, less than 0.2uM, less than 0.1uM when delivered to HuVEC cells as described herein.

**[0138]** In certain embodiments, the compounds as described herein are efficacious by virtue of having at least one of an *in vitro* $IC_{50}$ of less than 0.95uM, less than 0.90uM, less than 0.85uM, less than 0.80uM, less than 0.75uM, less than 0.70uM, less than 0.65uM, less than 0.60uM, less than 0.55uM, less than 0.50uM, less than 0.45uM, less than 0.40uM, less than 0.35uM, less than 0.30uM, less than 0.25uM, less than 0.20uM, less than 0.15uM, less than 0.10uM, less than 0.05uM, less than 0.04uM, less than 0.03uM, less than 0.02uM, less than 0.01uM when delivered to HuVEC cells as described herein.

**[0139]** In certain embodiments, the compound as described herein are efficacious by virtue of having at least one of an *in vitro* $IC_{50}$ of less of less than 20uM, less than 15uM, less than 10uM, less than 5uM, less than 2 uM when delivered by free uptake methods to cancer cell lines as described herein.

**[0140]** In certain embodiments, the compounds 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 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 as described herein are highly tolerable as demonstrated by having no increase in liver, spleen, or kidney weight over saline treated animals. In certain disclosures, these compounds include ISIS 455265, ISIS 455269, ISIS 455271, ISIS 455272, ISIS 455291, ISIS 455371, ISIS 455394, ISIS 455703, ISIS 455429, ISIS 455471, ISIS 455527, ISIS 455530, ISIS 455536, ISIS 455548, ISIS 455611, ISIS 465236, ISIS 465237, ISIS 465588, ISIS 465740, ISIS 465754, ISIS 465830, ISIS 466670, ISIS 466720; ISIS 481374, ISIS 481390, ISIS 481420, ISIS 481431, ISIS 481453, ISIS 481464, ISIS 481475, ISIS 481495, ISIS 481500, ISIS 481501, ISIS 481525, ISIS 481548, ISIS 481549, ISIS 481597, ISIS 481695, ISIS 481700, ISIS 481702, ISIS 481710, ISIS 481725, ISIS 481750, and ISIS 481763. In certain disclosures, such compounds include compounds comprising the sequence of any one of SEQ ID NOs 57, 90, 90, 175, 223, 245, 267, 307, 317, 318, 366, 411, 413, 54, 258, 268, 272, 288, 464, 367, 393, 1564, 1568, 1571, 1572, 1590, 1670, 1693, 1728, 1770, 1826, 1829, 1835, 1847, 1910, 1997, 2168, 2198, 2325, 2339, 2720, 2731, 2732, and 2756.

***Antisense Compound Motifs***

**[0141]** In certain embodiments, antisense compounds targeted to a STAT3 nucleic acid have chemically modified subunits arranged in patterns, or motifs, to confer to the antisense compounds properties such as

enhanced inhibitory activity, increased binding affinity for a target nucleic acid, or resistance to degradation by *in vivo* nucleases.

**[0142]** Chimeric antisense compounds typically contain at least one region modified so as to confer increased resistance to nuclease degradation, increased cellular uptake, increased binding affinity for the target nucleic acid, and/or increased inhibitory activity. A second region of a chimeric antisense compound may optionally serve as a substrate for the cellular endonuclease RNase H, which cleaves the RNA strand of an RNA:DNA duplex.

**[0143]** Antisense compounds having a gapmer motif are considered chimeric antisense compounds. In a gapmer an internal region having a plurality of nucleotides that supports RNaseH cleavage is positioned between external regions having a plurality of nucleotides that are chemically distinct from the nucleosides of the internal region. In the case of an antisense oligonucleotide having a gapmer motif, the gap segment generally serves as the substrate for endonuclease cleavage, while the wing segments comprise modified nucleosides. In certain embodiments, the regions of a gapmer are differentiated by the types of sugar moieties comprising each distinct region. The types of sugar moieties that are used to differentiate the regions of a gapmer may in some embodiments include β-D-ribonucleosides, β-D-deoxyribonucleosides, 2'-modified nucleosides (such 2'-modified nucleosides may include 2'-MOE and 2'-O-$CH_3$, among others), and bicyclic sugar modified nucleosides (such bicyclic sugar modified nucleosides may include those having a constrained ethyl). In certain embodiments, wings may include several modified sugar moieties, including, for example 2'-MOE and constrained ethyl. In certain embodiments, wings may include several modified and unmodified sugar moieties. In certain embodiments, wings may include various combinations of 2'-MOE nucleosides, constrained ethyl nucleosides, and 2'-deoxynucleosides.

**[0144]** Each distinct region may comprise uniform sugar moieties, variant, or alternating sugar moieties. The wing-gap-wing motif is frequently described as "X-Y-Z", where "X" represents the length of the 5'-wing, "Y" represents the length of the gap, and "Z" represents the length of the 3'-wing. "X" and "Z" may comprise uniform, variant, or alternating sugar moieties. In certain embodiments, "X" and "Y" may include one or more 2'-deoxynucleosides.
"Y" may comprise 2'-deoxynucleosides. As used herein, a gapmer described as "X-Y-Z" has a configuration such that the gap is positioned immediately adjacent to each of the 5'-wing and the 3' wing. Thus, no intervening nucleotides exist between the 5'-wing and gap, or the gap and the 3'-wing. Any of the antisense compounds described herein can have a gapmer motif. In certain embodiments, "X" and "Z" are the same, in other embodiments they are different. In certain disclosures, "Y" is between 8 and 15 nucleosides. X, Y, or Z can be any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30 or more nucleosides.

**[0145]** In certain embodiments, the antisense compound targeted to a STAT3 nucleic acid has a 3-10-3 gapmer motif.

***Target Nucleic Acids, Target Regions and Nucleotide Sequences***

**[0146]** Nucleotide sequences that encode STAT3 include, without limitation, the following: GENBANK Accession No. NM_139276.2 (incorporated herein as SEQ ID NO: 1) and the complement of GENBANK Accession No. NT_010755.14 truncated from nucleotides 4185000 to 4264000 (incorporated herein as SEQ ID NO: 2).

**[0147]** 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 No) indicate a combination of nucleobase sequence and motif.

**[0148]** In certain embodiments, a target region is a structurally defined region of the target nucleic acid. For example, a target region may encompass a 3' UTR, a 5' UTR, an exon, an intron, an exon/intron junction, a coding region, a translation initiation region, translation termination region, or other defined nucleic acid region. The structurally defined regions for STAT3 can be obtained by accession number from sequence databases such as NCBI. In certain embodiments, a target region may encompass the sequence from a 5' target site of one target segment within the target region to a 3' target site of another target segment within the same target region.

**[0149]** Targeting includes determination of at least one target segment to which an antisense compound hybridizes, such that a desired effect occurs. In certain embodiments, the desired effect is a reduction in mRNA target nucleic acid levels. In certain embodiments, the desired effect is reduction of levels of protein encoded by the target nucleic acid or a phenotypic change associated with the target nucleic acid.

**[0150]** A target region may contain one or more target segments. Multiple target segments within a target region may be overlapping. Alternatively, they may be non-overlapping. In certain embodiments, target segments within a target region are separated by no more than about 300 nucleotides. In certain emodiments, target segments within a target region are separated by a number of nucleotides that is, is about, is no more than, is no more than about, 250, 200, 150, 100, 90, 80, 70, 60, 50, 40, 30, 20, or 10 nucleotides on the target nucleic acid, or is a range defined by any two of the preceeding values. In certain embodiments, target segments within a target region are separated by no more than, or no more than about, 5 nucleotides on the target nucleic acid. In certain embodiments, target segments are contiguous. Contemplated are target regions defined by a range having a starting nucleic acid that is any of the 5' target sites or 3' target sites listed herein.

**[0151]** Suitable target segments may be found within a 5' UTR, a coding region, a 3' UTR, an intron, an exon, or an exon/intron junction. Target segments containing a start codon or a stop codon are also suitable target segments. A suitable target segment may specifcally exclude a certain structurally defined region such as the start codon or stop codon.

**[0152]** The determination of suitable target segments may include a comparison of the sequence of a target nucleic acid to other sequences throughout the genome. For example, the BLAST algorithm may be used to identify regions of similarity amongst different nucleic acids. This comparison can prevent the selection of antisense compound sequences that may hybridize in a non-specific manner to sequences other than a selected target nucleic acid (i.e., non-target or off-target sequences).

**[0153]** There may be variation in activity (e.g., as defined by percent reduction of target nucleic acid levels) of the antisense compounds within an active target region. In certain embodiments, reductions in STAT3 mRNA levels are indicative of inhibition of STAT3 expression. Reductions in levels of a STAT3 protein are also indicative of inhibition of target mRNA expression. Further, phenotypic changes are indicative of inhibition of STAT3 expression. In certain embodiments, reduced cellular growth, reduced tumor growth, and reduced tumor volume can be indicative of inhibition of STAT3 expression. In certain embodiments, amelioration of symptoms associated with cancer can be indicative of inhibition of STAT3 expression. In certain embodiments, reduction of cachexia is indicative of inhibition of STAT3 expression. In certain embodiments, reduction of cancer markers can be indicative of inhibition of STAT3 expression.

***Hybridization***

**[0154]** In some embodiments, hybridization occurs between an antisense compound disclosed herein and a STAT3 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.

**[0155]** Hybridization can occur under varying conditions. Stringent conditions are sequence-dependent and are determined by the nature and composition of the nucleic acid molecules to be hybridized.

**[0156]** 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 STAT3 nucleic acid.

***Complementarity***

**[0157]** An antisense compound and a target nucleic acid are complementary to each other when a sufficient number of nucleobases of the antisense compound can hydrogen bond with the corresponding nucleobases of the target nucleic acid, such that a desired effect will occur (e.g., antisense inhibition of a target nucleic acid, such as a STAT3 nucleic acid).

**[0158]** Non-complementary nucleobases between an antisense compound and a STAT3 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 STAT3 nucleic acid such that intervening or adjacent segments are not involved in the hybridization event (e.g., a loop structure, mismatch or hairpin structure).

**[0159]** 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 STAT3 nucleic acid, a target region, target segment, or specified portion thereof. Percent complementarity of an antisense compound with a target nucleic acid can be determined using routine methods.

**[0160]** 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).

**[0161]** 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 STAT3 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.

**[0162]** 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.

**[0163]** 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 STAT3 nucleic acid, or specified portion thereof.

**[0164]** 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 STAT3 nucleic acid, or specified portion thereof.

**[0165]** The antisense compounds provided herein 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***

**[0166]** 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.

**[0167]** In certain embodiments, the antisense compounds, or portions thereof, are at least 70%, 75%, 80%, 85%, 90%, 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.

**[0168]** 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.

**[0169]** 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***

**[0170]** A nucleoside is a base-sugar combination. The nucleobase (also known as base) portion of the nucleoside is normally a heterocyclic base moiety. Nucleotides are nucleosides that further include a phosphate group covalently linked to the sugar portion of the nucleoside. For those nucleosides that include a pentofuranosyl sugar, the phosphate group can be linked to the 2', 3' or 5' hydroxyl moiety of the sugar. Oligonucleotides are formed through the covalent linkage of adjacent nucleosides to one another, to form a linear polymeric oligonucleotide. Within the oligonucleotide structure, the phosphate groups are commonly referred to as forming the internucleoside linkages of the oligonucleotide.

**[0171]** 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.

**[0172]** 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***

**[0173]** 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.

**[0174]** 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.

**[0175]** In certain embodiments, antisense compounds targeted to a STAT3 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.

***Modified Sugar Moieties***

**[0176]** Antisense compounds provided herein 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, nucleosides comprise a chemically modified ribofuranose ring moiety. Examples of chemically modified ribofuranose rings include, without limitation, addition of substitutent groups (including 5' and 2' substituent groups); bridging of non-geminal ring atoms to form bicyclic nucleic acids (BNA); replacement of the ribosyl ring oxygen atom with S, N(R), or C(R1)(R)2(R = H, $C_1$-$C_{12}$ alkyl or a protecting group); and combinations thereof. Examples of chemically modified sugars include, 2'-F-5'-methyl substituted nucleoside (*see,* PCT International Application WO 2008/101157, published on 8/21/08 for other disclosed 5',2'-bis substituted nucleosides), replacement of the ribosyl ring oxygen atom with S with further substitution at the 2'-position (*see,* published U.S. Patent Application US2005/0130923, published on June 16, 2005), or, alternatively, 5'-substitution of a BNA (*see,* PCT International Application WO 2007/134181, published on 11/22/07, wherein LNA is substituted with, for example, a 5'-methyl or a 5'-vinyl group).

**[0177]** Examples of nucleosides having modified sugar moieties include, without limitation, nucleosides comprising 5'-vinyl, 5'-methyl (R or S), 4'-S, 2'-F, 2'-$OCH_3$, and 2'-$O(CH_2)2OCH_3$ substituent groups. The substituent at the 2' position can also be selected from allyl, amino, azido, thio, O-allyl, O-$C_1$-$C_{10}$ alkyl, $OCF_3$, $O(CH_2)2SCH_3$, $O(CH_2)2$-O-N(Rm)(Rn), and O-$CH_2$-C(=O)-N(Rm)(Rn), where each Rm and Rn is, independently, H or substituted or unsubstituted $C_1$-$C_{10}$ alkyl.

**[0178]** As used herein, "bicyclic nucleosides" refer to modified nucleosides comprising a bicyclic sugar moiety. Examples of bicyclic nucleosides include, without limitation, nucleosides comprising a bridge between the 4' and the 2' ribosyl ring atoms. In certain embodiments, antisense compounds provided herein include one or more bicyclic nucleosides wherein the bridge comprises a 4' to 2' bicyclic nucleoside. Examples of such 4' to 2' bicyclic nucleosides, include, but are not limited to, one of the formulae: 4'-$(CH_2)$-O-2'(LNA); 4'-$(CH_2)$-S-2'; 4'-$(CH_2)_2$-O-2'(ENA); 4'-$CH(CH_3)$-O-2' and 4'-$CH(CH_2OCH_3)$-O-2', and analogs thereof (*see,* U.S. Patent 7,399,845, issued on July 15, 2008); 4'-$C(CH_3)(CH_3)$-O-2', and analogs thereof (*see,* published PCT International Application WO2009/006478, published January 8, 2009); 4'-$CH_2$-$N(OCH_3)$-2', and analogs thereof (*see,* published PCT International Application WO2008/150729, published December 11, 2008); 4'-$CH_2$-O-$N(CH_3)$-2' (*see,* published U.S. Patent Application US2004/0171570, published September 2, 2004); 4'-$CH_2$-N(R)-O-2', wherein R is H, $C_1$-$C_{12}$ alkyl, or a protecting group (*see,* U.S. Patent 7,427,672, issued on September 23, 2008); 4'-$CH_2$-C(H)$(CH_3)$-2' (*see,* Chattopadhyaya, et al., J. Org. Chem.,2009, 74, 118-134); and 4'-$CH_2$-C(=$CH_2$)-2', and analogs thereof (*see,* published PCT International Application WO 2008/154401, published on December 8, 2008). Also see, for example: 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., 129(26) 8362-8379 (Jul. 4, 2007); 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 U.S. 6,670,461, 7,053,207, 6,268,490, 6,770,748, 6,794,499, 7,034,133, 6,525,191, 7,399,845; published PCT International applications WO 2004/106356, WO 94/14226, WO 2005/021570, and WO 2007/134181; U.S. Patent Publication Nos. US2004/0171570, US2007/0287831, and US2008/0039618; and 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 Application Nos. PCT/US2008/064591, PCT/US2008/066154, and PCT/US2008/068922. Each of the foregoing bicyclic nucleosides can be prepared having one or more stereochemical sugar configurations including for example α-L-ribofuranose and β-D-ribofuranose (see PCT international application PCT/DK98/00393, published on March 25, 1999 as WO 99/14226).

**[0179]** In certain embodiments, bicyclic sugar moieties of BNA nucleosides include, but are not limited to, compounds having at least one bridge between the 4' and the 2' position of the pentofuranosyl sugar moiety wherein such bridges independently comprises 1 or from 2 to 4 linked groups independently selected from -$[C(R_a)(R_b)]_n$-, -$C(R_a)=C(R_b)$-, -$C(R_a)=N$-, -$C(=NR_a)$-, -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;

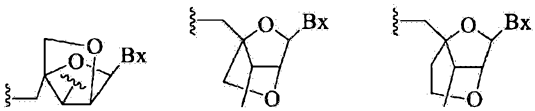
each $R_a$ and $R_b$ is, independently, H, a protecting group, hydroxyl, $C_1$-$C_{12}$ alkyl, substituted $C_1$-$C_{12}$ alkyl, $C_2$-$C_{12}$ alkenyl, substituted $C_2$-$C_{12}$ alkenyl, $C_2$-$C_{12}$ alkynyl, substituted $C_2$-$C_{12}$ alkynyl, $C_5$-$C_{20}$ aryl, substituted $C_5$-$C_{20}$ aryl, 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

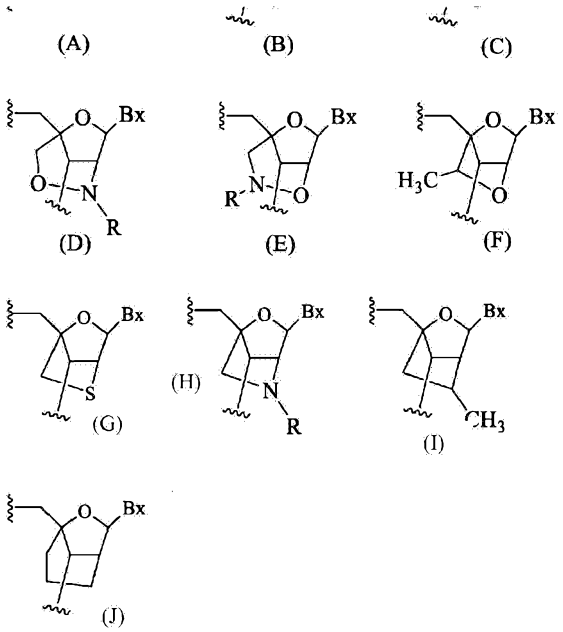
each $J_1$ and $J_2$ is, independently, H, $C_1$-$C_{12}$ alkyl, substituted $C_1$-$C_{12}$ alkyl, $C_2$-$C_{12}$ alkenyl, substituted $C_2$-$C_{12}$ alkenyl, $C_2$-$C_{12}$ alkynyl, substituted $C_2$-$C_{12}$ alkynyl, $C_5$-$C_{20}$ aryl, substituted $C_5$-$C_{20}$ aryl, acyl (C(=O)-H), substituted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

**[0180]** In certain embodiments, the bridge of a bicyclic sugar moiety is, -$[C(R_a)(R_b)]_n$-, -$[C(R_a)(R_b)]_n$-O-, -$C(R_aR_b)$-N(R)-O- or, -$C(R_aR_b)$-O-N(R)-. In certain embodiments, the bridge is 4'-$CH_2$-2', 4'-$(CH_2)_2$-2', 4'-$(CH_2)_3$-2', 4'-$CH_2$-O-2', 4'-$(CH_2)_2$-O-2', 4'-$CH_2$-O-N(R)-2', and 4'-$CH_2$-N(R)-O-2'-, wherein each Ris, independently, H, a protecting group, or $C_1$-$C_{12}$ alkyl.

**[0181]** In certain embodiments, bicyclic nucleosides are further defined by isomeric configuration. For example, a nucleoside comprising a 4'-2' methylene-oxy bridge, may be in the α-L configuration or in the β-D configuration. Previously, α-L-methyleneoxy (4'-$CH_2$-O-2') BNA's have been incorporated into antisense oligonucleotides that showed antisense activity (Frieden et al., Nucleic Acids Research, 2003, 21, 6365-6372).

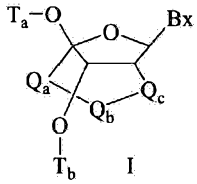
**[0182]** In certain embodiments, bicyclic nucleosides include, but are not limited to, (A) α-L-Methyleneoxy (4'-$CH_2$-O-2') BNA, (B) β-D-Methyleneoxy (4'-$CH_2$-O-2') BNA, (C) Ethyleneoxy (4'-$(CH_2)_2$-O-2') BNA, (D) Aminooxy (4'-$CH_2$-O-N(R)-2') BNA, (E) Oxyamino (4'-$CH_2$-N(R)-O-2') BNA, (F) Methyl(methyleneoxy) (4'-$CH(CH_3)$-O-2') BNA, (G) methylene-thio (4'-$CH_2$-S-2') BNA, (H) methylene-amino (4'-CH2-N(R)-2') BNA, (I) methyl carbocyclic (4'-$CH_2$-$CH(CH_3)$-2') BNA, and (J) propylene carbocyclic (4'-$(CH_2)_3$-2') BNA as depicted below.






wherein Bx is the base moiety and R is, independently, H, a protecting group or $C_1$-$C_{12}$ alkyl.

**[0183]** In certain embodiments, bicyclic nucleoside having Formula I:



I

wherein:

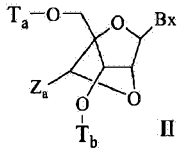
Bx is a heterocyclic base moiety;

$-Q_a-Q_b-Q_c-$ is $-CH_2-N(R_c)-CH_2-$, $-C(=O)-N(R_c)-CH_2-$, $-CH_2-O-N(R_c)-$, $-CH_2-N(R_c)-O-$, or $-N(R_c)-O-CH_2$;

$R_c$ is $C_1$-$C_{12}$ alkyl or an amino protecting group; and

$T_a$ and $T_b$ are each, independently, H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety, or a covalent attachment to a support medium.

**[0184]** In certain embodiments, bicyclic nucleoside having Formula II:



II

wherein:

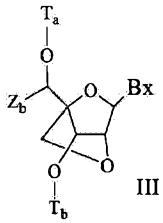
Bx is a heterocyclic base moiety;

$T_a$ and $T_b$ are each, independently, H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety, or a covalent attachment to a support medium;

$Z_a$ is $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, substituted $C_1$-$C_6$ alkyl, substituted $C_2$-$C_6$ alkenyl, substituted $C_2$-$C_6$ alkynyl, acyl, substituted acyl, substituted amide, thiol, or substituted thio.

**[0185]** In one embodiment, each of the substituted groups is, independently, mono or poly substituted with substituent groups independently selected from halogen, oxo, hydroxyl, $OJ_c$, $NJ_cJ_d$, $SJ_c$, $N_3$, $OC(=X)J_c$, and $NJ_eC(=X)NJ_cJ_d$, wherein each $J_c$, $J_d$, and $J_e$ is, independently, H, $C_1$-$C_6$ alkyl, or substituted $C_1$-$C_6$ alkyl and X is O or $NJ_c$.

**[0186]** In certain embodiments, bicyclic nucleoside having Formula III:



III

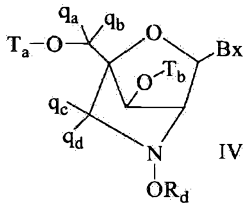
wherein:

Bx is a heterocyclic base moiety;

$T_a$ and $T_b$ are each, independently, H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety, or a covalent attachment to a support medium;

$Z_b$ is $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, substituted $C_1$-$C_6$ alkyl, substituted $C_2$-$C_6$ alkenyl, substituted $C_2$-$C_6$ alkynyl, or substituted acyl (C(=O)-).

**[0187]** In certain embodiments, bicyclic nucleoside having Formula IV:



IV

wherein:

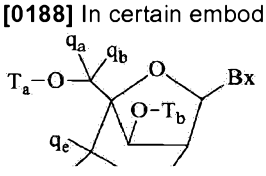
Bx is a heterocyclic base moiety;

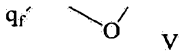
$T_a$ and $T_b$ are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety, or a covalent attachment to a support medium;

$R_d$ is $C_1$-$C_6$ 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;

each $q_a$, $q_b$, $q_c$ and $q_d$ is, independently, H, halogen, $C_1$-$C_6$ 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, $C_1$-$C_6$ alkoxyl, substituted $C_1$-$C_6$ alkoxyl, acyl, substituted acyl, $C_1$-$C_6$ aminoalkyl, or substituted $C_1$-$C_6$ aminoalkyl;

**[0188]** In certain embodiments, bicyclic nucleoside having Formula V:





V

wherein:

Bx is a heterocyclic base moiety;

$T_a$ and $T_b$ are each, independently, H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety, or a covalent attachment to a support medium;

$q_a$, $q_b$, $q_e$ and $q_f$ are each, independently, hydrogen, halogen, $C_1$-$C_{12}$ 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, $C_1$-$C_{12}$ alkoxy, substituted $C_1$-$C_{12}$ alkoxy, $OJ_j$, $SJ_j$, $SOJ_j$, $SO_2J_j$, $NJ_jJ_k$, $N_3$, CN, $C(=O)OJ_j$, $C(=O)NJ_jJ_k$, $C(=O)J_j$, $O\text{-}C(=O)\text{-}NJ_jJ_k$, $N(H)C(=NH)NJ_jJ_k$, $N(H)C(=O)NJ_jJ_k$ or $N(H)C(=S)NJ_jJ_k$;

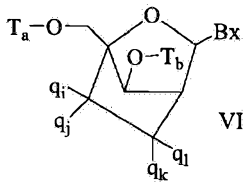
or $q_e$ and $q_f$ together are $=C(q_g)(q_h)$;

$q_g$ and $q_h$ are each, independently, H, halogen, $C_1$-$C_{12}$ alkyl, or substituted $C_1$-$C_{12}$ alkyl.

**[0189]** The synthesis and preparation of the methyleneoxy (4'-$CH_2$-O-2') BNA monomers adenine, cytosine, guanine, 5-methyl-cytosine, thymine, and uracil, along with their oligomerization, and nucleic acid recognition properties have been described (*see, e.g.,* Koshkin et al., Tetrahedron, 1998, 54, 3607-3630). BNAs and preparation thereof are also described in WO 98/39352 and WO 99/14226.

**[0190]** Analogs of methyleneoxy (4'-$CH_2$-O-2') BNA, methyleneoxy (4'-$CH_2$-O-2') BNA, and 2'-thio-BNAs, have also been prepared (*see, e.g.,* Kumar et al., Bioorg. Med. Chem. Lett., 1998, 8, 2219-2222). Preparation of locked nucleoside analogs comprising oligodeoxyribonucleotide duplexes as substrates for nucleic acid polymerases has also been described (*see, e.g.,* Wengel et al., WO 99/14226). Furthermore, synthesis of 2'-amino-BNA, a novel comformationally restricted high-affinity oligonucleotide analog, has been described in the art (*see, e.g.,* Singh et al., J. Org. Chem., 1998, 63, 10035-10039). In addition, 2'-amino- and 2'-methylamino-BNA's have been prepared and the thermal stability of their duplexes with complementary RNA and DNA strands has been previously reported.

**[0191]** In certain embodiments, bicyclic nucleoside having Formula VI:



VI

wherein:

Bx is a heterocyclic base moiety;

$T_a$ and $T_b$ are each, independently, H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety, or a covalent attachment to a support medium;

each $q_i$, $q_j$, $q_k$ and $q_l$ is, independently, H, halogen, $C_1$-$C_{12}$ 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, $C_1$-$C_{12}$ alkoxyl, substituted $C_1$-$C_{12}$ alkoxyl, $OJ_j$, $SJ_j$, $SOJ_j$, $SO_2J_j$, $NJ_jJ_k$, $N_3$, CN, $C(=O)OJ_j$, $C(=O)NJ_jJ_k$, $C(=O)J_j$, $O\text{-}C(=O)NJ_jJ_k$, $N(H)C(=NH)NJ_jJ_k$, $N(H)C(=O)NJ_jJ_k$, or $N(H)C(=S)NJ_jJ_k$; and

$q_i$ and $q_j$ or $q_l$ and $q_k$ together are $=C(q_g)(q_h)$, wherein $q_g$ and $q_h$ are each, independently, H, halogen, $C_1$-$C_{12}$

alkyl, or substituted $C_1$-$C_{12}$ alkyl.

**[0192]** One carbocyclic bicyclic nucleoside having a 4'-$(CH_2)_3$-2' bridge and the alkenyl analog, bridge 4'-CH=CH-$CH_2$-2', have been described (*see, e.g.,* Freier et al., Nucleic Acids Research, 1997, 25(22), 4429-4443 and Albaek et al., J. Org. Chem., 2006, 71, 7731-7740). The synthesis and preparation of carbocyclic bicyclic nucleosides along with their oligomerization and biochemical studies have also been described *(see, e.g.,* Srivastava et al., J. Am. Chem. Soc. 2007, 129(26), 8362-8379).

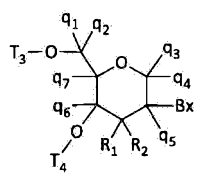
**[0193]** As used herein, "4'-2' bicyclic nucleoside" or "4' to 2' bicyclic nucleoside" refers to a bicyclic nucleoside comprising a furanose ring comprising a bridge connecting the 2' carbon atom and the 4' carbon atom.

**[0194]** As used herein, "monocylic nucleosides" refer to nucleosides comprising modified sugar moieties that are not bicyclic sugar moieties. In certain embodiments, the sugar moiety, or sugar moiety analogue, of a nucleoside may be modified or substituted at any position.

**[0195]** As used herein, "2'-modified sugar" means a furanosyl sugar modified at the 2' position. In certain embodiments, such modifications include substituents selected from: a halide, including, but not limited to substituted and unsubstituted alkoxy, substituted and unsubstituted thioalkyl, substituted and unsubstituted amino alkyl, substituted and unsubstituted alkyl, substituted and unsubstituted allyl, and substituted and unsubstituted alkynyl. In certain embodiments, 2' modifications are selected from substituents including, but not limited to: $O[(CH_2)_nO]_mCH_3$, $O(CH_2)_nNH_2$, $O(CH_2)_nCH_3$, $O(CH_2)_nONH_2$, $OCH_2C(=O)N(H)CH_3$, and $O(CH_2)_nON[(CH_2)_nCH_3]_2$, where n and m are from 1 to about 10. Other 2'- substituent groups can also be selected from: $C_1$-$C_{12}$ alkyl; substituted alkyl; alkenyl; alkynyl; alkaryl; aralkyl; O-alkaryl or O-aralkyl; SH; $SCH_3$; OCN; Cl; Br; CN; $CF_3$; $OCF_3$; $SOCH_3$; $SO_2CH_3$; $ONO_2$; $NO_2$; $N_3$; $NH_2$; heterocycloalkyl; heterocycloalkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a reporter group; an intercalator; a group for improving pharmacokinetic properties; and a group for improving the pharmacodynamic properties of an antisense compound, and other substituents having similar properties. In certain embodiments, modifed nucleosides comprise a 2'-MOE side chain (*see, e.g.,* Baker et al., J. Biol. Chem., 1997, 272, 11944-12000). Such 2'-MOE substitution have been described as having improved binding affinity compared to unmodified nucleosides and to other modified nucleosides, such as 2'-*O*-methyl, *O*-propyl, and *O*-aminopropyl. Oligonucleotides having the 2'-MOE substituent also have been shown to be antisense inhibitors of gene expression with promising features for *in vivo* use (*see, e.g.,* Martin, P., Helv. Chim. Acta, 1995, 78, 486-504; Altmann et al., Chimia, 1996, 50, 168-176; Altmann et al., Biochem. Soc. Trans., 1996, 24, 630-637; and Altmann et al., Nucleosides Nucleotides, 1997, 16, 917-926).

**[0196]** As used herein, a "modified tetrahydropyran nucleoside" or "modified THP nucleoside" means a nucleoside having a six-membered tetrahydropyran "sugar" substituted in for the pentofuranosyl residue in normal nucleosides (a sugar surrogate). Modified THP nucleosides include, but are not limited to, what is referred to in the art as 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), or those compounds having Formula X:

Formula X:




X

wherein independently for each of said at least one tetrahydropyran nucleoside analog of Formula X:

Bx is a heterocyclic base moiety;

$T_3$ and $T_4$ are each, independently, an internucleoside linking group linking the tetrahydropyran nucleoside analog to the antisense compound or one of $T_3$ and $T_4$ is an internucleoside linking group linking the tetrahydropyran nucleoside analog to the antisense compound 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

one of $R_1$ and $R_2$ is hydrogen and the other is selected from 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.

**[0197]** In certain embodiments, the modified THP nucleosides of Formula X are provided wherein $q_m$, $q_n$, $q_p$, $q_r$, $q_s$, $q_t$, and $q_u$ are each H. In certain embodiments, at least one of $q_m$, $q_n$, $q_p$, $q_r$, $q_s$, $q_t$, and $q_u$ is other than H. In certain embodiments, at least one of $q_m$, $q_n$, $q_p$, $q_r$, $q_s$, $q_t$ and $q_u$ is methyl. In certain embodiments, THP nucleosides of Formula X are provided wherein one of $R_1$ and $R_2$ is F. In certain embodiments, $R_1$ is fluoro and $R_2$ is H, $R_1$ is methoxy and $R_2$ is H, and $R_1$ is methoxyethoxy and $R_2$ is H.

**[0198]** As used herein, "2'-modified" or "2'-substituted" refers to a nucleoside comprising a sugar comprising a substituent at the 2' position other than H or OH. 2'-modified nucleosides, include, but are not limited to, bicyclic nucleosides wherein the bridge connecting two carbon atoms of the sugar ring connects the 2' carbon and another carbon of the sugar ring and nucleosides with non-bridging 2'substituents, such as allyl, amino, azido, thio, O-allyl, O-$C_1$-$C_{10}$ alkyl, -$OCF_3$, O-$(CH_2)_2$-O-$CH_3$, 2'-O$(CH_2)_2SCH_3$, O-$(CH_2)_2$-O-$N(R_m)(R_n)$, or O-$CH_2$-C(=O)-$N(R_m)(R_n)$, where each $R_m$ and $R_n$ is, independently, H or substituted or unsubstituted $C_1$-$C_{10}$ alkyl. 2'-modifed nucleosides may further comprise other modifications, for example, at other positions of the sugar and/or at the nucleobase.

**[0199]** As used herein, "2'-F" refers to a sugar comprising a fluoro group at the 2' position.

**[0200]** As used herein, "2'-OMe" or "2'-$OCH_3$" or "2'-O-methyl" each refers to a nucleoside comprising a sugar comprising an -$OCH_3$ group at the 2' position of the sugar ring.

**[0201]** As used herein, "oligonucleotide" refers to a compound comprising a plurality of linked nucleosides. In certain embodiments, one or more of the plurality of nucleosides is modified. In certain embodiments, an oligonucleotide comprises one or more ribonucleosides (RNA) and/or deoxyribonucleosides (DNA).

**[0202]** Many other bicyclo and tricyclo sugar surrogate ring systems are also known in the art that can be used to modify nucleosides for incorporation into antisense compounds (*see, e.g.,* review article: Leumann, J. C, Bioorganic & Medicinal Chemistry, 2002, 10, 841-854).
Such ring systems can undergo various additional substitutions to enhance activity.

**[0203]** Methods for the preparations of modified sugars are well known to those skilled in the art.

**[0204]** In nucleotides having modified sugar moieties, the nucleobase moieties (natural, modified, or a combination thereof) are maintained for hybridization with an appropriate nucleic acid target.

**[0205]** In certain embodiments, antisense compounds comprise one or more nucleotides having modified sugar moieties. In certain embodiments, the modified sugar moiety is 2'-MOE. In certain embodiments, the 2'-MOE modified nucleotides are arranged in a gapmer motif. In certain embodiments, the modified sugar moiety is a cEt. In certain embodiments, the cEt modified nucleotides are arranged throughout the wings of a gapmer motif.

***Compositions and Methods for Formulating Pharmaceutical Compositions***

**[0206]** Antisense oligonucleotides may be admixed with pharmaceutically acceptable active or inert substances for the preparation of pharmaceutical compositions or formulations. 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.

**[0207]** An antisense compound targeted to a STAT3 nucleic acid can be utilized in pharmaceutical compositions by combining the antisense compound with a suitable pharmaceutically acceptable diluent or carrier. A pharmaceutically acceptable diluent includes phosphate-buffered saline (PBS). PBS is a diluent suitable for use in compositions to be delivered parenterally. Accordingly, in one embodiment, employed in the methods described herein is a pharmaceutical composition comprising an antisense compound targeted to a STAT3 nucleic acid and a pharmaceutically acceptable diluent. In certain embodiments, the pharmaceutically acceptable diluent is PBS. In certain embodiments, the antisense compound is an antisense oligonucleotide.

**[0208]** 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.

**[0209]** 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.

***Conjugated Antisense compounds***

**[0210]** Antisense compounds may be covalently linked to one or more moieties or conjugates which enhance the activity, cellular distribution or cellular uptake of the resulting antisense oligonucleotides. Typical conjugate groups include cholesterol moieties and lipid moieties. Additional conjugate groups include carbohydrates, phospholipids, biotin, phenazine, folate, phenanthridine, anthraquinone, acridine, fluoresceins, rhodamines, coumarins, and dyes.

**[0211]** Antisense compounds can also be modified to have one or more stabilizing groups that are generally attached to one or both termini of antisense compounds to enhance properties such as, for example, nuclease stability. Included in stabilizing groups are cap structures. These terminal modifications protect the antisense compound having terminal nucleic acid from exonuclease degradation, and can help in delivery and/or localization within a cell. The cap can be present at the 5'-terminus (5'-cap), or at the 3'-terminus (3'-cap), or can be present on both termini. Cap structures are well known in the art and include, for example, inverted deoxy abasic caps. Further 3' and 5'-stabilizing groups that can be used to cap one or both ends of an antisense compound to impart nuclease stability include those disclosed in WO 03/004602 published on

January 16, 2003.

***Cell culture and antisense compounds treatment***

**[0212]** The effects of antisense compounds on the level, activity or expression of STAT3 nucleic acids can be tested *in vitro* in a variety of cell types. Cell types used for such analyses are available from commerical vendors (*e.g.* American Type Culture Collection, Manassus, VA; Zen-Bio, Inc., Research Triangle Park, NC; Clonetics Corporation, Walkersville, MD) and are cultured according to the vendor's instructions using commercially available reagents (e.g. Invitrogen Life Technologies, Carlsbad, CA). Illustrative cell types include, but are not limited to, HuVEC cells, b.END cells, HepG2 cells, Hep3B cells, and primary hepatocytes.

***In vitro testing of antisense oligonucleotides***

**[0213]** Described herein are methods for treatment of cells with antisense oligonucleotides, which can be modified appropriately for treatment with other antisense compounds.

**[0214]** Cells may be treated with antisense oligonucleotides when the cells reach approximately 60-80% confluency in culture.

**[0215]** One reagent commonly used to introduce antisense oligonucleotides into cultured cells includes the cationic lipid transfection reagent LIPOFECTIN (Invitrogen, Carlsbad, CA). Antisense oligonucleotides may be mixed with LIPOFECTIN in OPTI-MEM 1 (Invitrogen, Carlsbad, CA) to achieve the desired final concentration of antisense oligonucleotide and a LIPOFECTIN concentration that may range from 2 to 12 ug/mL per 100 nM antisense oligonucleotide.

**[0216]** Another reagent used to introduce antisense oligonucleotides into cultured cells includes LIPOFECTAMINE (Invitrogen, Carlsbad, CA). Antisense oligonucleotide is mixed with LIPOFECTAMINE in OPTI-MEM 1 reduced serum medium (Invitrogen, Carlsbad, CA) to achieve the desired concentration of antisense oligonucleotide and a LIPOFECTAMINE concentration that may range from 2 to 12 ug/mL per 100 nM antisense oligonucleotide.

**[0217]** Another technique used to introduce antisense oligonucleotides into cultured cells includes electroporation.

**[0218]** Cells are treated with antisense oligonucleotides by routine methods. Cells may be harvested 16-24 hours after antisense oligonucleotide treatment, at which time RNA or protein levels of target nucleic acids are measured by methods known in the art and described herein. In general, when treatments are performed in multiple replicates, the data are presented as the average of the replicate treatments.

**[0219]** The concentration of antisense oligonucleotide used varies from cell line to cell line. Methods to determine the optimal antisense oligonucleotide concentration for a particular cell line are well known in the art. Antisense oligonucleotides are typically used at concentrations ranging from 1 nM to 300 nM when transfected with LIPOFECTAMINE. Antisense oligonucleotides are used at higher concentrations ranging from 625 to 20,000 nM when transfected using electroporation.

***Free Uptake Assays***

**[0220]** In certain embodiments, transfection-independent activity (i.e., free uptake) of antisense oligonucleotides in cancer cell lines is a measure of potency. Free uptake may be measured in cancer cell lines such as, for example, SK-BR-3 cells, U251-MG cells, MDA-MB-231 cells, H460 cells, A431 cells, colo205 cells, SNB-19 cells, SK-OV3 cells, H1993 lung cancer cells, H358 lung cancer cells, PC-9 lung cancer cells, KHM-35 lung cancer cells, Capan-1 pancreatic cancer cells, HPAF-11 pancreatic cancer cells, and Colo 201colorectal cancer cells.

**[0221]** In free uptake assays, antisense oligonucleotides are administered to cells lines without the aid of a transfection agent or electroporation. Antisense oligonucleotides are administered to cell lines at one or more doses and percent inhbition of target mRNA or protein expression is meausred. Where multiple doses are administered, IC50 may be measured. In certain embodiments, antisense oligonucleotides exhibiting a high degree of potency, as measured by percent inhbition after single dose or multiple doses, are preferred over antisense oligonucleotides exhibiting a lower degree of potency. Those antisense oligonucleotides exhibiting a high degree of *in vitro* potency are more likely to exhibit *in vivo* potency.

***RNA Isolation***

**[0222]** RNA analysis can be performed on total cellular RNA or poly(A)+ mRNA. Methods of RNA isolation are well known in the art. RNA is prepared using methods well known in the art, for example, using the TRIZOL Reagent (Invitrogen, Carlsbad, CA) according to the manufacturer's recommended protocols.

***Analysis of inhibition of target levels or expression***

**[0223]** Inhibition of levels or expression of a STAT3 nucleic acid can be assayed in a variety of ways known in the art. For example, target nucleic acid levels can be quantitated by, e.g., Northern blot analysis, competitive polymerase chain reaction (PCR), or quantitaive real-time PCR. RNA analysis can be performed on total cellular RNA or poly(A)+ mRNA. Methods of RNA isolation are well known in the art. Northern blot analysis is also routine in the art. Quantitative real-time PCR can be conveniently accomplished using the commercially available ABI PRISM 7600, 7700, or 7900 Sequence Detection System, available from PE-Applied Biosystems, Foster City, CA and used according to manufacturer's instructions.

***Quantitative Real-Time PCR Analysis of Target RNA Levels***

**[0224]** Quantitation of target RNA levels may be accomplished by quantitative real-time PCR using the ABI PRISM 7600, 7700, or 7900 Sequence Detection System (PE-Applied Biosystems, Foster City, CA) according to manufacturer's instructions. Methods of quantitative real-time PCR are well known in the art.

**[0225]** Prior to real-time PCR, the isolated RNA is subjected to a reverse transcriptase (RT) reaction, which produces complementary DNA (cDNA) that is then used as the substrate for the real-time PCR amplification. The RT and real-time PCR reactions are performed sequentially in the same sample well. RT and real-time PCR reagents may be obtained from Invitrogen (Carlsbad, CA). RT real-time-PCR reactions are carried out by methods well known to those skilled in the art.

**[0226]** Gene (or RNA) target quantities obtained by real time PCR are normalized using either the expression level of a gene whose expression is constant, such as cyclophilin A, or by quantifying total RNA using RIBOGREEN (Invitrogen, Inc. Carlsbad, CA). Cyclophilin A expression is quantified by real time PCR, by being run simultaneously with the target, multiplexing, or separately. Total RNA is quantified using RIBOGREEN RNA

quantification reagent (Invetrogen, Inc. Eugene, OR). Methods of RNA quantification by RIBOGREEN are taught in Jones, L.J., et al, (Analytical Biochemistry, 1998, 265, 368-374). A CYTOFLUOR 4000 instrument (PE Applied Biosystems) is used to measure RIBOGREEN fluorescence.

**[0227]** Probes and primers are designed to hybridize to a STAT3 nucleic acid. Methods for designing real-time PCR probes and primers are well known in the art, and may include the use of software such as PRIMER EXPRESS Software (Applied Biosystems, Foster City, CA).

***Analysis of Protein Levels***

**[0228]** Antisense inhibition of STAT3 nucleic acids can be assessed by measuring STAT3 protein levels. Protein levels of STAT3 can be evaluated or quantitated in a variety of ways well known in the art, such as immunoprecipitation, Western blot analysis (immunoblotting), enzyme-linked immunosorbent assay (ELISA), quantitative protein assays, protein activity assays (for example, caspase activity assays), immunohistochemistry, immunocytochemistry or fluorescence-activated cell sorting (FACS). Antibodies directed to a target can be identified and obtained from a variety of sources, such as the MSRS catalog of antibodies (Aerie Corporation, Birmingham, MI), or can be prepared via conventional monoclonal or polyclonal antibody generation methods well known in the art. Antibodies useful for the detection of mouse, rat, monkey, and human STAT3 are commercially available.

***In vivo testing of antisense compounds***

**[0229]** Antisense compounds, for example, antisense oligonucleotides, are tested in animals to assess their ability to inhibit expression of STAT3 and produce phenotypic changes, such as, reduced cellular growth, amelioration of symptoms associated with cancer, reduction of cachexia, and reduction of cancer markers. Testing may be performed in normal animals, or in experimental disease models. For administration to animals, antisense oligonucleotides are formulated in a pharmaceutically acceptable diluent, such as phosphate-buffered saline. Administration includes parenteral routes of administration, such as intraperitoneal, intravenous, subcutaneous, intrathecal, and intracerebroventricular. Calculation of antisense oligonucleotide dosage and dosing frequency is within the abilities of those skilled in the art, and depends upon factors such as route of administration and animal body weight. Following a period of treatment with antisense oligonucleotides, RNA is isolated from liver tissue and changes in STAT3 nucleic acid expression are measured. Changes in STAT3 protein levels are also measured.

**[0230]** In certain embodiments, xenograft tumor models are used to measure the effect of antisense oligonucleotides on tumor growth and metastasis. In xenograft tumor model described herein, cells from a cancerous cell line are inoculated into an animal. Such cell lines may include, for example, human breast cancer cells, MDA-MB-231, A431 human epidermoid carcinoma, U251 human glioma tumor cells, and human NCI-H460 non-small cell lung carcinoma cells. Certain compounds described herein and used in xenograft models described herein may target human STAT3, mouse STAT3, rat STAT3, and/or monkey STAT3. Certain compounds described herein and used in xenograft models described herein may cross-react with one or more species STAT3. In certain embodiments, compounds described herein and used in xenograft models described herein may be more potent inhibitors of tumor growth and tumor volume than the data suggests wherein endogenous STAT3 is not reduced (due to lack of cross-reactivity).

***Certain Indications***

**[0231]** In certain embodiments, provided are methods, compounds, and compositions of treating an individual comprising administering one or more pharmaceutical compositions provided herein. In certain embodiments, the individual has a hyperproliferative disease. In certain embodiments, the hyperproliferative disease is cancer, e.g., carcinomas, sarcomas, lymphomas, and leukemias as well as associated malignancies and metastases. In certain embodiments, the type of cancer is lung cancer, including non small cell lung cancer (NSCLC), pancreatic cancer, colorectal cancer, multiple myeloma, hepatocellular carcinoma (HCC), glioblastoma, ovarian cancer, osteosarcoma, head and neck cancer, breast cancer, epidermoid carcinomas, intestinal adenomas, prostate cancer, and gastric cancer. In certain embodiments, the individual is at risk for a hyperproliferative disease, including, cancer, e.g., carcinomas, sarcomas, lymphomas, and leukemias as well as associated malignancies and metastases. This includes individuals having one or more risk factors for developing a hyperproliferative disease, including, growing older; tobacco use; exposure to sunlight and ionizing radiation; contact with certain chemicals; infection with certain viruses and bacteria; certain hormone therapies; genetic predisposition; alcohol use; and certain lifestyle choices including poor diet, lack of physical activity, and/or being overweight. In certain embodiments, the individual has been identified as in need of treatment for a hyperproliferative disease. In certain embodiments, are provided methods for prophylactically reducing STAT3 expression in an individual. Certain embodiments include treating an individual in need thereof by administering to an individual a therapeutically effective amount of an antisense compound targeted to a STAT3 nucleic acid.

**[0232]** In certain embodiments, treatment with the methods, compounds, and compositions described herein is useful for preventing metastasis of a cancer associated with the upregulation of certain genes, such as STAT3, at the tumor bone interface to bone. In certain embodiments, treatment with the methods, compounds, and compositions described herein is useful for preventing cancer from metastasizing to bone. In certain embodiments, treatment with the methods, compounds, and compositions described herein is useful for preventing renal cell carcinoma, breast cancer, non small cell lung carcinoma, and prostate cancer from metastasizing to bone.

**[0233]** In one embodiment, administration of a therapeutically effective amount of an antisense compound targeted to a STAT3 nucleic acid is accompanied by monitoring of STAT3 levels in the serum of an individual to determine an individual's response to administration of the antisense compound. An individual's response to administration of the antisense compound is used by a physician to determine the amount and duration of therapeutic intervention.

**[0234]** In certain embodiments, administration of an antisense compound targeted to a STAT3 nucleic acid results in reduction of STAT3 expression by at least 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 99%, or a range defined by any two of these values. In certain embodiments, administration of an antisense compound targeted to a STAT3 nucleic acid results in reduced cellular growth, reduced tumor growth, reduced tumor volume, amelioration of symptoms associated with cancer, and reduction of cancer markers. In certain embodiments, administration of a STAT3 antisense compound decreases cellular growth, tumor growth, and tumor volume by at least 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 99%, or a range defined by any two of these values.

**[0235]** In certain embodiments, pharmaceutical compositions comprising an antisense compound targeted to STAT3 are used for the preparation of a medicament for treating a patient suffering or susceptible to a hyperproliferative disease.

***Certain Combination Therapies***

**[0236]** In certain embodiments, one or more pharmaceutical compositions provided herein are co-administered with one or more other pharmaceutical agents. In certain embodiments, such one or more other

pharmaceutical agents are designed to treat the same disease, disorder, or condition as the one or more pharmaceutical compositions provided herein. In certain embodiments, such one or more other pharmaceutical agents are designed to treat a different disease, disorder, or condition as the one or more pharmaceutical compositions provided herein. In certain embodiments, such one or more other pharmaceutical agents are designed to treat an undesired side effect of one or more pharmaceutical compositions provided herein. In certain embodiments, one or more pharmaceutical compositions provided herein are co-administered with another pharmaceutical agent to treat an undesired effect of that other pharmaceutical agent. In certain embodiments, one or more pharmaceutical compositions provided herein are co-administered with another pharmaceutical agent to produce a combinational effect. In certain embodiments, one or more pharmaceutical compositions provided herein are co-administered with another pharmaceutical agent to produce a synergistic effect.

**[0237]** In certain embodiments, one or more pharmaceutical compositions provided herein and one or more other pharmaceutical agents are administered at the same time. In certain embodiments, one or more pharmaceutical compositions provided herein and one or more other pharmaceutical agents are administered at different times. In certain embodiments, one or more pharmaceutical compositions provided herein and one or more other pharmaceutical agents are prepared together in a single formulation. In certain embodiments, one or more pharmaceutical compositions provided herein and one or more other pharmaceutical agents are prepared separately. In certain embodiments, one or more other pharmaceutical agents include all-trans retinoic acid, azacitidine, azathioprine, bleomycin, carboplatin, capecitabine, cisplatin, chlorambucil, cyclophosphamide, cytarabine, daunorubicin, docetaxel, doxifluridine, doxorubicin, epirubicin, epothilone, etoposide, fluorouracil, gemcitabine, hydroxyurea, idarubicin, imatinib, mechlorethamine, mercaptopurine, methotrexate, mitoxantrone, oxaliplatin, paclitaxel, pemetrexed, teniposide, tioguanine, valrubicin, vinblastine, vincristine, vindesine, or vinorelbine. In certain embodiments, one or more other pharmaceutical agents include another antisense oligonucleotide. In certain embodiments, another antisense oligonucleotide is a second STAT3 antisense oligonucleotide.

**[0238]** In certain embodiments, one or more other pharmaceutical agents include molecular targeted therapies. In certain embodiments, the molecular targeted therapy is an EGFR inhibitor, a mTOR inhibitor, a HER2 inhibitor, or a VEGF/VEGFR inhibitor. In certain embodiments, EGFR inhibitors include gefitinib, erlotinib, lapatinib, cetuximab, panitumumbo. In certain embodiments, mTOR inhibitors include everolimus and temsirolimus. In certain embodiments, HER2 inhibitors include trastuzumab and lapatinib. In certain embodiments, VEGF/VEGFR inhibitors include pazopanib, bevacizumab, sunitinib, and sorafenib.

**[0239]** In certain embodiments, one more pharmaceutical compositions provided herein are administered with radiation therapy. In certain embodiments, one or more pharmaceutical compositions are administered at the same time as radiation therapy. In certain embodiments, one or more pharmaceutical compositions are administered before radiation therapy. In certain embodiments, one or more pharmaceutical compositions are administered after radiation therapy. In certain embodiments, one or more pharmaceutical compositions are administered at various time points throughout a radiation therapy regimen.

**[0240]** In certain embodiments, radiation therapy is useful for inhibiting tumor growth. In certain embodiments, radiation therapy is useful for increasing overall survival. In certain embodiments, radiation therapy used in conjunction with administration of one or more pharmaceuticals provided herein is advantageous over using either therapy alone because both radiation therapy and administration with one or more pharmaceuticals can be limited to achieve effective antiproliferative response with limited toxicity.

**[0241]** In certain embodiments, a physician designs a therapy regimen including both radiation therapy and administration of one more pharmaceutical compositions provided herein. In certain embodiments, a physician designs a therapy regimen including radiation therapy, administration of one or more pharmaceutical compositions provided herein, and administration of one or more other chemotherapeutic agents.

***Tolerability***

**[0242]** In certain embodiments, the compounds provided herein display minimal side effects. Side effects include responses to the administration of the antisense compound that are typically unrelated to the targeting of STAT3, such as an inflammatory response in the animal. In certain embodiments compounds are well tolerated by the animal. Increased tolerability can depend on a number of factors, including, but not limited to, the nucleotide sequence of the antisense compound, chemical modifications to the nucleotides, the particular motif of unmodified and modified nucleosides in the antisense compound, or combinations thereof. Tolerability may be determined by a number of factors. Such factors include body weight, organ weight, liver function, kidney function, platelet count, white blood cell count.

**[0243]** In certain embodiments, the compounds provided herein demonstrate minimal effect on organ weight. In certain embodiments, the compounds demonstrate less than a 7-fold, 6-fold, 5-fold, 4-fold, 3-fold, 2-fold or no significant increase in spleen and/or liver weight.

**[0244]** In certain embodiments, the compounds provided herein demonstrate minimal effect on liver function. Factors for the evaluation of liver function include ALT levels, AST levels, plasma bilirubin levels and plasma albumin levels. In certain embodiments the compounds provided herein demonstrate less than a 7-fold, less than a 6-fold, less than a 5-fold, less than a 4-fold, less than a 3-fold or less than a 2-fold or no significant increase in ALT or AST. In certain embodiments the compounds provided herein demonstrate less than a 3-fold, less than a 2-fold or no significant increase in plasma bilirubin levels.

**[0245]** In certain embodiments, the compounds provided herein demonstrate minimal effect on kidney function. In certain embodiments, the compounds provided herein demonstrate less than a 3-fold, less than a 2-fold, or no significant increase in plasma concentrations of blood urea nitrogen (BUN). In certain embodiments, the compounds provided herein demonstrate less than a 6-fold, 5-fold, 4-fold, 3-fold, 2-fold, or no significant increase in the ratio of urine protein to creatinine.

**[0246]** In certain embodiments, the compounds provided herein demonstrate minimal effect on hematological factors. In certain embodiments, the compounds provided herein demonstrate less than a 60%, 50%, 40%, 30%, 20%, 10% or 5% decrease in platelet count. In certain embodiments, the compounds provided herein demonstrate less than a 4-fold, less than a 3-fold, less than a 2-fold or no significant increase in monocyte count.

**[0247]** In certain embodiments compounds further display favorable pharmacokinetics. In certain embodiments, antisense compounds exhibit relatively high half-lives in relevant biological fluids or tissues.

**[0248]** In certain embodiments, compounds or compositions further display favorable viscosity. In certain embodiments, the viscosity of the compound or composition is no more than 40cP at a concentration of 165-185 mg/mL.

**[0249]** In other embodiments, the compounds display combinations of the characteristics above and reduce STAT3 mRNA expression in an animal model with high efficiency.

**EXAMPLES**

***Non-limiting disclosure and incorporation by reference***

**[0250]** 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.

**Example 1: Antisense inhibition of human STAT3 in HuVEC cells**

**[0251]** Antisense oligonucleotides were designed targeting a human STAT3 nucleic acid and were tested for their effect on human STAT3 mRNA expression *in vitro.* The chimeric antisense oligonucleotides presented in Tables 1 and 2 were designed as either 2-10-2 cEt gapmers or 3-10-3 cEt gapmers. The 2-10-2 cEt gapmers are 14 nucleotides in length, wherein the central gap segment comprises ten 2'-deoxynucleosides and is flanked on both sides (in the 5' and 3' directions) by wings comprising two nucleosides each. The 3-10-3 cEt gapmers are 16 nucleosides in length, wherein the central gap segment comprises ten 2'-deoxynucleosides and is flanked on both sides (in the 5' and 3' directions) by wings comprising three nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has an cEt sugar modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines.

**[0252]** Potency of cEt gapmers was compared to ISIS 337332, ISIS 337333, and ISIS 345785, which are 5-10-5 MOE gapmers targeting human STAT3 and are further described in USPN 7,307,069.

**[0253]** Cultured HuVEC 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 STAT3 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS199 (forward sequence ACATGCCACTTTGGTGTTTCATAA, designated herein as SEQ ID NO: 6; reverse sequence TCTTCGTAGATTGTGCTGATAGAGAAC, designated herein as SEQ ID NO: 7; probe sequence CAGTATAGCCGCTTCCTGCAAGAGTCGAA, designated herein as SEQ ID NO: 8) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells. All cEt gapmers and MOE gapmers were tested under the same conditions.

**[0254]** "Human Target start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Human Target stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in Table 1 is targeted to human STAT3 mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_139276.2). Each gapmer listed in Table 2 is targeted to the human STAT3 genomic sequence, designated herein as SEQ ID NO: 2 (the complement of GENBANK Accession No. NT_010755.14 truncated from nucleotides 4185000 to 4264000).

**Table 1**

Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1

| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
|---|---|---|---|---|---|---|---|
| 481350 | 76 | 91 | TCCAGGATCCGGTTGG | 3-10-3 | cEt | 52 | 9 |
| 481575 | 77 | 90 | CCAGGATCCGGTTG | 2-10-2 | cEt | 41 | 10 |
| 481351 | 132 | 147 | GGCCGAAGGGCCTCTC | 3-10-3 | cEt | 14 | 11 |
| 481576 | 133 | 146 | GCCGAAGGGCCTCT | 2-10-2 | cEt | 8 | 12 |
| 481352 | 225 | 240 | CCTGCTAAAATCAGGG | 3-10-3 | cEt | 15 | 13 |
| 481577 | 226 | 239 | CT GCTAAAAT CAGG | 2-10-2 | cEt | 12 | 14 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481353 | 240 | 255 | ATTCCATTGGGCCATC | 3-10-3 | cEt | 78 | 15 |
| 481578 | 241 | 254 | TTCCATTGGGCCAT | 2-10-2 | cEt | 51 | 16 |
| 481354 | 264 | 279 | CCGTGTGTCAAGCTGC | 3-10-3 | cEt | 98 | 17 |
| 481579 | 265 | 278 | CGTGTGTCAAGCTG | 2-10-2 | cEt | 91 | 18 |
| 481355 | 322 | 337 | ACTGCCGCAGCTCCAT | 3-10-3 | cEt | 95 | 19 |
| 481580 | 323 | 336 | CTGCCGCAGCTCCA | 2-10-2 | cEt | 76 | 20 |
| 481356 | 346 | 361 | GACTCTCAATCCAAGG | 3-10-3 | cEt | 83 | 21 |
| 481581 | 347 | 360 | ACTCTCAATCCAAG | 2-10-2 | cEt | 31 | 22 |
| 481357 | 375 | 390 | TTCTTTGCTGGCCGCA | 3-10-3 | cEt | 97 | 23 |
| 481582 | 376 | 389 | TCTTTGCTGGCCGC | 2-10-2 | cEt | 87 | 24 |
| 481358 | 403 | 418 | GATTATGAAACACCAA | 3-10-3 | cEt | 85 | 25 |
| 481583 | 404 | 417 | ATTATGAAACACCA | 2-10-2 | cEt | 20 | 26 |
| 481359 | 429 | 444 | ATACTGCTGGTCAATC | 3-10-3 | cEt | 90 | 27 |
| 481584 | 430 | 443 | TACTGCTGGTCAAT | 2-10-2 | cEt | 42 | 28 |
| 481360 | 459 | 474 | GAGAACATTCGACTCT | 3-10-3 | cEt | 75 | 29 |
| 481585 | 460 | 473 | AGAACATTCGACTC | 2-10-2 | cEt | 77 | 30 |
| 481361 | 474 | 489 | TAGATTGTGCTGATAG | 3-10-3 | cEt | 90 | 31 |
| 481586 | 475 | 488 | AGATTGTGCTGATA | 2-10-2 | cEt | 81 | 32 |
| 481362 | 490 | 505 | ACTGCTTGATTCTTCG | 3-10-3 | cEt | 59 | 33 |
| 481587 | 491 | 504 | CTGCTTGATTCTTC | 2-10-2 | cEt | 23 | 34 |
| 481363 | 511 | 526 | CAAGATACCTGCTCTG | 3-10-3 | cEt | 84 | 35 |
| 481588 | 512 | 525 | AAGATACCTGCTCT | 2-10-2 | cEt | 58 | 36 |
| 481364 | 542 | 557 | GCCACAATCCGGGCAA | 3-10-3 | cEt | 36 | 37 |
| 481589 | 543 | 556 | CCACAATCCGGGCA | 2-10-2 | cEt | 69 | 38 |
| 481365 | 589 | 604 | CAGTGGCTGCAGTCTG | 3-10-3 | cEt | 36 | 39 |
| 481590 | 590 | 603 | AGTGGCTGCAGTCT | 2-10-2 | cEt | 30 | 40 |
| 481366 | 607 | 622 | GGCCCCCTTGCTGGGC | 3-10-3 | cEt | 1 | 41 |
| 481591 | 608 | 621 | GCCCCCTTGCTGGG | 2-10-2 | cEt | 0 | 42 |
| 481367 | 638 | 653 | GTCACCACGGCTGCTG | 3-10-3 | cEt | 70 | 43 |
| 481592 | 639 | 652 | TCACCACGGCTGCT | 2-10-2 | cEt | 48 | 44 |
| 481368 | 659 | 674 | TCCAGCATCTGCTGCT | 3-10-3 | cEt | 81 | 45 |
| 481593 | 660 | 673 | CCAGCATCTGCTGC | 2-10-2 | cEt | 46 | 46 |
| 481369 | 675 | 690 | ATCCTGAAGGTGCTGC | 3-10-3 | cEt | 29 | 47 |
| 481594 | 676 | 689 | TCCTGAAGGTGCTG | 2-10-2 | cEt | 16 | 48 |
| 481370 | 701 | 716 | TCTAGATCCTGCACTC | 3-10-3 | cEt | 79 | 49 |
| 481595 | 702 | 715 | CTAGATCCTGCACT | 2-10-2 | cEt | 47 | 50 |
| 481371 | 709 | 724 | TTTTCTGTTCTAGATC | 3-10-3 | cEt | 83 | 51 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481596 | 710 | 723 | TTTCTGTTCTAGAT | 2-10-2 | cEt | 48 | 52 |
| 481372 | 730 | 745 | GGAGATTCTCTACCAC | 3-10-3 | cEt | 85 | 53 |
| 481597 | 731 | 744 | GAGATTCTCTACCA | 2-10-2 | cEt | 80 | 54 |
| 481373 | 751 | 766 | AGTTGAAATCAAAGTC | 3-10-3 | cEt | 87 | 55 |
| 481598 | 752 | 765 | GTTGAAATCAAAGT | 2-10-2 | cEt | 6 | 56 |
| 481374 | 788 | 803 | AGATCTTGCATGTCTC | 3-10-3 | cEt | 92 | 57 |
| 481599 | 789 | 802 | GATCTTGCATGTCT | 2-10-2 | cEt | 51 | 58 |
| 481375 | 799 | 814 | TGTTTCCATTCAGATC | 3-10-3 | cEt | 65 | 59 |
| 481600 | 800 | 813 | GTTTCCATTCAGAT | 2-10-2 | cEt | 42 | 60 |
| 481376 | 868 | 883 | TCCGCATCTGGTCCAG | 3-10-3 | cEt | 82 | 61 |
| 481601 | 869 | 882 | CCGCATCTGGTCCA | 2-10-2 | cEt | 70 | 62 |
| 481785 | 872 | 885 | TCTCCGCATCTGGT | 2-10-2 | cEt | 28 | 63 |
| 481377 | 884 | 899 | TCACTCACGATGCTTC | 3-10-3 | cEt | 85 | 64 |
| 481602 | 885 | 898 | CACTCACGATGCTT | 2-10-2 | cEt | 55 | 65 |
| 481378 | 892 | 907 | CCGCCAGCTCACTCAC | 3-10-3 | cEt | 89 | 66 |
| 481603 | 893 | 906 | CGCCAGCTCACTCA | 2-10-2 | cEt | 60 | 67 |
| 481379 | 955 | 970 | TCCAGTCAGCCAGCTC | 3-10-3 | cEt | 91 | 68 |
| 481604 | 956 | 969 | CCAGTCAGCCAGCT | 2-10-2 | cEt | 70 | 69 |
| 481380 | 963 | 978 | CCGCCTCTTCCAGTCA | 3-10-3 | cEt | 73 | 70 |
| 481605 | 964 | 977 | CGCCTCTTCCAGTC | 2-10-2 | cEt | 55 | 71 |
| 481381 | 1010 | 1025 | CGATCTAGGCAGATGT | 3-10-3 | cEt | 26 | 72 |
| 481606 | 1011 | 1024 | GATCTAGGCAGATG | 2-10-2 | cEt | 35 | 73 |
| 481382 | 1045 | 1060 | GAGATTCTGCTAATGA | 3-10-3 | cEt | 81 | 74 |
| 481607 | 1046 | 1059 | AGATTCTGCTAATG | 2-10-2 | cEt | 51 | 75 |
| 481383 | 1053 | 1068 | CTGAAGTTGAGATTCT | 3-10-3 | cEt | 84 | 76 |
| 481608 | 1054 | 1067 | TGAAGTTGAGATTC | 2-10-2 | cEt | 26 | 77 |
| 481384 | 1098 | 1113 | AACTTTTTGCTGCAAC | 3-10-3 | cEt | 76 | 78 |
| 481609 | 1099 | 1112 | ACTTTTTGCTGCAA | 2-10-2 | cEt | 34 | 79 |
| 481385 | 1113 | 1128 | GTCCCCTTTGTAGGAA | 3-10-3 | cEt | 41 | 80 |
| 481610 | 1114 | 1127 | TCCCCTTTGTAGGA | 2-10-2 | cEt | 37 | 81 |
| 481386 | 1186 | 1201 | AGGCACTTTTCATTAA | 3-10-3 | cEt | 45 | 82 |
| 481611 | 1187 | 1200 | GGCACTTTTCATTA | 2-10-2 | cEt | 32 | 83 |
| 481387 | 1225 | 1240 | CAGGAT GCAT GGGCAT | 3-10-3 | cEt | 92 | 84 |
| 481612 | 1226 | 1239 | AGGATGCATGGGCA | 2-10-2 | cEt | 86 | 85 |
| 481388 | 1269 | 1284 | TTTAGTAGTGAACTGG | 3-10-3 | cEt | 74 | 86 |
| 481613 | 1270 | 1283 | TTAGTAGTGAACTG | 2-10-2 | cEt | 22 | 87 |
| 481389 | 1282 | 1297 | CCAGCAACCTGACTTT | 3-10-3 | cEt | 66 | 88 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481614 | 1283 | 1296 | CAGCAACCTGACTT | 2-10-2 | cEt | 34 | 89 |
| 481390 | 1305 | 1320 | ATAATTCAACTCAGGG | 3-10-3 | cEt | 92 | 90 |
| 481615 | 1306 | 1319 | TAATTCAACTCAGG | 2-10-2 | cEt | 48 | 91 |
| 481391 | 1314 | 1329 | TTTAAGCTGATAATTC | 3-10-3 | cEt | 44 | 92 |
| 481616 | 1315 | 1328 | TTAAGCTGATAATT | 2-10-2 | cEt | 0 | 93 |
| 481392 | 1326 | 1341 | GCACACTTTAATTTTA | 3-10-3 | cEt | 49 | 94 |
| 481617 | 1327 | 1340 | CACACTTTAATTTT | 2-10-2 | cEt | 1 | 95 |
| 481393 | 1347 | 1362 | GTCCCCAGAGTCTTTG | 3-10-3 | cEt | 39 | 96 |
| 481618 | 1348 | 1361 | TCCCCAGAGTCTTT | 2-10-2 | cEt | 41 | 97 |
| 481394 | 1437 | 1452 | GAGGCTGCCGTTGTTG | 3-10-3 | cEt | 62 | 98 |
| 481619 | 1438 | 1451 | AGGCTGCCGTTGTT | 2-10-2 | cEt | 29 | 99 |
| 481395 | 1468 | 1483 | CCCTCAGGGTCAAGTG | 3-10-3 | cEt | 72 | 100 |
| 481620 | 1469 | 1482 | CCTCAGGGTCAAGT | 2-10-2 | cEt | 37 | 101 |
| 481396 | 1480 | 1495 | CACATCTCTGCTCCCT | 3-10-3 | cEt | 92 | 102 |
| 481621 | 1481 | 1494 | ACATCTCTGCTCCC | 2-10-2 | cEt | 74 | 103 |
| 481397 | 1517 | 1532 | ATCAGGGAAGCATCAC | 3-10-3 | cEt | 59 | 104 |
| 481622 | 1518 | 1531 | TCAGGGAAGCATCA | 2-10-2 | cEt | 49 | 105 |
| 481398 | 1542 | 1557 | GATCAGGTGCAGCTCC | 3-10-3 | cEt | 73 | 106 |
| 481623 | 1543 | 1556 | ATCAGGTGCAGCTC | 2-10-2 | cEt | 40 | 107 |
| 481399 | 1563 | 1578 | ATACACCTCGGTCTCA | 3-10-3 | cEt | 73 | 108 |
| 481624 | 1564 | 1577 | TACACCTCGGTCTC | 2-10-2 | cEt | 43 | 109 |
| 481400 | 1579 | 1594 | TCTTGAGGCCTTGGTG | 3-10-3 | cEt | 47 | 110 |
| 481625 | 1580 | 1593 | CTTGAGGCCTTGGT | 2-10-2 | cEt | 16 | 111 |
| 481401 | 1589 | 1604 | TCTAGGTCAATCTTGA | 3-10-3 | cEt | 74 | 112 |
| 481626 | 1590 | 1603 | CTAGGTCAATCTTG | 2-10-2 | cEt | 54 | 113 |
| 481402 | 1599 | 1614 | GGAGTGGGTCTCTAGG | 3-10-3 | cEt | 52 | 114 |
| 481627 | 1600 | 1613 | GAGTGGGTCTCTAG | 2-10-2 | cEt | 13 | 115 |
| 481789 | 1604 | 1617 | CAAGGAGTGGGTCT | 2-10-2 | cEt | 10 | 116 |
| 481403 | 1607 | 1622 | ACTGGCAAGGAGTGGG | 3-10-3 | cEt | 58 | 117 |
| 481628 | 1608 | 1621 | CTGGCAAGGAGTGG | 2-10-2 | cEt | 38 | 118 |
| 481404 | 1633 | 1648 | TCTGACAGATGTTGGA | 3-10-3 | cEt | 50 | 119 |
| 481629 | 1634 | 1647 | CTGACAGATGTTGG | 2-10-2 | cEt | 64 | 120 |
| 481405 | 1641 | 1656 | ATTTGGCATCTGACAG | 3-10-3 | cEt | 75 | 121 |
| 481630 | 1642 | 1655 | TTTGGCATCTGACA | 2-10-2 | cEt | 39 | 122 |
| 481406 | 1691 | 1706 | TTCTTGGGATTGTTGG | 3-10-3 | cEt | 72 | 123 |
| 481631 | 1692 | 1705 | TCTTGGGATTGTTG | 2-10-2 | cEt | 33 | 124 |
| 481407 | 1729 | 1744 | CCCAGGTTCCAATTGG | 3-10-3 | cEt | 50 | 125 |

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|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481632 | 1730 | 1743 | CCAGGTTCCAATTG | 2-10-2 | cEt | 32 | 126 |
| 481408 | 1780 | 1795 | CTCGCTTGGTGGTGGA | 3-10-3 | cEt | 53 | 127 |
| 481633 | 1781 | 1794 | TCGCTTGGTGGTGG | 2-10-2 | cEt | 35 | 128 |
| 481409 | 1795 | 1810 | GCTCGATGCTCAGTCC | 3-10-3 | cEt | 86 | 129 |
| 481634 | 1796 | 1809 | CTCGATGCTCAGTC | 2-10-2 | cEt | 43 | 130 |
| 481410 | 1825 | 1840 | CCAAGAGTTTCTCTGC | 3-10-3 | cEt | 91 | 131 |
| 481635 | 1826 | 1839 | CAAGAGTTTCTCTG | 2-10-2 | cEt | 43 | 132 |
| 481411 | 1840 | 1855 | AATTCACACCAGGTCC | 3-10-3 | cEt | 72 | 133 |
| 481636 | 1841 | 1854 | ATTCACACCAGGTC | 2-10-2 | cEt | 42 | 134 |
| 481412 | 1858 | 1873 | TGATCTGACACCCTGA | 3-10-3 | cEt | 90 | 135 |
| 481637 | 1859 | 1872 | GATCTGACACCCTG | 2-10-2 | cEt | 79 | 136 |
| 481413 | 1866 | 1881 | AGCCCATGTGATCTGA | 3-10-3 | cEt | 80 | 137 |
| 481638 | 1867 | 1880 | GCCCATGTGATCTG | 2-10-2 | cEt | 64 | 138 |
| 481414 | 1888 | 1903 | CCATGTTTTCTTTGCA | 3-10-3 | cEt | 69 | 139 |
| 481639 | 1889 | 1902 | CATGTTTTCTTTGC | 2-10-2 | cEt | 16 | 140 |
| 481415 | 1896 | 1911 | CTTGCCAGCCATGTTT | 3-10-3 | cEt | 88 | 141 |
| 481640 | 1897 | 1910 | TTGCCAGCCATGTT | 2-10-2 | cEt | 57 | 142 |
| 337332 | 1898 | 1917 | GAAGCCCTTGCCAGCCATGT | 5-10-5 | MOE | 63 | 143 |
| 481416 | 1901 | 1916 | AAGCCCTTGCCAGCCA | 3-10-3 | cEt | 87 | 144 |
| 481641 | 1902 | 1915 | AGCCCTTGCCAGCC | 2-10-2 | cEt | 68 | 145 |
| 337333 | 1903 | 1922 | AAGGAGAAGCCCTTGCCAGC | 5-10-5 | MOE | 49 | 146 |
| 481417 | 1903 | 1918 | AGAAGCCCTTGCCAGC | 3-10-3 | cEt | 97 | 147 |
| 481418 | 1904 | 1919 | GAGAAGCCCTTGCCAG | 3-10-3 | cEt | 92 | 148 |
| 481642 | 1904 | 1917 | GAAGCCCTTGCCAG | 2-10-2 | cEt | 67 | 149 |
| 481419 | 1905 | 1920 | GGAGAAGCCCTTGCCA | 3-10-3 | cEt | 83 | 150 |
| 481643 | 1905 | 1918 | AGAAGCCCTTGCCA | 2-10-2 | cEt | 58 | 151 |
| 481644 | 1906 | 1919 | GAGAAGCCCTTGCC | 2-10-2 | cEt | 45 | 152 |
| 481420 | 1948 | 1963 | ACTTTTTCACAAGGTC | 3-10-3 | cEt | 94 | 153 |
| 481645 | 1949 | 1962 | CTTTTTCACAAGGT | 2-10-2 | cEt | 50 | 154 |
| 481421 | 2021 | 2036 | CTCAAGATGGCCCGCT | 3-10-3 | cEt | 86 | 155 |
| 481646 | 2022 | 2035 | TCAAGATGGCCCGC | 2-10-2 | cEt | 41 | 156 |
| 481422 | 2036 | 2051 | CCTGGAGGCTTAGTGC | 3-10-3 | cEt | 80 | 157 |
| 481647 | 2037 | 2050 | CTGGAGGCTTAGTG | 2-10-2 | cEt | 0 | 158 |
| 481423 | 2077 | 2092 | CTCCTTCTTTGCTGCT | 3-10-3 | cEt | 69 | 159 |
| 481648 | 2078 | 2091 | TCCTTCTTTGCTGC | 2-10-2 | cEt | 51 | 160 |
| 481424 | 2093 | 2108 | CAAGTGAAAGTGACGC | 3-10-3 | cEt | 70 | 161 |
| 481649 | 2094 | 2107 | AAGTGAAAGTGACG | 2-10-2 | cEt | 25 | 162 |

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|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481425 | 2115 | 2130 | ACCGCTGATGTCCTTC | 3-10-3 | cEt | 78 | 163 |
| 481650 | 2116 | 2129 | CCGCTGATGTCCTT | 2-10-2 | cEt | 79 | 164 |
| 481426 | 2131 | 2146 | ACTGGATCTGGGTCTT | 3-10-3 | cEt | 80 | 165 |
| 481651 | 2132 | 2145 | CTGGATCTGGGTCT | 2-10-2 | cEt | 64 | 166 |
| 481427 | 2155 | 2170 | GCTGCTTTGTGTATGG | 3-10-3 | cEt | 75 | 167 |
| 481652 | 2156 | 2169 | CTGCTTTGTGTATG | 2-10-2 | cEt | 82 | 168 |
| 481428 | 2164 | 2179 | TGTTCAGCTGCTGCTT | 3-10-3 | cEt | 77 | 169 |
| 481653 | 2165 | 2178 | GTTCAGCTGCTGCT | 2-10-2 | cEt | 79 | 170 |
| 481429 | 2172 | 2187 | TGACATGTTGTTCAGC | 3-10-3 | cEt | 84 | 171 |
| 481654 | 2173 | 2186 | GACATGTTGTTCAG | 2-10-2 | cEt | 70 | 172 |
| 481430 | 2190 | 2205 | CATGATGATTTCAGCA | 3-10-3 | cEt | 67 | 173 |
| 481655 | 2191 | 2204 | ATGATGATTTCAGC | 2-10-2 | cEt | 31 | 174 |
| 481431 | 2206 | 2221 | CCATGATCTTATAGCC | 3-10-3 | cEt | 91 | 175 |
| 481656 | 2207 | 2220 | CATGATCTTATAGC | 2-10-2 | cEt | 0 | 176 |
| 481432 | 2233 | 2248 | GTGGAGACACCAGGAT | 3-10-3 | cEt | 55 | 177 |
| 481657 | 2234 | 2247 | TGGAGACACCAGGA | 2-10-2 | cEt | 58 | 178 |
| 481433 | 2256 | 2271 | AATGTCAGGATAGAGA | 3-10-3 | cEt | 73 | 179 |
| 481658 | 2257 | 2270 | ATGTCAGGATAGAG | 2-10-2 | cEt | 62 | 180 |
| 481434 | 2266 | 2281 | CCTCCTTGGGAATGTC | 3-10-3 | cEt | 73 | 181 |
| 345785 | 2267 | 2286 | TGCCTCCTCCTTGGGAATGT | 5-10-5 | MOE | 50 | 182 |
| 481659 | 2267 | 2280 | CTCCTTGGGAATGT | 2-10-2 | cEt | 51 | 183 |
| 481435 | 2269 | 2284 | CCTCCTCCTTGGGAAT | 3-10-3 | cEt | 49 | 184 |
| 481660 | 2270 | 2283 | CTCCTCCTTGGGAA | 2-10-2 | cEt | 54 | 185 |
| 481436 | 2275 | 2290 | CGAATGCCTCCTCCTT | 3-10-3 | cEt | 82 | 186 |
| 481661 | 2276 | 2289 | GAATGCCTCCTCCT | 2-10-2 | cEt | 76 | 187 |
| 481437 | 2296 | 2311 | TCTCTGGCCGACAATA | 3-10-3 | cEt | 49 | 188 |
| 481662 | 2297 | 2310 | CTCTGGCCGACAAT | 2-10-2 | cEt | 43 | 189 |
| 481438 | 2353 | 2368 | ACTTGGTCTTCAGGTA | 3-10-3 | cEt | 51 | 190 |
| 481663 | 2354 | 2367 | CTTGGTCTTCAGGT | 2-10-2 | cEt | 52 | 191 |
| 481439 | 2371 | 2386 | TTGGTGTCACACAGAT | 3-10-3 | cEt | 82 | 192 |
| 481664 | 2372 | 2385 | TGGTGTCACACAGA | 2-10-2 | cEt | 89 | 193 |
| 481440 | 2387 | 2402 | GTATTGCTGCAGGTCG | 3-10-3 | cEt | 79 | 194 |
| 481665 | 2388 | 2401 | TATTGCTGCAGGTC | 2-10-2 | cEt | 43 | 195 |
| 481441 | 2395 | 2410 | GGTCAATGGTATTGCT | 3-10-3 | cEt | 55 | 196 |
| 481666 | 2396 | 2409 | GTCAATGGTATTGC | 2-10-2 | cEt | 36 | 197 |
| 481442 | 2403 | 2418 | CATCGGCAGGTCAATG | 3-10-3 | cEt | 44 | 198 |
| 481667 | 2404 | 2417 | ATCGGCAGGTCAAT | 2-10-2 | cEt | 31 | 199 |

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|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481443 | 2423 | 2438 | GAATCTAAAGTGCGGG | 3-10-3 | cEt | 78 | 200 |
| 481668 | 2424 | 2437 | AATCTAAAGTGCGG | 2-10-2 | cEt | 41 | 201 |
| 481444 | 2431 | 2446 | GCATCAATGAATCTAA | 3-10-3 | cEt | 66 | 202 |
| 481669 | 2432 | 2445 | CATCAATGAATCTA | 2-10-2 | cEt | 0 | 203 |
| 481445 | 2439 | 2454 | TCCAAACTGCATCAAT | 3-10-3 | cEt | 70 | 204 |
| 481670 | 2440 | 2453 | CCAAACTGCATCAA | 2-10-2 | cEt | 60 | 205 |
| 481446 | 2460 | 2475 | TTCAGCACCTTCACCA | 3-10-3 | cEt | 44 | 206 |
| 481671 | 2461 | 2474 | TCAGCACCTTCACC | 2-10-2 | cEt | 41 | 207 |
| 481447 | 2476 | 2491 | GCCCTCCTGCTGAGGG | 3-10-3 | cEt | 10 | 208 |
| 481672 | 2477 | 2490 | CCCTCCTGCTGAGG | 2-10-2 | cEt | 15 | 209 |
| 481448 | 2484 | 2499 | CTCAAACTGCCCTCCT | 3-10-3 | cEt | 29 | 210 |
| 481797 | 2484 | 2497 | CAAACTGCCCTCCT | 2-10-2 | cEt | 11 | 211 |
| 481673 | 2485 | 2498 | TCAAACTGCCCTCC | 2-10-2 | cEt | 33 | 212 |
| 481449 | 2503 | 2518 | CCATGTCAAAGGTGAG | 3-10-3 | cEt | 77 | 213 |
| 481674 | 2504 | 2517 | CATGTCAAAGGTGA | 2-10-2 | cEt | 31 | 214 |
| 481450 | 2530 | 2545 | GGGAGGTAGCGCACTC | 3-10-3 | cEt | 53 | 215 |
| 481675 | 2531 | 2544 | GGAGGTAGCGCACT | 2-10-2 | cEt | 41 | 216 |
| 481451 | 2592 | 2607 | GAATGCAGGTAGGCGC | 3-10-3 | cEt | 55 | 217 |
| 481676 | 2593 | 2606 | AATGCAGGTAGGCG | 2-10-2 | cEt | 39 | 218 |
| 481452 | 2631 | 2646 | TTTCAGATGATCTGGG | 3-10-3 | cEt | 71 | 219 |
| 481677 | 2632 | 2645 | TTCAGATGATCTGG | 2-10-2 | cEt | 38 | 220 |
| 481574 | 2650 | 2665 | GGAACCACAAAGTTAG | 3-10-3 | cEt | 69 | 221 |
| 481799 | 2651 | 2664 | GAACCACAAAGTTA | 2-10-2 | cEt | 50 | 222 |
| 481453 | 2681 | 2696 | GATAGCAGAAGTAGGA | 3-10-3 | cEt | 92 | 223 |
| 481678 | 2682 | 2695 | ATAGCAGAAGTAGG | 2-10-2 | cEt | 78 | 224 |
| 481454 | 2702 | 2717 | AAAGTGCCCAGATTGC | 3-10-3 | cEt | 85 | 225 |
| 481679 | 2703 | 2716 | AAGTGCCCAGATTG | 2-10-2 | cEt | 69 | 226 |
| 481455 | 2722 | 2737 | CACTCATTTCTCTATT | 3-10-3 | cEt | 74 | 227 |
| 481680 | 2723 | 2736 | ACTCATTTCTCTAT | 2-10-2 | cEt | 39 | 228 |
| 481456 | 2767 | 2782 | AACACATCCTTATTTG | 3-10-3 | cEt | 48 | 229 |
| 481681 | 2768 | 2781 | ACACATCCTTATTT | 2-10-2 | cEt | 47 | 230 |
| 481457 | 2779 | 2794 | TGGGTCTCAGAGAACA | 3-10-3 | cEt | 88 | 231 |
| 481682 | 2780 | 2793 | GGGTCTCAGAGAAC | 2-10-2 | cEt | 77 | 232 |
| 481458 | 2832 | 2847 | CAAGACATTTCCTTTT | 3-10-3 | cEt | 54 | 233 |
| 481683 | 2833 | 2846 | AAGACATTTCCTTT | 2-10-2 | cEt | 29 | 234 |
| 481459 | 2908 | 2923 | GGAGGCACTTGTCTAA | 3-10-3 | cEt | 76 | 235 |
| 481684 | 2909 | 2922 | GAGGCACTTGTCTA | 2-10-2 | cEt | 89 | 236 |

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|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481460 | 2943 | 2958 | TTACAGAAACAGGCAG | 3-10-3 | cEt | 83 | 237 |
| 481685 | 2944 | 2957 | TACAGAAACAGGCA | 2-10-2 | cEt | 36 | 238 |
| 481461 | 2969 | 2984 | AGCTATAGGTGGCCTG | 3-10-3 | cEt | 75 | 239 |
| 481686 | 2970 | 2983 | GCTATAGGTGGCCT | 2-10-2 | cEt | 70 | 240 |
| 481462 | 2984 | 2999 | ATGCCAGGAGTATGTA | 3-10-3 | cEt | 89 | 241 |
| 481687 | 2985 | 2998 | TGCCAGGAGTATGT | 2-10-2 | cEt | 80 | 242 |
| 481463 | 3001 | 3016 | CAAGGTTAAAAAGTGC | 3-10-3 | cEt | 88 | 243 |
| 481688 | 3002 | 3015 | AAGGTTAAAAAGTG | 2-10-2 | cEt | 13 | 244 |
| 481464 | 3016 | 3031 | CTATTTGGATGTCAGC | 3-10-3 | cEt | 97 | 245 |
| 481689 | 3017 | 3030 | TATTTGGATGTCAG | 2-10-2 | cEt | 40 | 246 |
| 481465 | 3032 | 3047 | TAGATAGTCCTATCTT | 3-10-3 | cEt | 51 | 247 |
| 481690 | 3033 | 3046 | AGATAGTCCTATCT | 2-10-2 | cEt | 64 | 248 |
| 481466 | 3047 | 3062 | AAGAAACCTAGGGCTT | 3-10-3 | cEt | 74 | 249 |
| 481691 | 3048 | 3061 | AGAAACCTAGGGCT | 2-10-2 | cEt | 77 | 250 |
| 481467 | 3097 | 3112 | GCTGATACAGTGTTTT | 3-10-3 | cEt | 74 | 251 |
| 481692 | 3098 | 3111 | CTGATACAGTGTTT | 2-10-2 | cEt | 74 | 252 |
| 481468 | 3112 | 3127 | ATACAGAAAGGCTATG | 3-10-3 | cEt | 71 | 253 |
| 481693 | 3113 | 3126 | TACAGAAAGGCTAT | 2-10-2 | cEt | 25 | 254 |
| 481469 | 3127 | 3142 | GCTTAAGTTTCTTAAA | 3-10-3 | cEt | 61 | 255 |
| 481694 | 3128 | 3141 | CTTAAGTTTCTTAA | 2-10-2 | cEt | 0 | 256 |
| 481470 | 3461 | 3476 | AGCACCAAGGAGGCTG | 3-10-3 | cEt | 49 | 257 |
| 481695 | 3462 | 3475 | GCACCAAGGAGGCT | 2-10-2 | cEt | 83 | 258 |
| 481471 | 3476 | 3491 | AAGCTGAATGCTTAAA | 3-10-3 | cEt | 36 | 259 |
| 481696 | 3477 | 3490 | AGCTGAATGCTTAA | 2-10-2 | cEt | 33 | 260 |
| 481472 | 3491 | 3506 | TTACCAGCCTGAAGGA | 3-10-3 | cEt | 76 | 261 |
| 481697 | 3492 | 3505 | TACCAGCCTGAAGG | 2-10-2 | cEt | 63 | 262 |
| 481473 | 3506 | 3521 | CAGGGATTATATAAAT | 3-10-3 | cEt | 53 | 263 |
| 481698 | 3507 | 3520 | AGGGATTATATAAA | 2-10-2 | cEt | 15 | 264 |
| 481474 | 3521 | 3536 | ACCTGAAGCCCGTTTC | 3-10-3 | cEt | 80 | 265 |
| 481699 | 3522 | 3535 | CCTGAAGCCCGTTT | 2-10-2 | cEt | 57 | 266 |
| 481475 | 3536 | 3551 | TGTCTTAAGGGTTTGA | 3-10-3 | cEt | 93 | 267 |
| 481700 | 3537 | 3550 | GTCTTAAGGGTTTG | 2-10-2 | cEt | 89 | 268 |
| 481476 | 3551 | 3566 | GGTTGCAGCTTCAGAT | 3-10-3 | cEt | 92 | 269 |
| 481701 | 3552 | 3565 | GTTGCAGCTTCAGA | 2-10-2 | cEt | 60 | 270 |
| 481477 | 3567 | 3582 | TCAACACCAAAGGCCA | 3-10-3 | cEt | 95 | 271 |
| 481702 | 3568 | 3581 | CAACACCAAAGGCC | 2-10-2 | cEt | 89 | 272 |
| 481478 | 3585 | 3600 | TCCTTAAACCTTCCTA | 3-10-3 | cEt | 84 | 273 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481703 | 3586 | 3599 | CCTTAAACCTTCCT | 2-10-2 | cEt | 57 | 274 |
| 481479 | 3600 | 3615 | AAAATGCTTAGATTCT | 3-10-3 | cEt | 80 | 275 |
| 481704 | 3601 | 3614 | AAATGCTTAGATTC | 2-10-2 | cEt | 32 | 276 |
| 481480 | 3628 | 3643 | AAATAAGTCTATTTAT | 3-10-3 | cEt | 5 | 277 |
| 481705 | 3629 | 3642 | AATAAGTCTATTTA | 2-10-2 | cEt | 25 | 278 |
| 481481 | 3648 | 3663 | GGCCAATACATTACAA | 3-10-3 | cEt | 63 | 279 |
| 481706 | 3649 | 3662 | GCCAATACATTACA | 2-10-2 | cEt | 56 | 280 |
| 481482 | 3670 | 3685 | TGCCCAGCCTTACTCA | 3-10-3 | cEt | 55 | 281 |
| 481707 | 3671 | 3684 | GCCCAGCCTTACTC | 2-10-2 | cEt | 43 | 282 |
| 481483 | 3685 | 3700 | GTTGTAAGCACCCTCT | 3-10-3 | cEt | 1 | 283 |
| 481708 | 3686 | 3699 | TTGTAAGCACCCTC | 2-10-2 | cEt | 56 | 284 |
| 481484 | 3700 | 3715 | AGAAAGGGAGTCAAGG | 3-10-3 | cEt | 60 | 285 |
| 481709 | 3701 | 3714 | GAAAGGGAGTCAAG | 2-10-2 | cEt | 27 | 286 |
| 481485 | 3717 | 3732 | GCAGATCAAGTCCAGG | 3-10-3 | cEt | 90 | 287 |
| 481710 | 3718 | 3731 | CAGATCAAGTCCAG | 2-10-2 | cEt | 88 | 288 |
| 481486 | 3730 | 3745 | AGCCTCTGAAACAGCA | 3-10-3 | cEt | 75 | 289 |
| 481711 | 3731 | 3744 | GCCTCTGAAACAGC | 2-10-2 | cEt | 74 | 290 |
| 481487 | 3746 | 3761 | CCCACAGAAACAACCT | 3-10-3 | cEt | 66 | 291 |
| 481712 | 3747 | 3760 | CCACAGAAACAACC | 2-10-2 | cEt | 45 | 292 |
| 481488 | 3761 | 3776 | AGCCCTGATAAGGCAC | 3-10-3 | cEt | 23 | 293 |
| 481713 | 3762 | 3775 | GCCCTGATAAGGCA | 2-10-2 | cEt | 18 | 294 |
| 481489 | 3776 | 3791 | AATCAGAAGTATCCCA | 3-10-3 | cEt | 60 | 295 |
| 481714 | 3777 | 3790 | ATCAGAAGTATCCC | 2-10-2 | cEt | 43 | 296 |
| 481490 | 3833 | 3848 | GCCTCTAGCAGGATCA | 3-10-3 | cEt | 78 | 297 |
| 481715 | 3834 | 3847 | CCTCTAGCAGGATC | 2-10-2 | cEt | 79 | 298 |
| 481491 | 3848 | 3863 | CACGCAAGGAGACATG | 3-10-3 | cEt | 70 | 299 |
| 481716 | 3849 | 3862 | ACGCAAGGAGACAT | 2-10-2 | cEt | 68 | 300 |
| 481492 | 3863 | 3878 | TGAGGGACCTTTAGAC | 3-10-3 | cEt | 61 | 301 |
| 481717 | 3864 | 3877 | GAGGGACCTTTAGA | 2-10-2 | cEt | 44 | 302 |
| 481493 | 3886 | 3901 | CAGGATTCCTAAAACA | 3-10-3 | cEt | 43 | 303 |
| 481718 | 3887 | 3900 | AGGATTCCTAAAAC | 2-10-2 | cEt | 7 | 304 |
| 481494 | 3901 | 3916 | ATGAGGTCCTGAGACC | 3-10-3 | cEt | 60 | 305 |
| 481719 | 3902 | 3915 | TGAGGTCCTGAGAC | 2-10-2 | cEt | 29 | 306 |
| 481495 | 3940 | 3955 | CATCATGTCCAACCTG | 3-10-3 | cEt | 92 | 307 |
| 481720 | 3941 | 3954 | ATCATGTCCAACCT | 2-10-2 | cEt | 63 | 308 |
| 481496 | 3955 | 3970 | GGGCCCCATAGTGTGC | 3-10-3 | cEt | 29 | 309 |
| 481721 | 3956 | 3969 | GGCCCCATAGTGTG | 2-10-2 | cEt | 19 | 310 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481497 | 3977 | 3992 | AGCTCAACCAGACACG | 3-10-3 | cEt | 67 | 311 |
| 481722 | 3978 | 3991 | GCTCAACCAGACAC | 2-10-2 | cEt | 69 | 312 |
| 481498 | 3992 | 4007 | GAACCATATTCCCTGA | 3-10-3 | cEt | 90 | 313 |
| 481723 | 3993 | 4006 | AACCATATTCCCTG | 2-10-2 | cEt | 49 | 314 |
| 481499 | 4007 | 4022 | CAAGAAACTGGCTAAG | 3-10-3 | cEt | 43 | 315 |
| 481724 | 4008 | 4021 | AAGAAACTGGCTAA | 2-10-2 | cEt | 17 | 316 |
| 481500 | 4022 | 4037 | GCCACTGGATATCACC | 3-10-3 | cEt | 92 | 317 |
| 481501 | 4048 | 4063 | AACTGAATGAAGACGC | 3-10-3 | cEt | 91 | 318 |
| 481726 | 4049 | 4062 | ACTGAATGAAGACG | 2-10-2 | cEt | 56 | 319 |
| 481502 | 4063 | 4078 | CCTTTGCCCTGCATGA | 3-10-3 | cEt | 85 | 320 |
| 481727 | 4064 | 4077 | CTTTGCCCTGCATG | 2-10-2 | cEt | 70 | 321 |
| 481503 | 4078 | 4093 | AAGTTTATCAGTAAGC | 3-10-3 | cEt | 57 | 322 |
| 481728 | 4079 | 4092 | AGTTTATCAGTAAG | 2-10-2 | cEt | 22 | 323 |
| 481504 | 4093 | 4108 | TACGAGGGCAGACTCA | 3-10-3 | cEt | 60 | 324 |
| 481729 | 4094 | 4107 | ACGAGGGCAGACTC | 2-10-2 | cEt | 22 | 325 |
| 481505 | 4108 | 4123 | AGGTATACACCCTCAT | 3-10-3 | cEt | 45 | 326 |
| 481730 | 4109 | 4122 | GGTATACACCCTCA | 2-10-2 | cEt | 47 | 327 |
| 481506 | 4123 | 4138 | CCTCAGAGGGAGGCCA | 3-10-3 | cEt | 32 | 328 |
| 481731 | 4124 | 4137 | CTCAGAGGGAGGCC | 2-10-2 | cEt | 0 | 329 |
| 481507 | 4138 | 4153 | GGGAGGAGTCACCAGC | 3-10-3 | cEt | 64 | 330 |
| 481732 | 4139 | 4152 | GGAGGAGTCACCAG | 2-10-2 | cEt | 59 | 331 |
| 481508 | 4205 | 4220 | TAGCCAGCCAAGGCGG | 3-10-3 | cEt | 33 | 332 |
| 481733 | 4206 | 4219 | AGCCAGCCAAGGCG | 2-10-2 | cEt | 50 | 333 |
| 481509 | 4220 | 4235 | ACAGGAGAGGCGAGCT | 3-10-3 | cEt | 46 | 334 |
| 481734 | 4221 | 4234 | CAGGAGAGGCGAGC | 2-10-2 | cEt | 28 | 335 |
| 481510 | 4237 | 4252 | TAGGTGTTCCCATACG | 3-10-3 | cEt | 95 | 336 |
| 481735 | 4238 | 4251 | AGGTGTTCCCATAC | 2-10-2 | cEt | 22 | 337 |
| 481511 | 4258 | 4273 | GGCAGCCCATCCAGCA | 3-10-3 | cEt | 43 | 338 |
| 481736 | 4259 | 4272 | GCAGCCCATCCAGC | 2-10-2 | cEt | 54 | 339 |
| 481512 | 4275 | 4290 | CATGCCTCTGAGTCAG | 3-10-3 | cEt | 30 | 340 |
| 481737 | 4276 | 4289 | ATGCCTCTGAGTCA | 2-10-2 | cEt | 31 | 341 |
| 481513 | 4290 | 4305 | GTTGCCAAATCCGGCC | 3-10-3 | cEt | 85 | 342 |
| 481738 | 4291 | 4304 | TTGCCAAATCCGGC | 2-10-2 | cEt | 70 | 343 |
| 481514 | 4305 | 4320 | GCAAGGTGGTTTTGAG | 3-10-3 | cEt | 85 | 344 |
| 481739 | 4306 | 4319 | CAAGGTGGTTTTGA | 2-10-2 | cEt | 60 | 345 |
| 481515 | 4325 | 4340 | AGAAACTCTGATCAGC | 3-10-3 | cEt | 88 | 346 |
| 481740 | 4326 | 4339 | GAAACTCTGATCAG | 2-10-2 | cEt | 71 | 347 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481516 | 4364 | 4379 | CAGAGACCAGCTAATT | 3-10-3 | cEt | 78 | 348 |
| 481741 | 4365 | 4378 | AGAGACCAGCTAAT | 2-10-2 | cEt | 80 | 349 |
| 481517 | 4394 | 4409 | ATCTTAGAGAAGGTCG | 3-10-3 | cEt | 87 | 350 |
| 481742 | 4395 | 4408 | TCTTAGAGAAGGTC | 2-10-2 | cEt | 64 | 351 |
| 481518 | 4425 | 4440 | CCAGGCAGGAGGACTG | 3-10-3 | cEt | 67 | 352 |
| 481743 | 4426 | 4439 | CAGGCAGGAGGACT | 2-10-2 | cEt | 75 | 353 |
| 481519 | 4437 | 4452 | CATCAACTGTCTCCAG | 3-10-3 | cEt | 29 | 354 |
| 481744 | 4438 | 4451 | ATCAACTGTCTCCA | 2-10-2 | cEt | 69 | 355 |
| 481520 | 4439 | 4454 | CACATCAACTGTCTCC | 3-10-3 | cEt | 73 | 356 |
| 481745 | 4440 | 4453 | ACATCAACTGTCTC | 2-10-2 | cEt | 74 | 357 |
| 481521 | 4459 | 4474 | GAAGTAAGAGCTCTGC | 3-10-3 | cEt | 86 | 358 |
| 481746 | 4460 | 4473 | AAGTAAGAGCTCTG | 2-10-2 | cEt | 67 | 359 |
| 481522 | 4474 | 4489 | AAGAGTGTTGCTGGAG | 3-10-3 | cEt | 92 | 360 |
| 481747 | 4475 | 4488 | AGAGTGTTGCTGGA | 2-10-2 | cEt | 95 | 361 |
| 481523 | 4489 | 4504 | GCTTATTATGTACTGA | 3-10-3 | cEt | 95 | 362 |
| 481748 | 4490 | 4503 | CTTATTATGTACTG | 2-10-2 | cEt | 15 | 363 |
| 481524 | 4530 | 4545 | GCCCAAGTCTCACCTT | 3-10-3 | cEt | 70 | 364 |
| 481749 | 4531 | 4544 | CCCAAGTCTCACCT | 2-10-2 | cEt | 70 | 365 |
| 481525 | 4541 | 4556 | CCCAATGGTAAGCCCA | 3-10-3 | cEt | 93 | 366 |
| 481750 | 4542 | 4555 | CCAATGGTAAGCCC | 2-10-2 | cEt | 94 | 367 |
| 481526 | 4543 | 4558 | AACCCAATGGTAAGCC | 3-10-3 | cEt | 82 | 368 |
| 481751 | 4544 | 4557 | ACCCAATGGTAAGC | 2-10-2 | cEt | 54 | 369 |
| 481527 | 4560 | 4575 | TAGGTCCCTATGATTT | 3-10-3 | cEt | 55 | 370 |
| 481752 | 4561 | 4574 | AGGTCCCTATGATT | 2-10-2 | cEt | 62 | 371 |
| 481528 | 4579 | 4594 | AAGCCCTGAACCCTCG | 3-10-3 | cEt | 77 | 372 |
| 481753 | 4580 | 4593 | AGCCCTGAACCCTC | 2-10-2 | cEt | 71 | 373 |
| 481529 | 4615 | 4630 | CCTAAGGCCATGAACT | 3-10-3 | cEt | 64 | 374 |
| 481754 | 4616 | 4629 | CTAAGGCCATGAAC | 2-10-2 | cEt | 53 | 375 |
| 481530 | 4630 | 4645 | ACCAGATACATGCTAC | 3-10-3 | cEt | 87 | 376 |
| 481755 | 4631 | 4644 | CCAGATACATGCTA | 2-10-2 | cEt | 84 | 377 |
| 481531 | 4646 | 4661 | TACAATCAGAGTTAAG | 3-10-3 | cEt | 66 | 378 |
| 481756 | 4647 | 4660 | ACAATCAGAGTTAA | 2-10-2 | cEt | 5 | 379 |
| 481532 | 4664 | 4679 | TCCTCTCAGAACTTTT | 3-10-3 | cEt | 65 | 380 |
| 481757 | 4665 | 4678 | CCTCTCAGAACTTT | 2-10-2 | cEt | 81 | 381 |
| 481533 | 4666 | 4681 | GCTCCTCTCAGAACTT | 3-10-3 | cEt | 80 | 382 |
| 481758 | 4667 | 4680 | CTCCTCTCAGAACT | 2-10-2 | cEt | 62 | 383 |
| 481534 | 4693 | 4708 | TTCTTTAATGGGCCAC | 3-10-3 | cEt | 79 | 384 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481759 | 4694 | 4707 | TCTTTAATGGGCCA | 2-10-2 | cEt | 74 | 385 |
| 481535 | 4767 | 4782 | ACGGGATTCCCTCGGC | 3-10-3 | cEt | 78 | 386 |
| 481760 | 4768 | 4781 | CGGGATTCCCTCGG | 2-10-2 | cEt | 78 | 387 |
| 481536 | 4782 | 4797 | GTAGGTAAGCAACCCA | 3-10-3 | cEt | 91 | 388 |
| 481761 | 4783 | 4796 | TAGGTAAGCAACCC | 2-10-2 | cEt | 78 | 389 |
| 481537 | 4830 | 4845 | GAATTTGAATGCAGTG | 3-10-3 | cEt | 84 | 390 |
| 481762 | 4831 | 4844 | AATTTGAATGCAGT | 2-10-2 | cEt | 2 | 391 |
| 481538 | 4844 | 4859 | TGAAGTACACATTGGA | 3-10-3 | cEt | 92 | 392 |
| 481763 | 4845 | 4858 | GAAGTACACATTGG | 2-10-2 | cEt | 96 | 393 |
| 481539 | 4860 | 4875 | ATAAATTTTTACACTA | 3-10-3 | cEt | 19 | 394 |
| 481764 | 4861 | 4874 | TAAATTTTTACACT | 2-10-2 | cEt | 1 | 395 |
| 481765 | 4869 | 4882 | CAATAATATAAATT | 2-10-2 | cEt | 0 | 396 |
| 481541 | 4934 | 4949 | CTGGAAGTTAAAGTAG | 3-10-3 | cEt | 71 | 397 |
| 481766 | 4935 | 4948 | TGGAAGTTAAAGTA | 2-10-2 | cEt | 10 | 398 |

**Table 2**

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481350 | 1065 | 1080 | TCCAGGATCCGGTTGG | 3-10-3 | cEt | 52 | 9 |
| 481575 | 1066 | 1079 | CCAGGATCCGGTTG | 2-10-2 | cEt | 41 | 10 |
| 481351 | 1121 | 1136 | GGCCGAAGGGCCTCTC | 3-10-3 | cEt | 14 | 11 |
| 481576 | 1122 | 1135 | GCCGAAGGGCCTCT | 2-10-2 | cEt | 8 | 12 |
| 481542 | 1988 | 2003 | GGCTCAATTATTTATC | 3-10-3 | cEt | 64 | 399 |
| 481767 | 1989 | 2002 | GCTCAATTATTTAT | 2-10-2 | cEt | 0 | 400 |
| 481543 | 1996 | 2011 | AATGCAATGGCTCAAT | 3-10-3 | cEt | 84 | 401 |
| 481768 | 1997 | 2010 | AT GCAATGGCTCAA | 2-10-2 | cEt | 95 | 402 |
| 481544 | 2004 | 2019 | ATCCAGTAAATGCAAT | 3-10-3 | cEt | 58 | 403 |
| 481769 | 2005 | 2018 | TCCAGTAAATGCAA | 2-10-2 | cEt | 55 | 404 |
| 481545 | 2061 | 2076 | AGAAAACTCCCACTCT | 3-10-3 | cEt | 36 | 405 |
| 481770 | 2062 | 2075 | GAAAACTCCCACTC | 2-10-2 | cEt | 42 | 406 |
| 481546 | 2113 | 2128 | CTGTCTTTGTTTCCCT | 3-10-3 | cEt | 70 | 407 |
| 481771 | 2114 | 2127 | TGTCTTTGTTTCCC | 2-10-2 | cEt | 75 | 408 |
| 481547 | 2121 | 2136 | AGGCCAGCCTGTCTTT | 3-10-3 | cEt | 87 | 409 |
| 481772 | 2122 | 2135 | GGCCAGCCTGTCTT | 2-10-2 | cEt | 53 | 410 |
| 481548 | 2705 | 2720 | CTAATGGTTCTTTGTG | 3-10-3 | cEt | 78 | 411 |
| 481773 | 2706 | 2719 | TAATGGTTCTTTGT | 2-10-2 | cEt | 9 | 412 |
| 481549 | 6476 | 6491 | GAAATTCATTCTTCCA | 3-10-3 | cEt | 96 | 413 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481774 | 6477 | 6490 | AAATTCATTCTTCC | 2-10-2 | cEt | 56 | 414 |
| 481550 | 10001 | 10016 | ACACACACAGATGTGA | 3-10-3 | cEt | 48 | 415 |
| 481775 | 10002 | 10015 | CACACACAGATGTG | 2-10-2 | cEt | 35 | 416 |
| 481551 | 10337 | 10352 | CTACCCAAACATCCCC | 3-10-3 | cEt | 69 | 417 |
| 481776 | 10338 | 10351 | TACCCAAACATCCC | 2-10-2 | cEt | 62 | 418 |
| 481552 | 10345 | 10360 | TACAAAAACTACCCAA | 3-10-3 | cEt | 30 | 419 |
| 481777 | 10346 | 10359 | ACAAAAACTACCCA | 2-10-2 | cEt | 1 | 420 |
| 481553 | 10364 | 10379 | AGTTTTCAGAAATGGC | 3-10-3 | cEt | 96 | 421 |
| 481778 | 10365 | 10378 | GTTTTCAGAAATGG | 2-10-2 | cEt | 47 | 422 |
| 481554 | 15469 | 15484 | CAAGCTTTTCTATGAA | 3-10-3 | cEt | 86 | 423 |
| 481779 | 15470 | 15483 | AAGCTTTTCTATGA | 2-10-2 | cEt | 60 | 424 |
| 481555 | 24588 | 24603 | TTATTCAGGTCACTTT | 3-10-3 | cEt | 73 | 425 |
| 481780 | 24589 | 24602 | TATTCAGGTCACTT | 2-10-2 | cEt | 60 | 426 |
| 481352 | 40953 | 40968 | CCTGCTAAAATCAGGG | 3-10-3 | cEt | 15 | 13 |
| 481577 | 40954 | 40967 | CTGCTAAAATCAGG | 2-10-2 | cEt | 12 | 14 |
| 481353 | 40968 | 40983 | ATTCCATTGGGCCATC | 3-10-3 | cEt | 78 | 15 |
| 481578 | 40969 | 40982 | TTCCATTGGGCCAT | 2-10-2 | cEt | 51 | 16 |
| 481354 | 40992 | 41007 | CCGTGTGTCAAGCTGC | 3-10-3 | cEt | 98 | 17 |
| 481579 | 40993 | 41006 | CGTGTGTCAAGCTG | 2-10-2 | cEt | 91 | 18 |
| 481355 | 41050 | 41065 | ACTGCCGCAGCTCCAT | 3-10-3 | cEt | 95 | 19 |
| 481580 | 41051 | 41064 | CTGCCGCAGCTCCA | 2-10-2 | cEt | 76 | 20 |
| 481356 | 41074 | 41089 | GACTCTCAATCCAAGG | 3-10-3 | cEt | 83 | 21 |
| 481581 | 41075 | 41088 | ACTCTCAATCCAAG | 2-10-2 | cEt | 31 | 22 |
| 481556 | 42765 | 42780 | GCATATGCCCTAGGAA | 3-10-3 | cEt | 23 | 430 |
| 481781 | 42766 | 42779 | CATATGCCCTAGGA | 2-10-2 | cEt | 15 | 431 |
| 481357 | 42778 | 42793 | TTCTTTGCTGGCCGCA | 3-10-3 | cEt | 97 | 23 |
| 481582 | 42779 | 42792 | TCTTTGCTGGCCGC | 2-10-2 | cEt | 87 | 24 |
| 481358 | 42806 | 42821 | GATTATGAAACACCAA | 3-10-3 | cEt | 85 | 25 |
| 481583 | 42807 | 42820 | ATTATGAAACACCA | 2-10-2 | cEt | 20 | 26 |
| 481359 | 42832 | 42847 | ATACTGCTGGTCAATC | 3-10-3 | cEt | 90 | 27 |
| 481584 | 42833 | 42846 | TACTGCTGGTCAAT | 2-10-2 | cEt | 42 | 28 |
| 481360 | 42862 | 42877 | GAGAACATTCGACTCT | 3-10-3 | cEt | 75 | 29 |
| 481585 | 42863 | 42876 | AGAACATTCGACTC | 2-10-2 | cEt | 77 | 30 |
| 481361 | 42877 | 42892 | TAGATTGTGCTGATAG | 3-10-3 | cEt | 90 | 31 |
| 481586 | 42878 | 42891 | AGATTGTGCTGATA | 2-10-2 | cEt | 81 | 32 |
| 481362 | 42893 | 42908 | ACTGCTTGATTCTTCG | 3-10-3 | cEt | 59 | 33 |
| 481587 | 42894 | 42907 | CTGCTTGATTCTTC | 2-10-2 | cEt | 23 | 34 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481557 | 43043 | 43058 | GCTAATTACTTCTCCT | 3-10-3 | cEt | 57 | 432 |
| 481782 | 43044 | 43057 | CTAATTACTTCTCC | 2-10-2 | cEt | 25 | 433 |
| 481588 | 43826 | 43839 | AAGATACCTGCTCT | 2-10-2 | cEt | 58 | 36 |
| 481364 | 43856 | 43871 | GCCACAATCCGGGCAA | 3-10-3 | cEt | 36 | 37 |
| 481589 | 43857 | 43870 | CCACAATCCGGGCA | 2-10-2 | cEt | 69 | 38 |
| 481365 | 43903 | 43918 | CAGTGGCTGCAGTCTG | 3-10-3 | cEt | 36 | 39 |
| 481590 | 43904 | 43917 | AGTGGCTGCAGTCT | 2-10-2 | cEt | 30 | 40 |
| 481558 | 50069 | 50084 | GCCCCCTTGCTGCCAA | 3-10-3 | cEt | 0 | 434 |
| 481783 | 50070 | 50083 | CCCCCTTGCTGCCA | 2-10-2 | cEt | 39 | 435 |
| 481367 | 50101 | 50116 | GTCACCACGGCTGCTG | 3-10-3 | cEt | 70 | 43 |
| 481592 | 50102 | 50115 | TCACCACGGCTGCT | 2-10-2 | cEt | 48 | 44 |
| 481368 | 50122 | 50137 | TCCAGCATCTGCTGCT | 3-10-3 | cEt | 81 | 45 |
| 481593 | 50123 | 50136 | CCAGCATCTGCTGC | 2-10-2 | cEt | 46 | 46 |
| 481369 | 50138 | 50153 | ATCCTGAAGGTGCTGC | 3-10-3 | cEt | 29 | 47 |
| 481594 | 50139 | 50152 | TCCTGAAGGTGCTG | 2-10-2 | cEt | 16 | 48 |
| 481559 | 50668 | 50683 | TGTTCTAGATCCTGTT | 3-10-3 | cEt | 72 | 436 |
| 481784 | 50669 | 50682 | GTTCTAGATCCTGT | 2-10-2 | cEt | 79 | 437 |
| 481371 | 50673 | 50688 | TTTTCTGTTCTAGATC | 3-10-3 | cEt | 83 | 51 |
| 481596 | 50674 | 50687 | TTTCTGTTCTAGAT | 2-10-2 | cEt | 48 | 52 |
| 481372 | 50694 | 50709 | GGAGATTCTCTACCAC | 3-10-3 | cEt | 85 | 53 |
| 481597 | 50695 | 50708 | GAGATTCTCTACCA | 2-10-2 | cEt | 80 | 54 |
| 481373 | 50715 | 50730 | AGTTGAAATCAAAGTC | 3-10-3 | cEt | 87 | 55 |
| 481598 | 50716 | 50729 | GTTGAAATCAAAGT | 2-10-2 | cEt | 6 | 56 |
| 481599 | 51626 | 51639 | GATCTTGCATGTCT | 2-10-2 | cEt | 51 | 58 |
| 481375 | 51636 | 51651 | TGTTTCCATTCAGATC | 3-10-3 | cEt | 65 | 59 |
| 481600 | 51637 | 51650 | GTTTCCATTCAGAT | 2-10-2 | cEt | 42 | 60 |
| 481376 | 51705 | 51720 | TCCGCATCTGGTCCAG | 3-10-3 | cEt | 82 | 61 |
| 481601 | 51706 | 51719 | CCGCATCTGGTCCA | 2-10-2 | cEt | 70 | 62 |
| 481560 | 51708 | 51723 | CTCTCCGCATCTGGTC | 3-10-3 | cEt | 63 | 438 |
| 481785 | 51709 | 51722 | TCTCCGCATCTGGT | 2-10-2 | cEt | 28 | 63 |
| 481378 | 51905 | 51920 | CCGCCAGCTCACTCAC | 3-10-3 | cEt | 89 | 66 |
| 481603 | 51906 | 51919 | CGCCAGCTCACTCA | 2-10-2 | cEt | 60 | 67 |
| 481379 | 51968 | 51983 | TCCAGTCAGCCAGCTC | 3-10-3 | cEt | 91 | 68 |
| 481604 | 51969 | 51982 | CCAGTCAGCCAGCT | 2-10-2 | cEt | 70 | 69 |
| 481380 | 51976 | 51991 | CCGCCTCTTCCAGTCA | 3-10-3 | cEt | 73 | 70 |
| 481605 | 51977 | 51990 | CGCCTCTTCCAGTC | 2-10-2 | cEt | 55 | 71 |
| 481381 | 52023 | 52038 | CGATCTAGGCAGATGT | 3-10-3 | cEt | 26 | 72 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481606 | 52024 | 52037 | GATCTAGGCAGATG | 2-10-2 | cEt | 35 | 73 |
| 481382 | 55443 | 55458 | GAGATTCTGCTAATGA | 3-10-3 | cEt | 81 | 74 |
| 481607 | 55444 | 55457 | AGATTCTGCTAATG | 2-10-2 | cEt | 51 | 75 |
| 481383 | 55451 | 55466 | CTGAAGTTGAGATTCT | 3-10-3 | cEt | 84 | 76 |
| 481608 | 55452 | 55465 | TGAAGTTGAGATTC | 2-10-2 | cEt | 26 | 77 |
| 481384 | 55496 | 55511 | AACTTTTTGCTGCAAC | 3-10-3 | cEt | 76 | 78 |
| 481609 | 55497 | 55510 | ACTTTTTGCTGCAA | 2-10-2 | cEt | 34 | 79 |
| 481385 | 55511 | 55526 | GTCCCCTTTGTAGGAA | 3-10-3 | cEt | 41 | 80 |
| 481610 | 55512 | 55525 | TCCCCTTTGTAGGA | 2-10-2 | cEt | 37 | 81 |
| 481387 | 55748 | 55763 | CAGGATGCATGGGCAT | 3-10-3 | cEt | 92 | 84 |
| 481612 | 55749 | 55762 | AGGATGCATGGGCA | 2-10-2 | cEt | 86 | 85 |
| 481388 | 55792 | 55807 | TTTAGTAGTGAACTGG | 3-10-3 | cEt | 74 | 86 |
| 481613 | 55793 | 55806 | TTAGTAGTGAACTG | 2-10-2 | cEt | 22 | 87 |
| 481561 | 57949 | 57964 | TGACCAGCAACCTATT | 3-10-3 | cEt | 43 | 439 |
| 481786 | 57950 | 57963 | GACCAGCAACCTAT | 2-10-2 | cEt | 59 | 440 |
| 481390 | 57969 | 57984 | ATAATTCAACTCAGGG | 3-10-3 | cEt | 92 | 90 |
| 481615 | 57970 | 57983 | TAATTCAACTCAGG | 2-10-2 | cEt | 48 | 91 |
| 481391 | 57978 | 57993 | TTTAAGCTGATAATTC | 3-10-3 | cEt | 44 | 92 |
| 481616 | 57979 | 57992 | TTAAGCTGATAATT | 2-10-2 | cEt | 0 | 93 |
| 481392 | 57990 | 58005 | GCACACTTTAATTTTA | 3-10-3 | cEt | 49 | 94 |
| 481617 | 57991 | 58004 | CACACTTTAATTTT | 2-10-2 | cEt | 1 | 95 |
| 481562 | 59703 | 59718 | CCCAGAGTCTCTGTAA | 3-10-3 | cEt | 36 | 441 |
| 481787 | 59704 | 59717 | CCAGAGTCTCTGTA | 2-10-2 | cEt | 22 | 442 |
| 481394 | 59895 | 59910 | GAGGCTGCCGTTGTTG | 3-10-3 | cEt | 62 | 98 |
| 481619 | 59896 | 59909 | AGGCTGCCGTTGTT | 2-10-2 | cEt | 29 | 99 |
| 481396 | 60034 | 60049 | CACATCTCTGCTCCCT | 3-10-3 | cEt | 92 | 102 |
| 481621 | 60035 | 60048 | ACATCTCTGCTCCC | 2-10-2 | cEt | 74 | 103 |
| 481563 | 60064 | 60079 | TTACATCACAATTGGC | 3-10-3 | cEt | 24 | 445 |
| 481788 | 60065 | 60078 | TACATCACAATTGG | 2-10-2 | cEt | 3 | 446 |
| 481398 | 63306 | 63321 | GATCAGGTGCAGCTCC | 3-10-3 | cEt | 73 | 106 |
| 481623 | 63307 | 63320 | ATCAGGTGCAGCTC | 2-10-2 | cEt | 40 | 107 |
| 481399 | 63327 | 63342 | ATACACCTCGGTCTCA | 3-10-3 | cEt | 73 | 108 |
| 481624 | 63328 | 63341 | TACACCTCGGTCTC | 2-10-2 | cEt | 43 | 109 |
| 481400 | 63343 | 63358 | TCTTGAGGCCTTGGTG | 3-10-3 | cEt | 47 | 110 |
| 481625 | 63344 | 63357 | CTTGAGGCCTTGGT | 2-10-2 | cEt | 16 | 111 |
| 481401 | 63353 | 63368 | TCTAGGTCAATCTTGA | 3-10-3 | cEt | 74 | 112 |
| 481626 | 63354 | 63367 | CTAGGTCAATCTTG | 2-10-2 | cEt | 54 | 113 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481564 | 64421 | 64436 | GCAAGGAGTGGGTCTG | 3-10-3 | cEt | 33 | 446 |
| 481789 | 64422 | 64435 | CAAGGAGTGGGTCT | 2-10-2 | cEt | 10 | 116 |
| 481403 | 64425 | 64440 | ACTGGCAAGGAGTGGG | 3-10-3 | cEt | 58 | 117 |
| 481628 | 64426 | 64439 | CTGGCAAGGAGTGG | 2-10-2 | cEt | 38 | 118 |
| 481404 | 64451 | 64466 | TCTGACAGATGTTGGA | 3-10-3 | cEt | 50 | 119 |
| 481629 | 64452 | 64465 | CTGACAGATGTTGG | 2-10-2 | cEt | 64 | 120 |
| 481405 | 64459 | 64474 | ATTTGGCATCTGACAG | 3-10-3 | cEt | 75 | 121 |
| 481630 | 64460 | 64473 | TTTGGCATCTGACA | 2-10-2 | cEt | 39 | 122 |
| 481407 | 64663 | 64678 | CCCAGGTTCCAATTGG | 3-10-3 | cEt | 50 | 125 |
| 481632 | 64664 | 64677 | CCAGGTTCCAATTG | 2-10-2 | cEt | 32 | 126 |
| 481408 | 64714 | 64729 | CTCGCTTGGTGGTGGA | 3-10-3 | cEt | 53 | 127 |
| 481633 | 64715 | 64728 | TCGCTTGGTGGTGG | 2-10-2 | cEt | 35 | 128 |
| 481409 | 64729 | 64744 | GCTCGATGCTCAGTCC | 3-10-3 | cEt | 86 | 129 |
| 481634 | 64730 | 64743 | CTCGATGCTCAGTC | 2-10-2 | cEt | 43 | 130 |
| 481410 | 64759 | 64774 | CCAAGAGTTTCTCTGC | 3-10-3 | cEt | 91 | 131 |
| 481635 | 64760 | 64773 | CAAGAGTTTCTCTG | 2-10-2 | cEt | 43 | 132 |
| 481411 | 65859 | 65874 | AATTCACACCAGGTCC | 3-10-3 | cEt | 72 | 133 |
| 481636 | 65860 | 65873 | ATTCACACCAGGTC | 2-10-2 | cEt | 42 | 134 |
| 481412 | 65877 | 65892 | TGATCTGACACCCTGA | 3-10-3 | cEt | 90 | 135 |
| 481637 | 65878 | 65891 | GATCTGACACCCTG | 2-10-2 | cEt | 79 | 136 |
| 481413 | 65885 | 65900 | AGCCCATGTGATCTGA | 3-10-3 | cEt | 80 | 137 |
| 481638 | 65886 | 65899 | GCCCATGTGATCTG | 2-10-2 | cEt | 64 | 138 |
| 481565 | 66119 | 66134 | TTTCCTGGAGAAAAGA | 3-10-3 | cEt | 4 | 447 |
| 481790 | 66120 | 66133 | TTCCTGGAGAAAAG | 2-10-2 | cEt | 3 | 448 |
| 481566 | 66127 | 66142 | AGCCATGTTTTCCTGG | 3-10-3 | cEt | 62 | 449 |
| 481791 | 66128 | 66141 | GCCATGTTTTCCTG | 2-10-2 | cEt | 73 | 450 |
| 481415 | 66133 | 66148 | CTTGCCAGCCATGTTT | 3-10-3 | cEt | 88 | 141 |
| 481640 | 66134 | 66147 | TTGCCAGCCATGTT | 2-10-2 | cEt | 57 | 142 |
| 337332 | 66135 | 66154 | GAAGCCCTTGCCAGCCATGT | 5-10-5 | MOE | 63 | 143 |
| 481416 | 66138 | 66153 | AAGCCCTTGCCAGCCA | 3-10-3 | cEt | 87 | 144 |
| 481641 | 66139 | 66152 | AGCCCTTGCCAGCC | 2-10-2 | cEt | 68 | 145 |
| 337333 | 66140 | 66159 | AAGGAGAAGCCCTTGCCAGC | 5-10-5 | MOE | 49 | 146 |
| 481417 | 66140 | 66155 | AGAAGCCCTTGCCAGC | 3-10-3 | cEt | 97 | 147 |
| 481418 | 66141 | 66156 | GAGAAGCCCTTGCCAG | 3-10-3 | cEt | 92 | 148 |
| 481642 | 66141 | 66154 | GAAGCCCTTGCCAG | 2-10-2 | cEt | 67 | 149 |
| 481419 | 66142 | 66157 | GGAGAAGCCCTTGCCA | 3-10-3 | cEt | 83 | 150 |
| 481643 | 66142 | 66155 | AGAAGCCCTTGCCA | 2-10-2 | cEt | 58 | 151 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481644 | 66143 | 66156 | GAGAAGCCCTTGCC | 2-10-2 | cEt | 45 | 152 |
| 481420 | 66185 | 66200 | ACTTTTTCACAAGGTC | 3-10-3 | cEt | 94 | 153 |
| 481645 | 66186 | 66199 | CTTTTTCACAAGGT | 2-10-2 | cEt | 50 | 154 |
| 481421 | 66374 | 66389 | CTCAAGATGGCCCGCT | 3-10-3 | cEt | 86 | 155 |
| 481646 | 66375 | 66388 | TCAAGATGGCCCGC | 2-10-2 | cEt | 41 | 156 |
| 481422 | 66389 | 66404 | CCTGGAGGCTTAGTGC | 3-10-3 | cEt | 80 | 157 |
| 481647 | 66390 | 66403 | CTGGAGGCTTAGTG | 2-10-2 | cEt | 0 | 158 |
| 481423 | 66430 | 66445 | CTCCTTCTTTGCTGCT | 3-10-3 | cEt | 69 | 159 |
| 481648 | 66431 | 66444 | TCCTTCTTTGCTGC | 2-10-2 | cEt | 51 | 160 |
| 481424 | 66446 | 66461 | CAAGTGAAAGTGACGC | 3-10-3 | cEt | 70 | 161 |
| 481649 | 66447 | 66460 | AAGTGAAAGTGACG | 2-10-2 | cEt | 25 | 162 |
| 481425 | 66468 | 66483 | ACCGCTGATGTCCTTC | 3-10-3 | cEt | 78 | 163 |
| 481650 | 66469 | 66482 | CCGCTGATGTCCTT | 2-10-2 | cEt | 79 | 164 |
| 481426 | 66993 | 67008 | ACTGGATCTGGGTCTT | 3-10-3 | cEt | 80 | 165 |
| 481651 | 66994 | 67007 | CTGGATCTGGGTCT | 2-10-2 | cEt | 64 | 166 |
| 481427 | 67017 | 67032 | GCTGCTTTGTGTATGG | 3-10-3 | cEt | 75 | 167 |
| 481652 | 67018 | 67031 | CTGCTTTGTGTATG | 2-10-2 | cEt | 82 | 168 |
| 481428 | 67026 | 67041 | TGTTCAGCTGCTGCTT | 3-10-3 | cEt | 77 | 169 |
| 481653 | 67027 | 67040 | GTTCAGCTGCTGCT | 2-10-2 | cEt | 79 | 170 |
| 481429 | 67034 | 67049 | TGACATGTTGTTCAGC | 3-10-3 | cEt | 84 | 171 |
| 481654 | 67035 | 67048 | GACATGTTGTTCAG | 2-10-2 | cEt | 70 | 172 |
| 481430 | 67052 | 67067 | CATGATGATTTCAGCA | 3-10-3 | cEt | 67 | 173 |
| 481655 | 67053 | 67066 | ATGATGATTTCAGC | 2-10-2 | cEt | 31 | 174 |
| 481431 | 67068 | 67083 | CCATGATCTTATAGCC | 3-10-3 | cEt | 91 | 175 |
| 481656 | 67069 | 67082 | CATGATCTTATAGC | 2-10-2 | cEt | 0 | 176 |
| 481432 | 67095 | 67110 | GTGGAGACACCAGGAT | 3-10-3 | cEt | 55 | 177 |
| 481657 | 67096 | 67109 | TGGAGACACCAGGA | 2-10-2 | cEt | 58 | 178 |
| 481433 | 67118 | 67133 | AATGTCAGGATAGAGA | 3-10-3 | cEt | 73 | 179 |
| 481658 | 67119 | 67132 | ATGTCAGGATAGAG | 2-10-2 | cEt | 62 | 180 |
| 481434 | 67128 | 67143 | CCTCCTTGGGAATGTC | 3-10-3 | cEt | 73 | 181 |
| 345785 | 67129 | 67148 | TGCCTCCTCCTTGGGAATGT | 5-10-5 | MOE | 50 | 182 |
| 481659 | 67129 | 67142 | CTCCTTGGGAATGT | 2-10-2 | cEt | 51 | 183 |
| 481435 | 67131 | 67146 | CCTCCTCCTTGGGAAT | 3-10-3 | cEt | 49 | 184 |
| 481660 | 67132 | 67145 | CTCCTCCTTGGGAA | 2-10-2 | cEt | 54 | 185 |
| 481436 | 67137 | 67152 | CGAATGCCTCCTCCTT | 3-10-3 | cEt | 82 | 186 |
| 481661 | 67138 | 67151 | GAATGCCTCCTCCT | 2-10-2 | cEt | 76 | 187 |
| 481437 | 67158 | 67173 | TCTCTGGCCGACAATA | 3-10-3 | cEt | 49 | 188 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481662 | 67159 | 67172 | CTCTGGCCGACAAT | 2-10-2 | cEt | 43 | 189 |
| 481567 | 67194 | 67209 | AACAACTACCTGGGTC | 3-10-3 | cEt | 20 | 451 |
| 481792 | 67195 | 67208 | ACAACTACCTGGGT | 2-10-2 | cEt | 0 | 452 |
| 481438 | 72272 | 72287 | ACTTGGTCTTCAGGTA | 3-10-3 | cEt | 51 | 190 |
| 481663 | 72273 | 72286 | CTTGGTCTTCAGGT | 2-10-2 | cEt | 52 | 191 |
| 481568 | 72290 | 72305 | ACGGTGTCACACAGAT | 3-10-3 | cEt | 85 | 453 |
| 481793 | 72291 | 72304 | CGGTGTCACACAGA | 2-10-2 | cEt | 93 | 454 |
| 481569 | 72430 | 72445 | AACACACAAGGTCACT | 3-10-3 | cEt | 62 | 455 |
| 481794 | 72431 | 72444 | ACACACAAGGTCAC | 2-10-2 | cEt | 81 | 456 |
| 481570 | 72438 | 72453 | GCTTTTTAAACACACA | 3-10-3 | cEt | 79 | 457 |
| 481795 | 72439 | 72452 | CTTTTTAAACACAC | 2-10-2 | cEt | 0 | 458 |
| 481571 | 72528 | 72543 | TGACAAGACACAATGG | 3-10-3 | cEt | 12 | 459 |
| 481796 | 72529 | 72542 | GACAAGACACAATG | 2-10-2 | cEt | 36 | 460 |
| 481440 | 72586 | 72601 | GTATTGCTGCAGGTCG | 3-10-3 | cEt | 79 | 194 |
| 481665 | 72587 | 72600 | TATTGCTGCAGGTC | 2-10-2 | cEt | 43 | 195 |
| 481441 | 72594 | 72609 | GGTCAATGGTATTGCT | 3-10-3 | cEt | 55 | 196 |
| 481666 | 72595 | 72608 | GTCAATGGTATTGC | 2-10-2 | cEt | 36 | 197 |
| 481442 | 72602 | 72617 | CATCGGCAGGTCAATG | 3-10-3 | cEt | 44 | 198 |
| 481667 | 72603 | 72616 | ATCGGCAGGTCAAT | 2-10-2 | cEt | 31 | 199 |
| 481443 | 72622 | 72637 | GAATCTAAAGTGCGGG | 3-10-3 | cEt | 78 | 200 |
| 481668 | 72623 | 72636 | AATCTAAAGTGCGG | 2-10-2 | cEt | 41 | 201 |
| 481444 | 72630 | 72645 | GCATCAATGAATCTAA | 3-10-3 | cEt | 66 | 202 |
| 481669 | 72631 | 72644 | CATCAATGAATCTA | 2-10-2 | cEt | 0 | 203 |
| 481445 | 72638 | 72653 | TCCAAACTGCATCAAT | 3-10-3 | cEt | 70 | 204 |
| 481670 | 72639 | 72652 | CCAAACTGCATCAA | 2-10-2 | cEt | 60 | 205 |
| 481446 | 72659 | 72674 | TTCAGCACCTTCACCA | 3-10-3 | cEt | 44 | 206 |
| 481671 | 72660 | 72673 | TCAGCACCTTCACC | 2-10-2 | cEt | 41 | 207 |
| 481447 | 72675 | 72690 | GCCCTCCTGCTGAGGG | 3-10-3 | cEt | 10 | 208 |
| 481672 | 72676 | 72689 | CCCTCCTGCTGAGG | 2-10-2 | cEt | 15 | 209 |
| 481572 | 72682 | 72697 | CCAAACTGCCCTCCTG | 3-10-3 | cEt | 51 | 461 |
| 481797 | 72683 | 72696 | CAAACTGCCCTCCT | 2-10-2 | cEt | 11 | 211 |
| 481573 | 73535 | 73550 | GGTCAGAAAAGCCAGA | 3-10-3 | cEt | 55 | 462 |
| 481798 | 73536 | 73549 | GTCAGAAAAGCCAG | 2-10-2 | cEt | 59 | 463 |
| 481449 | 73690 | 73705 | CCATGTCAAAGGTGAG | 3-10-3 | cEt | 77 | 213 |
| 481674 | 73691 | 73704 | CATGTCAAAGGTGA | 2-10-2 | cEt | 31 | 214 |
| 481450 | 73717 | 73732 | GGGAGGTAGCGCACTC | 3-10-3 | cEt | 53 | 215 |
| 481675 | 73718 | 73731 | GGAGGTAGCGCACT | 2-10-2 | cEt | 41 | 216 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481451 | 73779 | 73794 | GAAT GCAGGTAGGC GC | 3-10-3 | cEt | 55 | 217 |
| 481676 | 73780 | 73793 | AATGCAGGTAGGCG | 2-10-2 | cEt | 39 | 218 |
| 481452 | 73818 | 73833 | TTTCAGATGATCTGGG | 3-10-3 | cEt | 71 | 219 |
| 481677 | 73819 | 73832 | TTCAGATGATCTGG | 2-10-2 | cEt | 38 | 220 |
| 481574 | 73837 | 73852 | GGAACCACAAAGTTAG | 3-10-3 | cEt | 69 | 221 |
| 481799 | 73838 | 73851 | GAACCACAAAGTTA | 2-10-2 | cEt | 50 | 222 |
| 481453 | 73868 | 73883 | GATAGCAGAAGTAGGA | 3-10-3 | cEt | 92 | 223 |
| 481678 | 73869 | 73882 | ATAGCAGAAGTAGG | 2-10-2 | cEt | 78 | 224 |
| 481454 | 73889 | 73904 | AAAGTGCCCAGATTGC | 3-10-3 | cEt | 85 | 225 |
| 481679 | 73890 | 73903 | AAGTGCCCAGATTG | 2-10-2 | cEt | 69 | 226 |
| 481455 | 73909 | 73924 | CACTCATTTCTCTATT | 3-10-3 | cEt | 74 | 227 |
| 481680 | 73910 | 73923 | ACTCATTTCTCTAT | 2-10-2 | cEt | 39 | 228 |
| 481456 | 73954 | 73969 | AACACATCCTTATTTG | 3-10-3 | cEt | 48 | 229 |
| 481681 | 73955 | 73968 | ACACATCCTTATTT | 2-10-2 | cEt | 47 | 230 |
| 481457 | 73966 | 73981 | TGGGTCTCAGAGAACA | 3-10-3 | cEt | 88 | 231 |
| 481682 | 73967 | 73980 | GGGTCTCAGAGAAC | 2-10-2 | cEt | 77 | 232 |
| 481458 | 74019 | 74034 | CAAGACATTTCCTTTT | 3-10-3 | cEt | 54 | 233 |
| 481683 | 74020 | 74033 | AAGACATTTCCTTT | 2-10-2 | cEt | 29 | 234 |
| 481459 | 74095 | 74110 | GGAGGCACTTGTCTAA | 3-10-3 | cEt | 76 | 235 |
| 481684 | 74096 | 74109 | GAGGCACTTGTCTA | 2-10-2 | cEt | 89 | 236 |
| 481460 | 74130 | 74145 | TTACAGAAACAGGCAG | 3-10-3 | cEt | 83 | 237 |
| 481685 | 74131 | 74144 | TACAGAAACAGGCA | 2-10-2 | cEt | 36 | 238 |
| 481461 | 74156 | 74171 | AGCTATAGGTGGCCTG | 3-10-3 | cEt | 75 | 239 |
| 481686 | 74157 | 74170 | GCTATAGGTGGCCT | 2-10-2 | cEt | 70 | 240 |
| 481462 | 74171 | 74186 | ATGCCAGGAGTATGTA | 3-10-3 | cEt | 89 | 241 |
| 481687 | 74172 | 74185 | TGCCAGGAGTATGT | 2-10-2 | cEt | 80 | 242 |
| 481463 | 74188 | 74203 | CAAGGTTAAAAAGTGC | 3-10-3 | cEt | 88 | 243 |
| 481688 | 74189 | 74202 | AAGGTTAAAAAGTG | 2-10-2 | cEt | 13 | 244 |
| 481464 | 74203 | 74218 | CTATTTGGATGTCAGC | 3-10-3 | cEt | 97 | 245 |
| 481689 | 74204 | 74217 | TATTTGGATGTCAG | 2-10-2 | cEt | 40 | 246 |
| 481465 | 74219 | 74234 | TAGATAGTCCTATCTT | 3-10-3 | cEt | 51 | 247 |
| 481690 | 74220 | 74233 | AGATAGTCCTATCT | 2-10-2 | cEt | 64 | 248 |
| 481466 | 74234 | 74249 | AAGAAACCTAGGGCTT | 3-10-3 | cEt | 74 | 249 |
| 481691 | 74235 | 74248 | AGAAACCTAGGGCT | 2-10-2 | cEt | 77 | 250 |
| 481467 | 74284 | 74299 | GCTGATACAGTGTTTT | 3-10-3 | cEt | 74 | 251 |
| 481692 | 74285 | 74298 | CTGATACAGTGTTT | 2-10-2 | cEt | 74 | 252 |
| 481468 | 74299 | 74314 | ATACAGAAAGGCTATG | 3-10-3 | cEt | 71 | 253 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481693 | 74300 | 74313 | TACAGAAAGGCTAT | 2-10-2 | cEt | 25 | 254 |
| 481469 | 74314 | 74329 | GCTTAAGTTTCTTAAA | 3-10-3 | cEt | 61 | 255 |
| 481694 | 74315 | 74328 | CTTAAGTTTCTTAA | 2-10-2 | cEt | 0 | 256 |
| 481470 | 74648 | 74663 | AGCACCAAGGAGGCTG | 3-10-3 | cEt | 49 | 257 |
| 481695 | 74649 | 74662 | GCACCAAGGAGGCT | 2-10-2 | cEt | 83 | 258 |
| 481471 | 74663 | 74678 | AAGCTGAATGCTTAAA | 3-10-3 | cEt | 36 | 259 |
| 481696 | 74664 | 74677 | AGCTGAATGCTTAA | 2-10-2 | cEt | 33 | 260 |
| 481472 | 74678 | 74693 | TTACCAGCCTGAAGGA | 3-10-3 | cEt | 76 | 261 |
| 481697 | 74679 | 74692 | TACCAGCCTGAAGG | 2-10-2 | cEt | 63 | 262 |
| 481473 | 74693 | 74708 | CAGGGATTATATAAAT | 3-10-3 | cEt | 53 | 263 |
| 481698 | 74694 | 74707 | AGGGATTATATAAA | 2-10-2 | cEt | 15 | 264 |
| 481474 | 74708 | 74723 | ACCTGAAGCCCGTTTC | 3-10-3 | cEt | 80 | 265 |
| 481699 | 74709 | 74722 | CCTGAAGCCCGTTT | 2-10-2 | cEt | 57 | 266 |
| 481475 | 74723 | 74738 | TGTCTTAAGGGTTTGA | 3-10-3 | cEt | 93 | 267 |
| 481700 | 74724 | 74737 | GTCTTAAGGGTTTG | 2-10-2 | cEt | 89 | 268 |
| 481476 | 74738 | 74753 | GGTTGCAGCTTCAGAT | 3-10-3 | cEt | 92 | 269 |
| 481701 | 74739 | 74752 | GTTGCAGCTTCAGA | 2-10-2 | cEt | 60 | 270 |
| 481477 | 74754 | 74769 | TCAACACCAAAGGCCA | 3-10-3 | cEt | 95 | 271 |
| 481702 | 74755 | 74768 | CAACACCAAAGGCC | 2-10-2 | cEt | 89 | 272 |
| 481478 | 74772 | 74787 | TCCTTAAACCTTCCTA | 3-10-3 | cEt | 84 | 273 |
| 481703 | 74773 | 74786 | CCTTAAACCTTCCT | 2-10-2 | cEt | 57 | 274 |
| 481479 | 74787 | 74802 | AAAATGCTTAGATTCT | 3-10-3 | cEt | 80 | 275 |
| 481704 | 74788 | 74801 | AAATGCTTAGATTC | 2-10-2 | cEt | 32 | 276 |
| 481480 | 74815 | 74830 | AAATAAGTCTATTTAT | 3-10-3 | cEt | 5 | 277 |
| 481705 | 74816 | 74829 | AATAAGTCTATTTA | 2-10-2 | cEt | 25 | 278 |
| 481481 | 74835 | 74850 | GGCCAATACATTACAA | 3-10-3 | cEt | 63 | 279 |
| 481706 | 74836 | 74849 | GCCAATACATTACA | 2-10-2 | cEt | 56 | 280 |
| 481482 | 74857 | 74872 | TGCCCAGCCTTACTCA | 3-10-3 | cEt | 55 | 281 |
| 481707 | 74858 | 74871 | GCCCAGCCTTACTC | 2-10-2 | cEt | 43 | 282 |
| 481483 | 74872 | 74887 | GTTGTAAGCACCCTCT | 3-10-3 | cEt | 1 | 283 |
| 481708 | 74873 | 74886 | TTGTAAGCACCCTC | 2-10-2 | cEt | 56 | 284 |
| 481484 | 74887 | 74902 | AGAAAGGGAGTCAAGG | 3-10-3 | cEt | 60 | 285 |
| 481709 | 74888 | 74901 | GAAAGGGAGTCAAG | 2-10-2 | cEt | 27 | 286 |
| 481485 | 74904 | 74919 | GCAGATCAAGTCCAGG | 3-10-3 | cEt | 90 | 287 |
| 481710 | 74905 | 74918 | CAGATCAAGTCCAG | 2-10-2 | cEt | 88 | 288 |
| 481486 | 74917 | 74932 | AGCCTCTGAAACAGCA | 3-10-3 | cEt | 75 | 289 |
| 481711 | 74918 | 74931 | GCCTCTGAAACAGC | 2-10-2 | cEt | 74 | 290 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481487 | 74933 | 74948 | CCCACAGAAACAACCT | 3-10-3 | cEt | 66 | 291 |
| 481712 | 74934 | 74947 | CCACAGAAACAACC | 2-10-2 | cEt | 45 | 292 |
| 481488 | 74948 | 74963 | AGCCCTGATAAGGCAC | 3-10-3 | cEt | 23 | 293 |
| 481713 | 74949 | 74962 | GCCCTGATAAGGCA | 2-10-2 | cEt | 18 | 294 |
| 481489 | 74963 | 74978 | AATCAGAAGTATCCCA | 3-10-3 | cEt | 60 | 295 |
| 481714 | 74964 | 74977 | ATCAGAAGTATCCC | 2-10-2 | cEt | 43 | 296 |
| 481490 | 75020 | 75035 | GCCTCTAGCAGGATCA | 3-10-3 | cEt | 78 | 297 |
| 481715 | 75021 | 75034 | CCTCTAGCAGGATC | 2-10-2 | cEt | 79 | 298 |
| 481491 | 75035 | 75050 | CACGCAAGGAGACATG | 3-10-3 | cEt | 70 | 299 |
| 481716 | 75036 | 75049 | ACGCAAGGAGACAT | 2-10-2 | cEt | 68 | 300 |
| 481492 | 75050 | 75065 | TGAGGGACCTTTAGAC | 3-10-3 | cEt | 61 | 301 |
| 481717 | 75051 | 75064 | GAGGGACCTTTAGA | 2-10-2 | cEt | 44 | 302 |
| 481493 | 75073 | 75088 | CAGGATTCCTAAAACA | 3-10-3 | cEt | 43 | 303 |
| 481718 | 75074 | 75087 | AGGATTCCTAAAAC | 2-10-2 | cEt | 7 | 304 |
| 481494 | 75088 | 75103 | ATGAGGTCCTGAGACC | 3-10-3 | cEt | 60 | 305 |
| 481719 | 75089 | 75102 | TGAGGTCCTGAGAC | 2-10-2 | cEt | 29 | 306 |
| 481495 | 75127 | 75142 | CATCATGTCCAACCTG | 3-10-3 | cEt | 92 | 307 |
| 481720 | 75128 | 75141 | ATCATGTCCAACCT | 2-10-2 | cEt | 63 | 308 |
| 481496 | 75142 | 75157 | GGGCCCCATAGTGTGC | 3-10-3 | cEt | 29 | 309 |
| 481721 | 75143 | 75156 | GGCCCCATAGTGTG | 2-10-2 | cEt | 19 | 310 |
| 481497 | 75164 | 75179 | AGCTCAACCAGACACG | 3-10-3 | cEt | 67 | 311 |
| 481722 | 75165 | 75178 | GCTCAACCAGACAC | 2-10-2 | cEt | 69 | 312 |
| 481498 | 75179 | 75194 | GAACCATATTCCCTGA | 3-10-3 | cEt | 90 | 313 |
| 481723 | 75180 | 75193 | AACCATATTCCCTG | 2-10-2 | cEt | 49 | 314 |
| 481499 | 75194 | 75209 | CAAGAAACTGGCTAAG | 3-10-3 | cEt | 43 | 315 |
| 481724 | 75195 | 75208 | AAGAAACTGGCTAA | 2-10-2 | cEt | 17 | 316 |
| 481500 | 75209 | 75224 | GCCACTGGATATCACC | 3-10-3 | cEt | 92 | 317 |
| 481725 | 75210 | 75223 | CCACTGGATATCAC | 2-10-2 | cEt | 88 | 464 |
| 481501 | 75235 | 75250 | AACTGAATGAAGACGC | 3-10-3 | cEt | 91 | 318 |
| 481726 | 75236 | 75249 | ACTGAATGAAGACG | 2-10-2 | cEt | 56 | 319 |
| 481502 | 75250 | 75265 | CCTTTGCCCTGCATGA | 3-10-3 | cEt | 85 | 320 |
| 481727 | 75251 | 75264 | CTTTGCCCTGCATG | 2-10-2 | cEt | 70 | 321 |
| 481503 | 75265 | 75280 | AAGTTTATCAGTAAGC | 3-10-3 | cEt | 57 | 322 |
| 481728 | 75266 | 75279 | AGTTTATCAGTAAG | 2-10-2 | cEt | 22 | 323 |
| 481504 | 75280 | 75295 | TACGAGGGCAGACTCA | 3-10-3 | cEt | 60 | 324 |
| 481729 | 75281 | 75294 | ACGAGGGCAGACTC | 2-10-2 | cEt | 22 | 325 |
| 481505 | 75295 | 75310 | AGGTATACACCCTCAT | 3-10-3 | cEt | 45 | 326 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481730 | 75296 | 75309 | GGTATACACCCTCA | 2-10-2 | cEt | 47 | 327 |
| 481506 | 75310 | 75325 | CCTCAGAGGGAGGCCA | 3-10-3 | cEt | 32 | 328 |
| 481731 | 75311 | 75324 | CTCAGAGGGAGGCC | 2-10-2 | cEt | 0 | 329 |
| 481507 | 75325 | 75340 | GGGAGGAGTCACCAGC | 3-10-3 | cEt | 64 | 330 |
| 481732 | 75326 | 75339 | GGAGGAGTCACCAG | 2-10-2 | cEt | 59 | 331 |
| 481508 | 75392 | 75407 | TAGCCAGCCAAGGCGG | 3-10-3 | cEt | 33 | 332 |
| 481733 | 75393 | 75406 | AGCCAGCCAAGGCG | 2-10-2 | cEt | 50 | 333 |
| 481509 | 75407 | 75422 | ACAGGAGAGGCGAGCT | 3-10-3 | cEt | 46 | 334 |
| 481734 | 75408 | 75421 | CAGGAGAGGCGAGC | 2-10-2 | cEt | 28 | 335 |
| 481510 | 75424 | 75439 | TAGGTGTTCCCATACG | 3-10-3 | cEt | 95 | 336 |
| 481735 | 75425 | 75438 | AGGTGTTCCCATAC | 2-10-2 | cEt | 22 | 337 |
| 481511 | 75445 | 75460 | GGCAGCCCATCCAGCA | 3-10-3 | cEt | 43 | 338 |
| 481736 | 75446 | 75459 | GCAGCCCATCCAGC | 2-10-2 | cEt | 54 | 339 |
| 481512 | 75462 | 75477 | CATGCCTCTGAGTCAG | 3-10-3 | cEt | 30 | 340 |
| 481737 | 75463 | 75476 | ATGCCTCTGAGTCA | 2-10-2 | cEt | 31 | 341 |
| 481513 | 75477 | 75492 | GTTGCCAAATCCGGCC | 3-10-3 | cEt | 85 | 342 |
| 481738 | 75478 | 75491 | TTGCCAAATCCGGC | 2-10-2 | cEt | 70 | 343 |
| 481514 | 75492 | 75507 | GCAAGGTGGTTTTGAG | 3-10-3 | cEt | 85 | 344 |
| 481739 | 75493 | 75506 | CAAGGTGGTTTTGA | 2-10-2 | cEt | 60 | 345 |
| 481515 | 75512 | 75527 | AGAAACTCTGATCAGC | 3-10-3 | cEt | 88 | 346 |
| 481740 | 75513 | 75526 | GAAACTCTGATCAG | 2-10-2 | cEt | 71 | 347 |
| 481516 | 75551 | 75566 | CAGAGACCAGCTAATT | 3-10-3 | cEt | 78 | 348 |
| 481741 | 75552 | 75565 | AGAGACCAGCTAAT | 2-10-2 | cEt | 80 | 349 |
| 481517 | 75581 | 75596 | ATCTTAGAGAAGGTCG | 3-10-3 | cEt | 87 | 350 |
| 481742 | 75582 | 75595 | TCTTAGAGAAGGTC | 2-10-2 | cEt | 64 | 351 |
| 481518 | 75612 | 75627 | CCAGGCAGGAGGACTG | 3-10-3 | cEt | 67 | 352 |
| 481743 | 75613 | 75626 | CAGGCAGGAGGACT | 2-10-2 | cEt | 75 | 353 |
| 481519 | 75624 | 75639 | CATCAACTGTCTCCAG | 3-10-3 | cEt | 29 | 354 |
| 481744 | 75625 | 75638 | ATCAACTGTCTCCA | 2-10-2 | cEt | 69 | 355 |
| 481520 | 75626 | 75641 | CACATCAACTGTCTCC | 3-10-3 | cEt | 73 | 356 |
| 481745 | 75627 | 75640 | ACATCAACTGTCTC | 2-10-2 | cEt | 74 | 357 |
| 481521 | 75646 | 75661 | GAAGTAAGAGCTCTGC | 3-10-3 | cEt | 86 | 358 |
| 481746 | 75647 | 75660 | AAGTAAGAGCTCTG | 2-10-2 | cEt | 67 | 359 |
| 481522 | 75661 | 75676 | AAGAGTGTTGCTGGAG | 3-10-3 | cEt | 92 | 360 |
| 481747 | 75662 | 75675 | AGAGTGTTGCTGGA | 2-10-2 | cEt | 95 | 361 |
| 481523 | 75676 | 75691 | GCTTATTATGTACTGA | 3-10-3 | cEt | 95 | 362 |
| 481748 | 75677 | 75690 | CTTATTATGTACTG | 2-10-2 | cEt | 15 | 363 |

| Inhibition of human STAT3 mRNA levels by cEt and MOE chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | Motif | Wing Chem | % inhibition | SEQ ID NO |
| 481524 | 75717 | 75732 | GCCCAAGTCTCACCTT | 3-10-3 | cEt | 70 | 364 |
| 481749 | 75718 | 75731 | CCCAAGTCTCACCT | 2-10-2 | cEt | 70 | 365 |
| 481525 | 75728 | 75743 | CCCAATGGTAAGCCCA | 3-10-3 | cEt | 93 | 366 |
| 481750 | 75729 | 75742 | CCAATGGTAAGCCC | 2-10-2 | cEt | 94 | 367 |
| 481526 | 75730 | 75745 | AACCCAATGGTAAGCC | 3-10-3 | cEt | 82 | 368 |
| 481751 | 75731 | 75744 | ACCCAATGGTAAGC | 2-10-2 | cEt | 54 | 369 |
| 481527 | 75747 | 75762 | TAGGTCCCTATGATTT | 3-10-3 | cEt | 55 | 370 |
| 481752 | 75748 | 75761 | AGGTCCCTATGATT | 2-10-2 | cEt | 62 | 371 |
| 481528 | 75766 | 75781 | AAGCCCTGAACCCTCG | 3-10-3 | cEt | 77 | 372 |
| 481753 | 75767 | 75780 | AGCCCTGAACCCTC | 2-10-2 | cEt | 71 | 373 |
| 481529 | 75802 | 75817 | CCTAAGGCCATGAACT | 3-10-3 | cEt | 64 | 374 |
| 481754 | 75803 | 75816 | CTAAGGCCATGAAC | 2-10-2 | cEt | 53 | 375 |
| 481530 | 75817 | 75832 | ACCAGATACATGCTAC | 3-10-3 | cEt | 87 | 376 |
| 481755 | 75818 | 75831 | CCAGATACATGCTA | 2-10-2 | cEt | 84 | 377 |
| 481531 | 75833 | 75848 | TACAATCAGAGTTAAG | 3-10-3 | cEt | 66 | 378 |
| 481756 | 75834 | 75847 | ACAATCAGAGTTAA | 2-10-2 | cEt | 5 | 379 |
| 481532 | 75851 | 75866 | TCCTCTCAGAACTTTT | 3-10-3 | cEt | 65 | 380 |
| 481757 | 75852 | 75865 | CCTCTCAGAACTTT | 2-10-2 | cEt | 81 | 381 |
| 481533 | 75853 | 75868 | GCTCCTCTCAGAACTT | 3-10-3 | cEt | 80 | 382 |
| 481758 | 75854 | 75867 | CTCCTCTCAGAACT | 2-10-2 | cEt | 62 | 383 |
| 481534 | 75880 | 75895 | TTCTTTAATGGGCCAC | 3-10-3 | cEt | 79 | 384 |
| 481759 | 75881 | 75894 | TCTTTAATGGGCCA | 2-10-2 | cEt | 74 | 385 |
| 481535 | 75954 | 75969 | ACGGGATTCCCTCGGC | 3-10-3 | cEt | 78 | 386 |
| 481760 | 75955 | 75968 | CGGGATTCCCTCGG | 2-10-2 | cEt | 78 | 387 |
| 481536 | 75969 | 75984 | GTAGGTAAGCAACCCA | 3-10-3 | cEt | 91 | 388 |
| 481761 | 75970 | 75983 | TAGGTAAGCAACCC | 2-10-2 | cEt | 78 | 389 |
| 481537 | 76017 | 76032 | GAATTTGAATGCAGTG | 3-10-3 | cEt | 84 | 390 |
| 481762 | 76018 | 76031 | AATTTGAATGCAGT | 2-10-2 | cEt | 2 | 391 |
| 481538 | 76031 | 76046 | TGAAGTACACATTGGA | 3-10-3 | cEt | 92 | 392 |
| 481763 | 76032 | 76045 | GAAGTACACATTGG | 2-10-2 | cEt | 96 | 393 |
| 481539 | 76047 | 76062 | ATAAATTTTTACACTA | 3-10-3 | cEt | 19 | 394 |
| 481764 | 76048 | 76061 | TAAATTTTTACACT | 2-10-2 | cEt | 1 | 395 |
| 481765 | 76056 | 76069 | CAATAATATAAATT | 2-10-2 | cEt | 0 | 396 |
| 481541 | 76121 | 76136 | CTGGAAGTTAAAGTAG | 3-10-3 | cEt | 71 | 397 |
| 481766 | 76122 | 76135 | TGGAAGTTAAAGTA | 2-10-2 | cEt | 10 | 398 |

**Example 2: Antisense inhibition of murine STAT3 in b.END cells**

**[0255]** Antisense oligonucleotides tested in the study described in Example 1 were also tested for their effects on STAT3 mRNA in b.END cells. Cultured b.END cells at a density of 20,000 cells per well were transfected using electroporation with 7,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Murine primer probe set RTS2381 (forward sequence GCCACGTTGGTGTTTCATAATCT, designated herein as SEQ ID NO: 465; reverse sequence GATAGAGGACATTGGACTCTTGCA, designated herein as SEQ ID NO: 466; probe sequence TTGGGTGAAATTGACCAGCAATATAGCCG, designated herein as SEQ ID NO: 467) was used to measure RNA. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®.

**[0256]** Certain sequences complementary to the STAT3 mouse gene sequence showed good inhibition in b. END cells. Results are presented in Table 3 as percent inhibition of STAT3, relative to untreated control cells. The human oligonucleotides in Table 3 were compared to the mouse STAT-3 genomic sequence, designated herein as SEQ ID NO: 3 (the complement of GENBANK Accession No. NT_165773.2 truncated from nucleotides 12286001 to 12344000). "Mouse Target start site" indicates the 5'-most nucleotide to which the gapmer is targeted in the murine sequence. "Mouse Target stop site" indicates the 3'-most nucleotide to which the gapmer is targeted murine sequence.

Table 3

| Inhibition of human STAT3 mRNA levels by certain cEt chimeric antisense oligonucleotides complementary to SEQ ID NO: 1 and SEQ ID NO: 3 | | | | |
|---|---|---|---|---|
| ISIS NO | Mouse Start Site | Mouse Stop Site | % inhibition | SEQ ID NO |
| 481549 | 5283 | 5298 | 96 | 413 |
| 481553 | 9913 | 9928 | 94 | 421 |
| 481768 | 3189 | 3202 | 91 | 402 |
| 481356 | 30356 | 30371 | 83 | 21 |
| 481548 | 4045 | 4060 | 82 | 411 |
| 481554 | 14662 | 14677 | 82 | 423 |
| 481426 | 48328 | 48343 | 82 | 165 |
| 481580 | 30333 | 30346 | 81 | 20 |
| 481412 | 47413 | 47428 | 81 | 135 |
| 481417 | 47636 | 47651 | 81 | 147 |
| 481418 | 47637 | 47652 | 80 | 148 |
| 481355 | 30332 | 30347 | 79 | 19 |
| 481396 | 43120 | 43135 | 79 | 443 |
| 481416 | 47634 | 47649 | 79 | 144 |
| 481420 | 47681 | 47696 | 79 | 153 |
| 481358 | 32842 | 32857 | 78 | 25 |
| 481363 | 33520 | 33535 | 78 | 35 |
| 481570 | 51870 | 51885 | 78 | 457 |
| 481382 | 37857 | 37872 | 77 | 74 |
| 481378 | 36560 | 36575 | 76 | 66 |
| 481431 | 48403 | 48418 | 76 | 175 |
| 481453 | 53034 | 53049 | 76 | 223 |
| 481621 | 43121 | 43134 | 75 | 444 |

| Inhibition of human STAT3 mRNA levels by certain cEt chimeric antisense oligonucleotides complementary to SEQ ID NO: 1 and SEQ ID NO: 3 | | | | |
|---|---|---|---|---|
| ISIS NO | Mouse Start Site | Mouse Stop Site | % inhibition | SEQ ID NO |
| 481641 | 47635 | 47648 | 75 | 145 |
| 481637 | 47414 | 47427 | 74 | 136 |
| 481380 | 36631 | 36646 | 73 | 70 |
| 481574 | 53000 | 53015 | 73 | 221 |
| 481601 | 36392 | 36405 | 71 | 62 |
| 481419 | 47638 | 47653 | 71 | 150 |
| 481371 | 35938 | 35953 | 70 | 51 |
| 481642 | 47637 | 47650 | 70 | 149 |
| 481542 | 3180 | 3195 | 69 | 399 |
| 481547 | 3313 | 3328 | 69 | 409 |
| 481772 | 3314 | 3327 | 69 | 410 |
| 481362 | 32929 | 32944 | 69 | 33 |
| 481653 | 48362 | 48375 | 69 | 170 |
| 481786 | 38812 | 38825 | 68 | 440 |
| 481415 | 47629 | 47644 | 68 | 141 |
| 481543 | 3188 | 3203 | 67 | 401 |
| 481793 | 51714 | 51727 | 67 | 454 |
| 481443 | 52060 | 52075 | 67 | 200 |
| 481684 | 53229 | 53242 | 67 | 236 |
| 481398 | 45226 | 45241 | 66 | 106 |
| 481560 | 36394 | 36409 | 65 | 438 |
| 481643 | 47638 | 47651 | 65 | 151 |
| 481430 | 48387 | 48402 | 65 | 173 |
| 481440 | 52024 | 52039 | 65 | 194 |

**Example 3: Tolerability of antisense oligonucleotides targeting STAT3 in BALB/c mice**

**[0257]** Forty antisense oligonucleotides exhibiting a high level of potency, selected from among the 452 compounds evaluated in Example 1, were further tested for *in vivo* tolerability.

**[0258]** Groups of 2-4 male BALB/c mice were injected subcutaneously twice a week for 3 weeks with 25 mg/kg of ISIS antisense oligonucleotides. One group of 4 male BALB/c mice was injected subcutaneously twice a week for 3 weeks with PBS. This group of mice was utilized as a control group to which the treatment groups were compared. One day after the last dose, body weights were taken, mice were euthanized, and organs and plasma were harvested for further analysis.

**[0259]** The body weights of the mice were measured pre-dose and at the end of the treatment period. Percent increase over the initial body weight was calculated. Liver, spleen, and kidney weights were measured at the end of the study and were compared to PBS treated mice.

**[0260]** To evaluate the effect of ISIS oligonucleotides on metabolic function, plasma concentrations of transaminases and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). Plasma concentrations of ALT (alanine transaminase), AST (aspartate transaminase), and BUN were measured.

**[0261]** Among the forty antisense oligonucleotides tested, certain antisense oligonucleotides, including ISIS 481374, ISIS 481390, ISIS 481420, ISIS 481431, ISIS 481453, ISIS 481464, ISIS 481475, ISIS 481495, ISIS 481500, ISIS 481501, ISIS 481525, ISIS 481548, ISIS 481549, ISIS 481597, ISIS 481695, ISIS 481700, ISIS 481702, ISIS 481710, ISIS 481725, ISIS 481750, and ISIS 481763 met tolerability thresholds for body weight, organ weight, ALT, AST, and BUN parameters.

**Example 4: Dose-dependent antisense inhibition of human STAT3 in HuVEC cells**

**[0262]** Gapmers from Examples 1 and 2 exhibiting significant *in vitro* inhibition of STAT3 were tested at various doses in HuVEC cells. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 31.25 nM, 62.5 nM, 125 nM, 250 nM, 500 nM, and 1,0000 nM concentrations of antisense oligonucleotide, as specified in Table 4. After a treatment period of approximately 16 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199 (forward sequence ACATGCCACTTTGGTGTTTCATAA, designated herein as SEQ ID NO: 6; reverse sequence TCTTCGTAGATTGTGCTGATAGAGAAC, designated herein as SEQ ID NO: 7; probe sequence CAGTATAGCCGCTTCCTGCAAGAGTCGAA, designated herein as SEQ ID NO: 8) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0263]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 4 and was calculated by plotting the concentrations of oligonucleotides used versus the percent inhibition of STAT3 mRNA expression achieved at each concentration and noting the concentration of oligonucleotide at which 50% inhibition of STAT3 mRNA expression was achieved compared to the control. As illustrated in Table 4, STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 4**

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells using electroporation | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 31.25 nM | 62.5 nM | 125.0 nM | 250.0 nM | 500.0 nM | 1000.0 nM | $IC_{50}$ (μM) |
| 481355 | 19 | 15 | 36 | 61 | 75 | 89 | 0.18 |
| 481374 | 25 | 42 | 52 | 72 | 82 | 88 | 0.10 |
| 481390 | 17 | 37 | 44 | 60 | 73 | 86 | 0.15 |
| 481420 | 23 | 20 | 40 | 60 | 81 | 92 | 0.16 |
| 481453 | 21 | 37 | 52 | 69 | 79 | 88 | 0.12 |
| 481464 | 57 | 73 | 81 | 90 | 94 | 94 | <0.03 |
| 481475 | 22 | 46 | 54 | 78 | 83 | 92 | 0.10 |
| 481500 | 25 | 37 | 42 | 75 | 83 | 90 | 0.12 |
| 481501 | 32 | 57 | 69 | 82 | 94 | 94 | 0.05 |
| 481523 | 35 | 60 | 74 | 85 | 90 | 93 | 0.04 |
| 481525 | 36 | 53 | 60 | 79 | 89 | 92 | 0.06 |
| 481549 | 0 | 16 | 60 | 81 | 90 | 96 | 0.15 |
| 481554 | 0 | 15 | 28 | 49 | 70 | 86 | 0.25 |

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells using electroporation | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 31.25 nM | 62.5 nM | 125.0 nM | 250.0 nM | 500.0 nM | 1000.0 nM | $IC_{50}$ (μM) |
| 481597 | 8 | 18 | 39 | 48 | 64 | 83 | 0.24 |
| 481695 | 15 | 27 | 39 | 50 | 64 | 80 | 0.22 |
| 481700 | 0 | 17 | 44 | 58 | 80 | 88 | 0.20 |
| 481710 | 12 | 39 | 65 | 79 | 86 | 90 | 0.11 |
| 481715 | 11 | 26 | 32 | 44 | 53 | 69 | 0.36 |
| 481725 | 27 | 40 | 56 | 77 | 89 | 93 | 0.09 |
| 481750 | 7 | 24 | 46 | 63 | 83 | 89 | 0.16 |
| 481755 | 17 | 28 | 30 | 54 | 68 | 80 | 0.20 |
| 481768 | 7 | 21 | 27 | 44 | 67 | 85 | 0.26 |

**Example 5: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in SK-BR-3 cells**

**[0264]** Gapmers from Example 4 were tested at various doses in SK-BR-3 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated with 0.02 μM, 0.1 μM, 0.5 μM, 1 μM. 2.5 μM, and 10 μM concentrations of antisense oligonucleotide, as specified in Table 5. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0265]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 5. As illustrated in Table 5, most of the ISIS oligonucleotides were able to penetrate the cell membrane and STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 5**

| Dose-dependent antisense inhibition of human STAT3 by free-uptake of ISIS oligonucleotide by SK-BR-3 cells | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 1 μM | 2.5 μM | 10 μM | $IC_{50}$ (μM) |
| 481374 | 10 | 18 | 18 | 16 | 8 | 25 | 15.9 |
| 481390 | 0 | 10 | 11 | 12 | 40 | 72 | 3.2 |
| 481453 | 14 | 13 | 27 | 45 | 58 | 79 | 1.3 |
| 481464 | 23 | 32 | 57 | 70 | 85 | 93 | 0.5 |
| 481475 | 0 | 0 | 35 | 49 | 72 | 88 | 1.0 |
| 481500 | 7 | 9 | 26 | 45 | 49 | 75 | 1.7 |
| 481501 | 0 | 0 | 4 | 5 | 53 | 65 | 2.7 |
| 481523 | 9 | 24 | 56 | 67 | 83 | 92 | 0.5 |
| 481525 | 0 | 17 | 13 | 15 | 32 | 68 | 4.4 |
| 481549 | 0 | 0 | 0 | 16 | 33 | 54 | 8.2 |
| 481597 | 1 | 0 | 11 | 14 | 22 | 44 | 10.6 |
| 481710 | 5 | 0 | 10 | 13 | 27 | 66 | 6.0 |
| 481725 | 29 | 45 | 47 | 39 | 39 | 63 | 2.6 |

| Dose-dependent antisense inhibition of human STAT3 by free-uptake of ISIS oligonucleotide by SK-BR-3 cells | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 1 μM | 2.5 μM | 10 μM | $IC_{50}$ (μM) |
| 481750 | 19 | 24 | 36 | 42 | 71 | 80 | 1.1 |
| 481763 | 30 | 38 | 51 | 63 | 81 | 89 | 0.6 |
| 481768 | 12 | 5 | 34 | 25 | 32 | 35 | 12.4 |

**Example 6: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in U251-MG cells**

**[0266]** Gapmers from Example 5 were further tested at various doses in U251-MG cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated with 0.02 μM, 0.1 μM, 0.5 μM, 1 μM. 2.5 μM, and 10 μM concentrations of antisense oligonucleotide, as specified in Table 6. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0267]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 6. As illustrated in Table 6, most of the ISIS oligonucleotides were able to penetrate the cell membrane and STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 6**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by U251-MG cells | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 1 μM | 2.5 μM | 10 μM | $IC_{50}$ (μM) |
| 481374 | 0 | 0 | 10 | 0 | 12 | 25 | 15.7 |
| 481390 | 0 | 4 | 10 | 8 | 16 | 31 | 13.9 |
| 481453 | 4 | 3 | 15 | 16 | 20 | 42 | 11.0 |
| 481464 | 13 | 11 | 41 | 42 | 54 | 79 | 1.3 |
| 481475 | 3 | 13 | 26 | 37 | 41 | 67 | 2.6 |
| 481500 | 2 | 12 | 14 | 12 | 25 | 38 | 11.7 |
| 481501 | 0 | 0 | 2 | 1 | 14 | 47 | 10.3 |
| 481523 | 22 | 27 | 39 | 45 | 63 | 83 | 1.1 |
| 481525 | 1 | 1 | 17 | 17 | 35 | 60 | 6.3 |
| 481549 | 0 | 0 | 0 | 0 | 9 | 29 | 14.5 |
| 481597 | 3 | 3 | 12 | 18 | 18 | 47 | 10.1 |
| 481695 | 0 | 14 | 12 | 22 | 25 | 33 | 12.9 |
| 481710 | 0 | 0 | 0 | 0 | 6 | 23 | 16.8 |
| 481725 | 0 | 0 | 5 | 7 | 20 | 38 | 11.8 |
| 481750 | 4 | 15 | 18 | 18 | 17 | 33 | 13.2 |
| 481763 | 15 | 16 | 25 | 36 | 36 | 64 | 3.2 |
| 481768 | 22 | 16 | 18 | 22 | 21 | 37 | 12.2 |

**Example 7: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in U251-MG cells**

**[0268]** ISIS 481464 and ISIS 481549, from the studies described above, were further tested at different doses in U251-MG cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated with 0.1 μM, 1 μM, 5 μM, 10 μM, and 20 μM concentrations of antisense oligonucleotide, as specified in Table 7. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0269]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 7. As illustrated in Table 7, both the ISIS oligonucleotides were able to penetrate the cell membrane.

**Table 7**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by U251-MG cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.1 μM | 1 μM | 5 μM | 10 μM | 20 μM | $IC_{50}$ (μM) |
| 481464 | 0 | 30 | 69 | 80 | 79 | 2.3 |
| 481549 | 0 | 0 | 26 | 35 | 38 | >20 |

**Example 8: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in MDA-MB-231 cells**

**[0270]** ISIS 481464 and ISIS 481549 were further tested at different doses in MDA-MB-231 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated with 0.02 μM, 0.2 μM, 1.0 μM, 5.0 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 8. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0271]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 8. As illustrated in Table 8, both the ISIS oligonucleotides were able to penetrate the cell membrane and significantly reduce STAT3 mRNA levels in a dose-dependent manner.

**Table 8**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by MDA-MB-231 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.2 μM | 1.0 μM | 5.0 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 0 | 25 | 71 | 85 | 87 | 0.6 |
| 481549 | 0 | 2 | 33 | 49 | 66 | 4.4 |

**Example 9: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in A431 cells**

**[0272]** ISIS 481464 and ISIS 481549 were further tested at different doses in A431 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated with 0.02 μM, 0.2 μM, 1.0 μM, 5.0 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 9. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0273]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 9. As illustrated in Table 9, both the ISIS oligonucleotides were able to penetrate the cell membrane and significantly reduce STAT3 mRNA levels in a dose-dependent manner.

**Table 9**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by A431 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.2 μM | 1.0 μM | 5.0 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 79 | 93 | 98 | 98 | 98 | <0.02 |
| 481549 | 0 | 38 | 68 | 82 | 84 | 0.6 |

**Example 10: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in H460 cells**

**[0274]** ISIS 481464 and ISIS 481549 were further tested at different doses in H460 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated with 0.02 μM, 0.2 μM, 1.0 μM, 5.0 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 10. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0275]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 10. As illustrated in Table 10, both the ISIS oligonucleotides were able to penetrate the cell membrane and significantly reduce STAT3 mRNA levels in a dose-dependent manner.

**Table 10**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by H460 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.2 μM | 1.0 μM | 5.0 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 46 | 89 | 96 | 97 | 98 | 0.01 |
| 481549 | 8 | 53 | 78 | 96 | 98 | 0.23 |

**Example 11: Antisense inhibition of human STAT3 in HuVEC cells**

**[0276]** Antisense oligonucleotides were designed targeting a human STAT3 nucleic acid and were tested for their effect on human STAT3 mRNA expression *in vitro*. Cultured HuVEC 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 STAT3 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS199 (forward sequence ACATGCCACTTTGGTGTTTCATAA, designated herein as SEQ ID NO: 6; reverse sequence TCTTCGTAGATTGTGCTGATAGAGAAC, designated herein as SEQ ID NO: 7; probe sequence CAGTATAGCCGCTTCCTGCAAGAGTCGAA, designated herein as SEQ ID NO: 8) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0277]** The chimeric antisense oligonucleotides in Table 11 were designed as 3-10-3 MOE, deoxy, and cEt gapmers. The gapmers are 16 nucleotides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked on both sides (in the 5' and 3' directions) by wings comprising three nucleosides each. Each nucleoside in the 5'-wing segment has a 2'-MOE sugar modification. Each nucleoside in the 3'-wing segment has a cEt sugar modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. The chemistry column of Table 11 presents the sugar motif of each gapmer, wherein 'e' indicates a 2'-MOE nucleoside, 'k' indicates a constrained ethyl (cEt) nucleoside, and 'd' indicates a 2'-deoxynucleoside.

**[0278]** "Human Target start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Human Target stop site" indicates the 3'-most nucleoside to which the gapmer is targeted in the human gene sequence. Each gapmer listed in Table 11 is targeted to human STAT3 mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_139276.2).

**Table 11**

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1 | 16 | 528170 | CGCAGCTCCGGAAACC | e-e-e-$d_{(10)}$-k-k-k | 12 | 471 |
| 2 | 17 | 528171 | CCGCAGCTCCGGAAAC | e-e-e-$d_{(10)}$-k-k-k | 11 | 472 |
| 4 | 19 | 528172 | CGCCGCAGCTCCGGAA | e-e-e-$d_{(10)}$-k-k-k | 10 | 473 |
| 5 | 20 | 528173 | CCGCCGCAGCTCCGGA | e-e-e-$d_{(10)}$-k-k-k | 22 | 474 |
| 32 | 47 | 528174 | ACCCCCGGCTCCCCCT | e-e-e-$d_{(10)}$-k-k-k | 18 | 475 |
| 34 | 49 | 528175 | GAACCCCCGGCTCCCC | e-e-e-$d_{(10)}$-k-k-k | 17 | 476 |
| 35 | 50 | 528176 | GGAACCCCCGGCTCCC | e-e-e-$d_{(10)}$-k-k-k | 23 | 477 |
| 36 | 51 | 528177 | CGGAACCCCCGGCTCC | e-e-e-$d_{(10)}$-k-k-k | 15 | 478 |
| 38 | 53 | 528178 | GTCGGAACCCCCGGCT | e-e-e-$d_{(10)}$-k-k-k | 21 | 479 |
| 39 | 54 | 528179 | CGTCGGAACCCCCGGC | e-e-e-$d_{(10)}$-k-k-k | 19 | 480 |
| 57 | 72 | 528180 | TTGTTCCCTCGGCTGC | e-e-e-$d_{(10)}$-k-k-k | 40 | 481 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 58 | 73 | 528181 | CTTGTTCCCTCGGCTG | e-e-e-$d_{(10)}$-k-k-k | 28 | 482 |
| 60 | 75 | 528182 | GGCTTGTTCCCTCGGC | e-e-e-$d_{(10)}$-k-k-k | 25 | 483 |
| 61 | 76 | 528183 | GGGCTTGTTCCCTCGG | e-e-e-$d_{(10)}$-k-k-k | 34 | 484 |
| 75 | 90 | 528184 | CCAGGATCCGGTTGGG | e-e-e-$d_{(10)}$-k-k-k | 34 | 485 |
| 76 | 91 | 528185 | TCCAGGATCCGGTTGG | e-e-e-$d_{(10)}$-k-k-k | 15 | 9 |
| 77 | 92 | 528186 | GTCCAGGATCCGGTTG | e-e-e-$d_{(10)}$-k-k-k | 28 | 486 |
| 78 | 93 | 528187 | TGTCCAGGATCCGGTT | e-e-e-$d_{(10)}$-k-k-k | 27 | 487 |
| 79 | 94 | 528188 | CTGTCCAGGATCCGGT | e-e-e-$d_{(10)}$-k-k-k | 33 | 488 |
| 81 | 96 | 528189 | GCCTGTCCAGGATCCG | e-e-e-$d_{(10)}$-k-k-k | 63 | 489 |
| 83 | 98 | 528190 | GTGCCTGTCCAGGATC | e-e-e-$d_{(10)}$-k-k-k | 36 | 490 |
| 189 | 204 | 528191 | AGAGGCCGAGAGGCCG | e-e-e-$d_{(10)}$-k-k-k | 2 | 491 |
| 210 | 225 | 528192 | GGTCCCAACTGTTTCT | e-e-e-$d_{(10)}$-k-k-k | 11 | 492 |
| 232 | 247 | 528193 | GGGCCATCCTGCTAAA | e-e-e-$d_{(10)}$-k-k-k | 14 | 493 |
| 233 | 248 | 528194 | TGGGCCATCCTGCTAA | e-e-e-$d_{(10)}$-k-k-k | 16 | 494 |
| 234 | 249 | 528195 | TTGGGCCATCCTGCTA | e-e-e-$d_{(10)}$-k-k-k | 9 | 495 |
| 236 | 251 | 528196 | CATTGGGCCATCCTGC | e-e-e-$d_{(10)}$-k-k-k | 39 | 496 |
| 237 | 252 | 528197 | CCATTGGGCCATCCTG | e-e-e-$d_{(10)}$-k-k-k | 38 | 497 |
| 239 | 254 | 528198 | TTCCATTGGGCCATCC | e-e-e-$d_{(10)}$-k-k-k | 19 | 498 |
| 240 | 255 | 528199 | ATTCCATTGGGCCATC | e-e-e-$d_{(10)}$-k-k-k | 27 | 15 |
| 244 | 259 | 528200 | GCTGATTCCATTGGGC | e-e-e-$d_{(10)}$-k-k-k | 18 | 500 |
| 245 | 260 | 528201 | AGCTGATTCCATTGGG | e-e-e-$d_{(10)}$-k-k-k | 20 | 501 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 246 | 261 | 528202 | TAGCTGATTCCATTGG | e-e-e-$d_{(10)}$-k-k-k | 41 | 502 |
| 247 | 262 | 528203 | GTAGCTGATTCCATTG | e-e-e-$d_{(10)}$-k-k-k | 37 | 503 |
| 250 | 265 | 528204 | GCTGTAGCTGATTCCA | e-e-e-$d_{(10)}$-k-k-k | 83 | 504 |
| 251 | 266 | 528205 | TGCTGTAGCTGATTCC | e-e-e-$d_{(10)}$-k-k-k | 72 | 505 |
| 252 | 267 | 528206 | CTGCTGTAGCTGATTC | e-e-e-$d_{(10)}$-k-k-k | 44 | 506 |
| 253 | 268 | 528207 | GCTGCTGTAGCTGATT | e-e-e-$d_{(10)}$-k-k-k | 49 | 507 |
| 263 | 278 | 528208 | CGTGTGTCAAGCTGCT | e-e-e-$d_{(10)}$-k-k-k | 73 | 508 |
| 264 | 279 | 528209 | CCGTGTGTCAAGCTGC | e-e-e-$d_{(10)}$-k-k-k | 81 | 17 |
| 265 | 280 | 528210 | ACCGTGTGTCAAGCTG | e-e-e-$d_{(10)}$-k-k-k | 78 | 509 |
| 266 | 281 | 528211 | TACCGTGTGTCAAGCT | e-e-e-$d_{(10)}$-k-k-k | 72 | 510 |
| 267 | 282 | 528212 | GTACCGTGTGTCAAGC | e-e-e-$d_{(10)}$-k-k-k | 81 | 511 |
| 268 | 283 | 528213 | GGTACCGTGTGTCAAG | e-e-e-$d_{(10)}$-k-k-k | 46 | 512 |
| 270 | 285 | 528214 | CAGGTACCGTGTGTCA | e-e-e-$d_{(10)}$-k-k-k | 80 | 513 |
| 271 | 286 | 528215 | CCAGGTACCGTGTGTC | e-e-e-$d_{(10)}$-k-k-k | 69 | 514 |
| 272 | 287 | 528216 | TCCAGGTACCGTGTGT | e-e-e-$d_{(10)}$-k-k-k | 41 | 515 |
| 273 | 288 | 528217 | CTCCAGGTACCGTGTG | e-e-e-$d_{(10)}$-k-k-k | 44 | 516 |
| 274 | 289 | 528218 | GCTCCAGGTACCGTGT | e-e-e-$d_{(10)}$-k-k-k | 32 | 517 |
| 275 | 290 | 528219 | TGCTCCAGGTACCGTG | e-e-e-$d_{(10)}$-k-k-k | 50 | 518 |
| 291 | 306 | 528220 | GTAGAGCTGATGGAGC | e-e-e-$d_{(10)}$-k-k-k | 12 | 519 |
| 292 | 307 | 528221 | TGTAGAGCTGATGGAG | e-e-e-$d_{(10)}$-k-k-k | 0 | 520 |
| 295 | 310 | 528222 | CACTGTAGAGCTGATG | e-e-e-$d_{(10)}$-k-k-k | 0 | 521 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 297 | 312 | 528223 | GTCACTGTAGAGCTGA | e-e-e-$d_{(10)}$-k-k-k | 44 | 522 |
| 302 | 317 | 528224 | AAGCTGTCACTGTAGA | e-e-e-$d_{(10)}$-k-k-k | 20 | 523 |
| 303 | 318 | 528225 | GAAGCTGTCACTGTAG | e-e-e-$d_{(10)}$-k-k-k | 24 | 524 |
| 307 | 322 | 528226 | TTGGGAAGCTGTCACT | e-e-e-$d_{(10)}$-k-k-k | 35 | 525 |
| 308 | 323 | 528227 | ATTGGGAAGCTGTCAC | e-e-e-$d_{(10)}$-k-k-k | 29 | 526 |
| 310 | 325 | 528228 | CCATTGGGAAGCTGTC | e-e-e-$d_{(10)}$-k-k-k | 33 | 527 |
| 322 | 337 | 519639 | ACTGCCGCAGCTCCAT | e-e-e-$d_{(10)}$-k-k-k | 37 | 19 |
| 329 | 344 | 528229 | GCCAGAAACTGCCGCA | e-e-e-$d_{(10)}$-k-k-k | 20 | 528 |
| 330 | 345 | 528230 | GGCCAGAAACTGCCGC | e-e-e-$d_{(10)}$-k-k-k | 1 | 529 |
| 331 | 346 | 528231 | GGGCCAGAAACTGCCG | e-e-e-$d_{(10)}$-k-k-k | 1 | 530 |
| 345 | 360 | 528232 | ACTCTCAATCCAAGGG | e-e-e-$d_{(10)}$-k-k-k | 14 | 531 |
| 346 | 361 | 528233 | GACTCTCAATCCAAGG | e-e-e-$d_{(10)}$-k-k-k | 10 | 21 |
| 347 | 362 | 528234 | TGACTCTCAATCCAAG | e-e-e-$d_{(10)}$-k-k-k | 6 | 532 |
| 351 | 366 | 528235 | ATCTTGACTCTCAATC | e-e-e-$d_{(10)}$-k-k-k | 38 | 533 |
| 353 | 368 | 528236 | CAATCTTGACTCTCAA | e-e-e-$d_{(10)}$-k-k-k | 29 | 534 |
| 354 | 369 | 528237 | CCAATCTTGACTCTCA | e-e-e-$d_{(10)}$-k-k-k | 60 | 535 |
| 355 | 370 | 528238 | CCCAATCTTGACTCTC | e-e-e-$d_{(10)}$-k-k-k | 37 | 536 |
| 356 | 371 | 528239 | GCCCAATCTTGACTCT | e-e-e-$d_{(10)}$-k-k-k | 48 | 537 |
| 357 | 372 | 528240 | TGCCCAATCTTGACTC | e-e-e-$d_{(10)}$-k-k-k | 40 | 538 |
| 358 | 373 | 528241 | ATGCCCAATCTTGACT | e-e-e-$d_{(10)}$-k-k-k | 21 | 539 |
| 359 | 374 | 528242 | TATGCCCAATCTTGAC | e-e-e-$d_{(10)}$-k-k-k | 27 | 540 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 362 | 377 | 528243 | GCATATGCCCAATCTT | e-e-e-$d_{(10)}$-k-k-k | 16 | 541 |
| 363 | 378 | 528244 | CGCATATGCCCAATCT | e-e-e-$d_{(10)}$-k-k-k | 50 | 542 |
| 367 | 382 | 528245 | TGGCCGCATATGCCCA | e-e-e-$d_{(10)}$-k-k-k | 67 | 543 |
| 368 | 383 | 528246 | CTGGCCGCATATGCCC | e-e-e-$d_{(10)}$-k-k-k | 47 | 544 |
| 369 | 384 | 528247 | GCTGGCCGCATATGCC | e-e-e-$d_{(10)}$-k-k-k | 54 | 545 |
| 370 | 385 | 528248 | TGCTGGCCGCATATGC | e-e-e-$d_{(10)}$-k-k-k | 35 | 546 |
| 371 | 386 | 528249 | TTGCTGGCCGCATATG | e-e-e-$d_{(10)}$-k-k-k | 22 | 547 |
| 372 | 387 | 528250 | TTTGCTGGCCGCATAT | e-e-e-$d_{(10)}$-k-k-k | 19 | 548 |
| 373 | 388 | 528251 | CTTTGCTGGCCGCATA | e-e-e-$d_{(10)}$-k-k-k | 27 | 549 |
| 374 | 389 | 528252 | TCTTTGCTGGCCGCAT | e-e-e-$d_{(10)}$-k-k-k | 34 | 550 |
| 375 | 390 | 528253 | TTCTTTGCTGGCCGCA | e-e-e-$d_{(10)}$-k-k-k | 59 | 23 |
| 376 | 391 | 528254 | ATTCTTTGCTGGCCGC | e-e-e-$d_{(10)}$-k-k-k | 63 | 551 |
| 378 | 393 | 528255 | TGATTCTTTGCTGGCC | e-e-e-$d_{(10)}$-k-k-k | 30 | 552 |
| 379 | 394 | 528256 | GTGATTCTTTGCTGGC | e-e-e-$d_{(10)}$-k-k-k | 47 | 553 |
| 383 | 398 | 528257 | GCATGTGATTCTTTGC | e-e-e-$d_{(10)}$-k-k-k | 43 | 554 |
| 384 | 399 | 528258 | GGCATGTGATTCTTTG | e-e-e-$d_{(10)}$-k-k-k | 47 | 555 |
| 388 | 403 | 528259 | AAGTGGCATGTGATTC | e-e-e-$d_{(10)}$-k-k-k | 43 | 556 |
| 391 | 406 | 528260 | CCAAAGTGGCATGTGA | e-e-e-$d_{(10)}$-k-k-k | 46 | 557 |
| 393 | 408 | 528261 | CACCAAAGTGGCATGT | e-e-e-$d_{(10)}$-k-k-k | 32 | 558 |
| 395 | 410 | 528262 | AACACCAAAGTGGCAT | e-e-e-$d_{(10)}$-k-k-k | 41 | 559 |
| 397 | 412 | 528263 | GAAACACCAAAGTGGC | e-e-e-$d_{(10)}$-k-k-k | 69 | 560 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 427 | 442 | 528264 | ACTGCTGGTCAATCTC | e-e-e-$d_{(10)}$-k-k-k | 27 | 561 |
| 428 | 443 | 528265 | TACTGCTGGTCAATCT | e-e-e-$d_{(10)}$-k-k-k | 32 | 562 |
| 430 | 445 | 528266 | TATACTGCTGGTCAAT | e-e-e-$d_{(10)}$-k-k-k | 27 | 563 |
| 431 | 446 | 528267 | CTATACTGCTGGTCAA | e-e-e-$d_{(10)}$-k-k-k | 38 | 564 |
| 432 | 447 | 528268 | GCTATACTGCTGGTCA | e-e-e-$d_{(10)}$-k-k-k | 58 | 565 |
| 433 | 448 | 528269 | GGCTATACTGCTGGTC | e-e-e-$d_{(10)}$-k-k-k | 69 | 566 |
| 434 | 449 | 528270 | CGGCTATACTGCTGGT | e-e-e-$d_{(10)}$-k-k-k | 73 | 567 |
| 435 | 450 | 528271 | GCGGCTATACTGCTGG | e-e-e-$d_{(10)}$-k-k-k | 71 | 568 |
| 436 | 451 | 528272 | AGCGGCTATACTGCTG | e-e-e-$d_{(10)}$-k-k-k | 54 | 569 |
| 437 | 452 | 528273 | AAGCGGCTATACTGCT | e-e-e-$d_{(10)}$-k-k-k | 36 | 570 |
| 439 | 454 | 528274 | GGAAGCGGCTATACTG | e-e-e-$d_{(10)}$-k-k-k | 27 | 571 |
| 440 | 455 | 528275 | AGGAAGCGGCTATACT | e-e-e-$d_{(10)}$-k-k-k | 21 | 572 |
| 441 | 456 | 528276 | CAGGAAGCGGCTATAC | e-e-e-$d_{(10)}$-k-k-k | 12 | 573 |
| 442 | 457 | 528277 | GCAGGAAGCGGCTATA | e-e-e-$d_{(10)}$-k-k-k | 14 | 574 |
| 443 | 458 | 528278 | TGCAGGAAGCGGCTAT | e-e-e-$d_{(10)}$-k-k-k | 21 | 575 |
| 444 | 459 | 528279 | TTGCAGGAAGCGGCTA | e-e-e-$d_{(10)}$-k-k-k | 31 | 576 |
| 445 | 460 | 528280 | CTTGCAGGAAGCGGCT | e-e-e-$d_{(10)}$-k-k-k | 44 | 577 |
| 463 | 478 | 528281 | GATAGAGAACATTCGA | e-e-e-$d_{(10)}$-k-k-k | 25 | 578 |
| 464 | 479 | 528282 | TGATAGAGAACATTCG | e-e-e-$d_{(10)}$-k-k-k | 39 | 579 |
| 469 | 484 | 528283 | TGTGCTGATAGAGAAC | e-e-e-$d_{(10)}$-k-k-k | 41 | 580 |
| 471 | 486 | 528284 | ATTGTGCTGATAGAGA | e-e-e-$d_{(10)}$-k-k-k | 38 | 581 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 472 | 487 | 528285 | GATTGTGCTGATAGAG | e-e-e-$d_{(10)}$-k-k-k | 50 | 582 |
| 473 | 488 | 528286 | AGATTGTGCTGATAGA | e-e-e-$d_{(10)}$-k-k-k | 49 | 583 |
| 475 | 490 | 528287 | GTAGATTGTGCTGATA | e-e-e-$d_{(10)}$-k-k-k | 14 | 584 |
| 476 | 491 | 528288 | CGTAGATTGTGCTGAT | e-e-e-$d_{(10)}$-k-k-k | 8 | 585 |
| 490 | 505 | 528289 | ACTGCTTGATTCTTCG | e-e-e-$d_{(10)}$-k-k-k | 9 | 33 |
| 511 | 526 | 528290 | CAAGATACCTGCTCTG | e-e-e-$d_{(10)}$-k-k-k | 48 | 35 |
| 512 | 527 | 528291 | TCAAGATACCTGCTCT | e-e-e-$d_{(10)}$-k-k-k | 34 | 586 |
| 513 | 528 | 528292 | CTCAAGATACCTGCTC | e-e-e-$d_{(10)}$-k-k-k | 19 | 587 |
| 514 | 529 | 528293 | TCTCAAGATACCTGCT | e-e-e-$d_{(10)}$-k-k-k | 31 | 588 |
| 517 | 532 | 528294 | GCTTCTCAAGATACCT | e-e-e-$d_{(10)}$-k-k-k | 42 | 589 |
| 519 | 534 | 528295 | TGGCTTCTCAAGATAC | e-e-e-$d_{(10)}$-k-k-k | 37 | 590 |
| 522 | 537 | 528296 | CATTGGCTTCTCAAGA | e-e-e-$d_{(10)}$-k-k-k | 11 | 591 |
| 523 | 538 | 528297 | CCATTGGCTTCTCAAG | e-e-e-$d_{(10)}$-k-k-k | 23 | 592 |
| 530 | 545 | 528298 | GCAATCTCCATTGGCT | e-e-e-$d_{(10)}$-k-k-k | 46 | 593 |
| 531 | 546 | 528299 | GGCAATCTCCATTGGC | e-e-e-$d_{(10)}$-k-k-k | 37 | 594 |
| 532 | 547 | 528300 | GGGCAATCTCCATTGG | e-e-e-$d_{(10)}$-k-k-k | 24 | 595 |
| 533 | 548 | 528301 | CGGGCAATCTCCATTG | e-e-e-$d_{(10)}$-k-k-k | 15 | 596 |
| 534 | 549 | 528302 | CCGGGCAATCTCCATT | e-e-e-$d_{(10)}$-k-k-k | 30 | 597 |
| 535 | 550 | 528303 | TCCGGGCAATCTCCAT | e-e-e-$d_{(10)}$-k-k-k | 29 | 598 |
| 536 | 551 | 528304 | ATCCGGGCAATCTCCA | e-e-e-$d_{(10)}$-k-k-k | 32 | 599 |
| 537 | 552 | 528305 | AATCCGGGCAATCTCC | e-e-e-$d_{(10)}$-k-k-k | 32 | 600 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 538 | 553 | 528306 | CAATCCGGGCAATCTC | e-e-e-$d_{(10)}$-k-k-k | 24 | 601 |
| 539 | 554 | 528307 | ACAATCCGGGCAATCT | e-e-e-$d_{(10)}$-k-k-k | 21 | 602 |
| 540 | 555 | 528308 | CACAATCCGGGCAATC | e-e-e-$d_{(10)}$-k-k-k | 14 | 603 |
| 541 | 556 | 528309 | CCACAATCCGGGCAAT | e-e-e-$d_{(10)}$-k-k-k | 13 | 604 |
| 543 | 558 | 528310 | GGCCACAATCCGGGCA | e-e-e-$d_{(10)}$-k-k-k | 27 | 605 |
| 546 | 561 | 528311 | CCGGGCCACAATCCGG | e-e-e-$d_{(10)}$-k-k-k | 27 | 606 |
| 547 | 562 | 528312 | ACCGGGCCACAATCCG | e-e-e-$d_{(10)}$-k-k-k | 58 | 607 |
| 548 | 563 | 528313 | CACCGGGCCACAATCC | e-e-e-$d_{(10)}$-k-k-k | 25 | 608 |
| 549 | 564 | 528314 | GCACCGGGCCACAATC | e-e-e-$d_{(10)}$-k-k-k | 18 | 609 |
| 550 | 565 | 528315 | GGCACCGGGCCACAAT | e-e-e-$d_{(10)}$-k-k-k | 33 | 610 |
| 551 | 566 | 528316 | AGGCACCGGGCCACAA | e-e-e-$d_{(10)}$-k-k-k | 42 | 611 |
| 558 | 573 | 528317 | TTCCCACAGGCACCGG | e-e-e-$d_{(10)}$-k-k-k | 47 | 612 |
| 586 | 601 | 528318 | TGGCTGCAGTCTGTAG | e-e-e-$d_{(10)}$-k-k-k | 12 | 613 |
| 592 | 607 | 528319 | CCGCAGTGGCTGCAGT | e-e-e-$d_{(10)}$-k-k-k | 10 | 614 |
| 599 | 614 | 528320 | TGCTGGGCCGCAGTGG | e-e-e-$d_{(10)}$-k-k-k | 14 | 615 |
| 601 | 616 | 528321 | CTTGCTGGGCCGCAGT | e-e-e-$d_{(10)}$-k-k-k | 0 | 616 |
| 603 | 618 | 528322 | CCCTTGCTGGGCCGCA | e-e-e-$d_{(10)}$-k-k-k | 6 | 617 |
| 604 | 619 | 528323 | CCCCTTGCTGGGCCGC | e-e-e-$d_{(10)}$-k-k-k | 21 | 618 |
| 605 | 620 | 528324 | CCCCCTTGCTGGGCCG | e-e-e-$d_{(10)}$-k-k-k | 8 | 619 |
| 608 | 623 | 528325 | TGGCCCCCTTGCTGGG | e-e-e-$d_{(10)}$-k-k-k | 0 | 620 |
| 615 | 630 | 528326 | GTTGGCCTGGCCCCCT | e-e-e-$d_{(10)}$-k-k-k | 31 | 621 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 616 | 631 | 528327 | GGTTGGCCTGGCCCCC | e-e-e-$d_{(10)}$-k-k-k | 47 | 622 |
| 617 | 632 | 528328 | TGGTTGGCCTGGCCCC | e-e-e-$d_{(10)}$-k-k-k | 36 | 623 |
| 646 | 661 | 528329 | GCTTCTCCGTCACCAC | e-e-e-$d_{(10)}$-k-k-k | 28 | 624 |
| 647 | 662 | 528330 | TGCTTCTCCGTCACCA | e-e-e-$d_{(10)}$-k-k-k | 22 | 625 |
| 649 | 664 | 528331 | GCTGCTTCTCCGTCAC | e-e-e-$d_{(10)}$-k-k-k | 35 | 626 |
| 667 | 682 | 528332 | GGTGCTGCTCCAGCAT | e-e-e-$d_{(10)}$-k-k-k | 21 | 627 |
| 678 | 693 | 528333 | GACATCCTGAAGGTGC | e-e-e-$d_{(10)}$-k-k-k | 0 | 628 |
| 682 | 697 | 528334 | TCCGGACATCCTGAAG | e-e-e-$d_{(10)}$-k-k-k | 1 | 629 |
| 683 | 698 | 528335 | TTCCGGACATCCTGAA | e-e-e-$d_{(10)}$-k-k-k | 0 | 630 |
| 684 | 699 | 528336 | CTTCCGGACATCCTGA | e-e-e-$d_{(10)}$-k-k-k | 0 | 631 |
| 685 | 700 | 528337 | TCTTCCGGACATCCTG | e-e-e-$d_{(10)}$-k-k-k | 0 | 632 |
| 686 | 701 | 528338 | CTCTTCCGGACATCCT | e-e-e-$d_{(10)}$-k-k-k | 19 | 633 |
| 687 | 702 | 528339 | TCTCTTCCGGACATCC | e-e-e-$d_{(10)}$-k-k-k | 21 | 634 |
| 688 | 703 | 528340 | CTCTCTTCCGGACATC | e-e-e-$d_{(10)}$-k-k-k | 17 | 635 |
| 689 | 704 | 528341 | ACTCTCTTCCGGACAT | e-e-e-$d_{(10)}$-k-k-k | 37 | 636 |
| 727 | 742 | 528342 | GATTCTCTACCACTTT | e-e-e-$d_{(10)}$-k-k-k | 33 | 637 |
| 730 | 745 | 528343 | GGAGATTCTCTACCAC | e-e-e-$d_{(10)}$-k-k-k | 40 | 53 |
| 731 | 746 | 528344 | TGGAGATTCTCTACCA | e-e-e-$d_{(10)}$-k-k-k | 32 | 638 |
| 732 | 747 | 528345 | CTGGAGATTCTCTACC | e-e-e-$d_{(10)}$-k-k-k | 18 | 639 |
| 733 | 748 | 528346 | CCTGGAGATTCTCTAC | e-e-e-$d_{(10)}$-k-k-k | 12 | 640 |
| 738 | 753 | 528347 | GTCATCCTGGAGATTC | e-e-e-$d_{(10)}$-k-k-k | 54 | 641 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 764 | 779 | 528348 | TTGAGGGTTTTATAGT | e-e-e-$d_{(10)}$-k-k-k | 0 | 642 |
| 775 | 790 | 528349 | CTCCTTGACTCTTGAG | e-e-e-$d_{(10)}$-k-k-k | 21 | 643 |
| 781 | 796 | 528350 | GCATGTCTCCTTGACT | e-e-e-$d_{(10)}$-k-k-k | 29 | 644 |
| 782 | 797 | 528351 | TGCATGTCTCCTTGAC | e-e-e-$d_{(10)}$-k-k-k | 30 | 645 |
| 783 | 798 | 528352 | TTGCATGTCTCCTTGA | e-e-e-$d_{(10)}$-k-k-k | 17 | 646 |
| 787 | 802 | 528353 | GATCTTGCATGTCTCC | e-e-e-$d_{(10)}$-k-k-k | 61 | 647 |
| 788 | 803 | 518346 | AGATCTTGCATGTCTC | e-e-e-$d_{(10)}$-k-k-k | 36 | 57 |
| 790 | 805 | 528354 | TCAGATCTTGCATGTC | e-e-e-$d_{(10)}$-k-k-k | 43 | 648 |
| 792 | 807 | 528355 | ATTCAGATCTTGCATG | e-e-e-$d_{(10)}$-k-k-k | 9 | 649 |
| 794 | 809 | 528356 | CCATTCAGATCTTGCA | e-e-e-$d_{(10)}$-k-k-k | 37 | 650 |
| 795 | 810 | 528357 | TCCATTCAGATCTTGC | e-e-e-$d_{(10)}$-k-k-k | 55 | 651 |
| 796 | 811 | 528358 | TTCCATTCAGATCTTG | e-e-e-$d_{(10)}$-k-k-k | 17 | 652 |
| 803 | 818 | 528359 | TGGTTGTTTCCATTCA | e-e-e-$d_{(10)}$-k-k-k | 33 | 653 |
| 804 | 819 | 528360 | CTGGTTGTTTCCATTC | e-e-e-$d_{(10)}$-k-k-k | 18 | 654 |
| 806 | 821 | 528361 | GACTGGTTGTTTCCAT | e-e-e-$d_{(10)}$-k-k-k | 23 | 655 |
| 807 | 822 | 528362 | TGACTGGTTGTTTCCA | e-e-e-$d_{(10)}$-k-k-k | 33 | 656 |
| 813 | 828 | 528363 | GGTCACTGACTGGTTG | e-e-e-$d_{(10)}$-k-k-k | 43 | 657 |
| 814 | 829 | 528364 | TGGTCACTGACTGGTT | e-e-e-$d_{(10)}$-k-k-k | 62 | 658 |
| 848 | 863 | 528365 | GTGAGCATCTGTTCCA | e-e-e-$d_{(10)}$-k-k-k | 41 | 659 |
| 852 | 867 | 528366 | CGCAGTGAGCATCTGT | e-e-e-$d_{(10)}$-k-k-k | 0 | 660 |
| 853 | 868 | 528367 | GCGCAGTGAGCATCTG | e-e-e-$d_{(10)}$-k-k-k | 0 | 661 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 854 | 869 | 528368 | AGCGCAGTGAGCATCT | e-e-e-$d_{(10)}$-k-k-k | 7 | 662 |
| 855 | 870 | 528369 | CAGCGCAGTGAGCATC | e-e-e-$d_{(10)}$-k-k-k | 6 | 663 |
| 857 | 872 | 528370 | TCCAGCGCAGTGAGCA | e-e-e-$d_{(10)}$-k-k-k | 12 | 664 |
| 858 | 873 | 528371 | GTCCAGCGCAGTGAGC | e-e-e-$d_{(10)}$-k-k-k | 11 | 665 |
| 859 | 874 | 528372 | GGTCCAGCGCAGTGAG | e-e-e-$d_{(10)}$-k-k-k | 8 | 666 |
| 860 | 875 | 528373 | TGGTCCAGCGCAGTGA | e-e-e-$d_{(10)}$-k-k-k | 12 | 667 |
| 862 | 877 | 528374 | TCTGGTCCAGCGCAGT | e-e-e-$d_{(10)}$-k-k-k | 9 | 668 |
| 863 | 878 | 528375 | ATCTGGTCCAGCGCAG | e-e-e-$d_{(10)}$-k-k-k | 8 | 669 |
| 864 | 879 | 528376 | CATCTGGTCCAGCGCA | e-e-e-$d_{(10)}$-k-k-k | 0 | 670 |
| 865 | 880 | 528377 | GCATCTGGTCCAGCGC | e-e-e-$d_{(10)}$-k-k-k | 28 | 671 |
| 867 | 882 | 528378 | CCGCATCTGGTCCAGC | e-e-e-$d_{(10)}$-k-k-k | 72 | 672 |
| 868 | 883 | 528379 | TCCGCATCTGGTCCAG | e-e-e-$d_{(10)}$-k-k-k | 43 | 61 |
| 869 | 884 | 528380 | CTCCGCATCTGGTCCA | e-e-e-$d_{(10)}$-k-k-k | 34 | 673 |
| 870 | 885 | 528381 | TCTCCGCATCTGGTCC | e-e-e-$d_{(10)}$-k-k-k | 42 | 674 |
| 871 | 886 | 528382 | TTCTCCGCATCTGGTC | e-e-e-$d_{(10)}$-k-k-k | 37 | 675 |
| 872 | 887 | 528383 | CTTCTCCGCATCTGGT | e-e-e-$d_{(10)}$-k-k-k | 23 | 676 |
| 873 | 888 | 528384 | GCTTCTCCGCATCTGG | e-e-e-$d_{(10)}$-k-k-k | 36 | 677 |
| 875 | 890 | 528385 | ATGCTTCTCCGCATCT | e-e-e-$d_{(10)}$-k-k-k | 45 | 678 |
| 876 | 891 | 528386 | GATGCTTCTCCGCATC | e-e-e-$d_{(10)}$-k-k-k | 14 | 679 |
| 877 | 892 | 528387 | CGATGCTTCTCCGCAT | e-e-e-$d_{(10)}$-k-k-k | 25 | 680 |
| 878 | 893 | 528388 | ACGATGCTTCTCCGCA | e-e-e-$d_{(10)}$-k-k-k | 39 | 681 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 879 | 894 | 528389 | CACGATGCTTCTCCGC | e-e-e-$d_{(10)}$-k-k-k | 46 | 682 |
| 880 | 895 | 528390 | TCACGATGCTTCTCCG | e-e-e-$d_{(10)}$-k-k-k | 17 | 683 |
| 881 | 896 | 528391 | CTCACGATGCTTCTCC | e-e-e-$d_{(10)}$-k-k-k | 20 | 684 |
| 882 | 897 | 528392 | ACTCACGATGCTTCTC | e-e-e-$d_{(10)}$-k-k-k | 16 | 685 |
| 883 | 898 | 528393 | CACTCACGATGCTTCT | e-e-e-$d_{(10)}$-k-k-k | 39 | 686 |
| 885 | 900 | 528394 | CTCACTCACGATGCTT | e-e-e-$d_{(10)}$-k-k-k | 45 | 687 |
| 886 | 901 | 528395 | GCTCACTCACGATGCT | e-e-e-$d_{(10)}$-k-k-k | 37 | 688 |
| 888 | 903 | 528396 | CAGCTCACTCACGATG | e-e-e-$d_{(10)}$-k-k-k | 24 | 689 |
| 889 | 904 | 528397 | CCAGCTCACTCACGAT | e-e-e-$d_{(10)}$-k-k-k | 25 | 690 |
| 890 | 905 | 528398 | GCCAGCTCACTCACGA | e-e-e-$d_{(10)}$-k-k-k | 18 | 691 |
| 891 | 906 | 528399 | CGCCAGCTCACTCACG | e-e-e-$d_{(10)}$-k-k-k | 4 | 692 |
| 1068 | 1083 | 528477 | AATTTGTTGACGGGTC | e-e-e-$d_{(10)}$-k-k-k | 37 | 693 |
| 1069 | 1084 | 528478 | TAATTTGTTGACGGGT | e-e-e-$d_{(10)}$-k-k-k | 35 | 694 |
| 1070 | 1085 | 528479 | TTAATTTGTTGACGGG | e-e-e-$d_{(10)}$-k-k-k | 40 | 695 |
| 1072 | 1087 | 528480 | TCTTAATTTGTTGACG | e-e-e-$d_{(10)}$-k-k-k | 6 | 696 |
| 1087 | 1102 | 528481 | GCAACTCCTCCAGTTT | e-e-e-$d_{(10)}$-k-k-k | 42 | 697 |
| 1088 | 1103 | 528482 | TGCAACTCCTCCAGTT | e-e-e-$d_{(10)}$-k-k-k | 28 | 698 |
| 1094 | 1109 | 528483 | TTTTGCTGCAACTCCT | e-e-e-$d_{(10)}$-k-k-k | 49 | 699 |
| 1095 | 1110 | 528484 | TTTTTGCTGCAACTCC | e-e-e-$d_{(10)}$-k-k-k | 58 | 700 |
| 1114 | 1129 | 528485 | GGTCCCCTTTGTAGGA | e-e-e-$d_{(10)}$-k-k-k | 35 | 701 |
| 1115 | 1130 | 528486 | GGGTCCCCTTTGTAGG | e-e-e-$d_{(10)}$-k-k-k | 31 | 702 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1129 | 1144 | 528487 | GGTGCTGTACAATGGG | e-e-e-$d_{(10)}$-k-k-k | 61 | 703 |
| 1130 | 1145 | 528488 | CGGTGCTGTACAATGG | e-e-e-$d_{(10)}$-k-k-k | 61 | 704 |
| 1131 | 1146 | 528489 | CCGGTGCTGTACAATG | e-e-e-$d_{(10)}$-k-k-k | 37 | 705 |
| 1132 | 1147 | 528490 | GCCGGTGCTGTACAAT | e-e-e-$d_{(10)}$-k-k-k | 33 | 706 |
| 1133 | 1148 | 528491 | GGCCGGTGCTGTACAA | e-e-e-$d_{(10)}$-k-k-k | 39 | 707 |
| 1134 | 1149 | 528492 | CGGCCGGTGCTGTACA | e-e-e-$d_{(10)}$-k-k-k | 38 | 708 |
| 1136 | 1151 | 528493 | ATCGGCCGGTGCTGTA | e-e-e-$d_{(10)}$-k-k-k | 29 | 709 |
| 1137 | 1152 | 528494 | CATCGGCCGGTGCTGT | e-e-e-$d_{(10)}$-k-k-k | 43 | 710 |
| 1138 | 1153 | 528495 | GCATCGGCCGGTGCTG | e-e-e-$d_{(10)}$-k-k-k | 41 | 711 |
| 1139 | 1154 | 528496 | AGCATCGGCCGGTGCT | e-e-e-$d_{(10)}$-k-k-k | 18 | 712 |
| 1140 | 1155 | 528497 | CAGCATCGGCCGGTGC | e-e-e-$d_{(10)}$-k-k-k | 15 | 713 |
| 1141 | 1156 | 528498 | CCAGCATCGGCCGGTG | e-e-e-$d_{(10)}$-k-k-k | 39 | 714 |
| 1142 | 1157 | 528499 | TCCAGCATCGGCCGGT | e-e-e-$d_{(10)}$-k-k-k | 50 | 715 |
| 1144 | 1159 | 528500 | CCTCCAGCATCGGCCG | e-e-e-$d_{(10)}$-k-k-k | 58 | 716 |
| 1146 | 1161 | 528501 | CTCCTCCAGCATCGGC | e-e-e-$d_{(10)}$-k-k-k | 67 | 717 |
| 1147 | 1162 | 528502 | TCTCCTCCAGCATCGG | e-e-e-$d_{(10)}$-k-k-k | 76 | 718 |
| 1153 | 1168 | 528503 | CGATTCTCTCCTCCAG | e-e-e-$d_{(10)}$-k-k-k | 68 | 719 |
| 1154 | 1169 | 528504 | ACGATTCTCTCCTCCA | e-e-e-$d_{(10)}$-k-k-k | 69 | 720 |
| 1155 | 1170 | 528505 | CACGATTCTCTCCTCC | e-e-e-$d_{(10)}$-k-k-k | 68 | 721 |
| 1156 | 1171 | 528506 | CCACGATTCTCTCCTC | e-e-e-$d_{(10)}$-k-k-k | 45 | 722 |
| 1157 | 1172 | 528507 | TCCACGATTCTCTCCT | e-e-e-$d_{(10)}$-k-k-k | 42 | 723 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1158 | 1173 | 528508 | CTCCACGATTCTCTCC | e-e-e-$d_{(10)}$-k-k-k | 41 | 724 |
| 1159 | 1174 | 528509 | GCTCCACGATTCTCTC | e-e-e-$d_{(10)}$-k-k-k | 32 | 725 |
| 1160 | 1175 | 528510 | AGCTCCACGATTCTCT | e-e-e-$d_{(10)}$-k-k-k | 7 | 726 |
| 1161 | 1176 | 528511 | CAGCTCCACGATTCTC | e-e-e-$d_{(10)}$-k-k-k | 5 | 727 |
| 1162 | 1177 | 528512 | ACAGCTCCACGATTCT | e-e-e-$d_{(10)}$-k-k-k | 0 | 728 |
| 1163 | 1178 | 528513 | AACAGCTCCACGATTC | e-e-e-$d_{(10)}$-k-k-k | 8 | 729 |
| 1184 | 1199 | 528514 | GCACTTTTCATTAAGT | e-e-e-$d_{(10)}$-k-k-k | 14 | 730 |
| 1185 | 1200 | 528515 | GGCACTTTTCATTAAG | e-e-e-$d_{(10)}$-k-k-k | 15 | 731 |
| 1199 | 1214 | 528516 | CGCTCCACCACAAAGG | e-e-e-$d_{(10)}$-k-k-k | 46 | 732 |
| 1205 | 1220 | 528517 | GGCTGCCGCTCCACCA | e-e-e-$d_{(10)}$-k-k-k | 55 | 733 |
| 1206 | 1221 | 528518 | GGGCTGCCGCTCCACC | e-e-e-$d_{(10)}$-k-k-k | 80 | 734 |
| 1207 | 1222 | 528519 | AGGGCTGCCGCTCCAC | e-e-e-$d_{(10)}$-k-k-k | 61 | 735 |
| 1208 | 1223 | 528520 | CAGGGCTGCCGCTCCA | e-e-e-$d_{(10)}$-k-k-k | 63 | 736 |
| 1211 | 1226 | 528521 | ATGCAGGGCTGCCGCT | e-e-e-$d_{(10)}$-k-k-k | 37 | 737 |
| 1212 | 1227 | 528522 | CATGCAGGGCTGCCGC | e-e-e-$d_{(10)}$-k-k-k | 38 | 738 |
| 1221 | 1236 | 528523 | ATGCATGGGCATGCAG | e-e-e-$d_{(10)}$-k-k-k | 26 | 739 |
| 1222 | 1237 | 528524 | GATGCATGGGCATGCA | e-e-e-$d_{(10)}$-k-k-k | 42 | 740 |
| 1223 | 1238 | 528525 | GGATGCATGGGCATGC | e-e-e-$d_{(10)}$-k-k-k | 43 | 741 |
| 1252 | 1267 | 528526 | CGCCGGTCTTGATGAC | e-e-e-$d_{(10)}$-k-k-k | 11 | 742 |
| 1253 | 1268 | 528527 | ACGCCGGTCTTGATGA | e-e-e-$d_{(10)}$-k-k-k | 0 | 743 |
| 1265 | 1280 | 528528 | GTAGTGAACTGGACGC | e-e-e-$d_{(10)}$-k-k-k | 10 | 744 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1284 | 1299 | 528529 | GACCAGCAACCTGACT | e-e-e-$d_{(10)}$-k-k-k | 22 | 745 |
| 1285 | 1300 | 528530 | TGACCAGCAACCTGAC | e-e-e-$d_{(10)}$-k-k-k | 31 | 746 |
| 1288 | 1303 | 528531 | ATTTGACCAGCAACCT | e-e-e-$d_{(10)}$-k-k-k | 48 | 747 |
| 1289 | 1304 | 528532 | AATTTGACCAGCAACC | e-e-e-$d_{(10)}$-k-k-k | 22 | 748 |
| 1290 | 1305 | 528533 | GAATTTGACCAGCAAC | e-e-e-$d_{(10)}$-k-k-k | 11 | 749 |
| 1293 | 1308 | 528534 | AGGGAATTTGACCAGC | e-e-e-$d_{(10)}$-k-k-k | 67 | 750 |
| 1294 | 1309 | 528535 | CAGGGAATTTGACCAG | e-e-e-$d_{(10)}$-k-k-k | 50 | 751 |
| 1295 | 1310 | 528536 | TCAGGGAATTTGACCA | e-e-e-$d_{(10)}$-k-k-k | 38 | 752 |
| 1296 | 1311 | 528537 | CTCAGGGAATTTGACC | e-e-e-$d_{(10)}$-k-k-k | 17 | 753 |
| 1336 | 1351 | 528539 | CTTTGTCAATGCACAC | e-e-e-$d_{(10)}$-k-k-k | 67 | 754 |
| 1338 | 1353 | 528540 | GTCTTTGTCAATGCAC | e-e-e-$d_{(10)}$-k-k-k | 61 | 755 |
| 1339 | 1354 | 528541 | AGTCTTTGTCAATGCA | e-e-e-$d_{(10)}$-k-k-k | 65 | 756 |
| 1343 | 1358 | 528542 | CCAGAGTCTTTGTCAA | e-e-e-$d_{(10)}$-k-k-k | 10 | 757 |
| 1345 | 1360 | 528543 | CCCCAGAGTCTTTGTC | e-e-e-$d_{(10)}$-k-k-k | 7 | 758 |
| 1371 | 1386 | 528544 | CCGGGATCCTCTGAGA | e-e-e-$d_{(10)}$-k-k-k | 12 | 759 |
| 1372 | 1387 | 528545 | TCCGGGATCCTCTGAG | e-e-e-$d_{(10)}$-k-k-k | 11 | 760 |
| 1373 | 1388 | 528546 | TTCCGGGATCCTCTGA | e-e-e-$d_{(10)}$-k-k-k | 7 | 761 |
| 1374 | 1389 | 528547 | TTTCCGGGATCCTCTG | e-e-e-$d_{(10)}$-k-k-k | 14 | 762 |
| 1375 | 1390 | 528548 | ATTTCCGGGATCCTCT | e-e-e-$d_{(10)}$-k-k-k | 14 | 763 |
| 1376 | 1391 | 528549 | AATTTCCGGGATCCTC | e-e-e-$d_{(10)}$-k-k-k | 19 | 764 |
| 1377 | 1392 | 528550 | AAATTTCCGGGATCCT | e-e-e-$d_{(10)}$-k-k-k | 14 | 765 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1379 | 1394 | 528551 | TTAAATTTCCGGGATC | e-e-e-$d_{(10)}$-k-k-k | 1 | 766 |
| 1380 | 1395 | 528552 | GTTAAATTTCCGGGAT | e-e-e-$d_{(10)}$-k-k-k | 9 | 767 |
| 1381 | 1396 | 528553 | TGTTAAATTTCCGGGA | e-e-e-$d_{(10)}$-k-k-k | 0 | 768 |
| 1382 | 1397 | 528554 | ATGTTAAATTTCCGGG | e-e-e-$d_{(10)}$-k-k-k | 12 | 769 |
| 1384 | 1399 | 528555 | GAATGTTAAATTTCCG | e-e-e-$d_{(10)}$-k-k-k | 13 | 770 |
| 1392 | 1407 | 528556 | TGTGCCCAGAATGTTA | e-e-e-$d_{(10)}$-k-k-k | 18 | 771 |
| 1435 | 1450 | 528557 | GGCTGCCGTTGTTGGA | e-e-e-$d_{(10)}$-k-k-k | 48 | 772 |
| 1436 | 1451 | 528558 | AGGCTGCCGTTGTTGG | e-e-e-$d_{(10)}$-k-k-k | 38 | 773 |
| 1437 | 1452 | 528559 | GAGGCTGCCGTTGTTG | e-e-e-$d_{(10)}$-k-k-k | 24 | 98 |
| 1438 | 1453 | 528560 | AGAGGCTGCCGTTGTT | e-e-e-$d_{(10)}$-k-k-k | 27 | 774 |
| 1439 | 1454 | 528561 | GAGAGGCTGCCGTTGT | e-e-e-$d_{(10)}$-k-k-k | 10 | 775 |
| 1440 | 1455 | 528562 | AGAGAGGCTGCCGTTG | e-e-e-$d_{(10)}$-k-k-k | 17 | 776 |
| 1441 | 1456 | 528563 | CAGAGAGGCTGCCGTT | e-e-e-$d_{(10)}$-k-k-k | 27 | 777 |
| 1461 | 1476 | 528564 | GGTCAAGTGTTTGAAT | e-e-e-$d_{(10)}$-k-k-k | 7 | 778 |
| 1471 | 1486 | 528565 | GCTCCCTCAGGGTCAA | e-e-e-$d_{(10)}$-k-k-k | 48 | 779 |
| 1496 | 1511 | 528566 | GCTCGGCCCCCATTCC | e-e-e-$d_{(10)}$-k-k-k | 42 | 780 |
| 1497 | 1512 | 528567 | GGCTCGGCCCCCATTC | e-e-e-$d_{(10)}$-k-k-k | 45 | 781 |
| 1498 | 1513 | 528568 | TGGCTCGGCCCCCATT | e-e-e-$d_{(10)}$-k-k-k | 34 | 782 |
| 1499 | 1514 | 528569 | TTGGCTCGGCCCCCAT | e-e-e-$d_{(10)}$-k-k-k | 49 | 783 |
| 1517 | 1532 | 528570 | ATCAGGGAAGCATCAC | e-e-e-$d_{(10)}$-k-k-k | 22 | 104 |
| 1519 | 1534 | 528571 | CAATCAGGGAAGCATC | e-e-e-$d_{(10)}$-k-k-k | 13 | 784 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1523 | 1538 | 528572 | GTCACAATCAGGGAAG | e-e-e-$d_{(10)}$-k-k-k | 30 | 785 |
| 1525 | 1540 | 528573 | CAGTCACAATCAGGGA | e-e-e-$d_{(10)}$-k-k-k | 27 | 786 |
| 1526 | 1541 | 528574 | TCAGTCACAATCAGGG | e-e-e-$d_{(10)}$-k-k-k | 51 | 787 |
| 1529 | 1544 | 528575 | TCCTCAGTCACAATCA | e-e-e-$d_{(10)}$-k-k-k | 14 | 788 |
| 1537 | 1552 | 528576 | GGTGCAGCTCCTCAGT | e-e-e-$d_{(10)}$-k-k-k | 28 | 789 |
| 1543 | 1558 | 528577 | TGATCAGGTGCAGCTC | e-e-e-$d_{(10)}$-k-k-k | 30 | 790 |
| 1544 | 1559 | 528578 | GTGATCAGGTGCAGCT | e-e-e-$d_{(10)}$-k-k-k | 36 | 791 |
| 1545 | 1560 | 528579 | GGTGATCAGGTGCAGC | e-e-e-$d_{(10)}$-k-k-k | 39 | 792 |
| 1576 | 1591 | 528580 | TGAGGCCTTGGTGATA | e-e-e-$d_{(10)}$-k-k-k | 10 | 793 |
| 1578 | 1593 | 528581 | CTTGAGGCCTTGGTGA | e-e-e-$d_{(10)}$-k-k-k | 5 | 794 |
| 1579 | 1594 | 528582 | TCTTGAGGCCTTGGTG | e-e-e-$d_{(10)}$-k-k-k | 15 | 110 |
| 1580 | 1595 | 528583 | ATCTTGAGGCCTTGGT | e-e-e-$d_{(10)}$-k-k-k | 5 | 795 |
| 1581 | 1596 | 528584 | AATCTTGAGGCCTTGG | e-e-e-$d_{(10)}$-k-k-k | 15 | 796 |
| 1582 | 1597 | 528585 | CAATCTTGAGGCCTTG | e-e-e-$d_{(10)}$-k-k-k | 7 | 797 |
| 1583 | 1598 | 528586 | TCAATCTTGAGGCCTT | e-e-e-$d_{(10)}$-k-k-k | 9 | 798 |
| 1584 | 1599 | 528587 | GTCAATCTTGAGGCCT | e-e-e-$d_{(10)}$-k-k-k | 25 | 799 |
| 1585 | 1600 | 528588 | GGTCAATCTTGAGGCC | e-e-e-$d_{(10)}$-k-k-k | 26 | 800 |
| 1586 | 1601 | 528589 | AGGTCAATCTTGAGGC | e-e-e-$d_{(10)}$-k-k-k | 31 | 801 |
| 1587 | 1602 | 528590 | TAGGTCAATCTTGAGG | e-e-e-$d_{(10)}$-k-k-k | 27 | 802 |
| 1588 | 1603 | 528591 | CTAGGTCAATCTTGAG | e-e-e-$d_{(10)}$-k-k-k | 24 | 803 |
| 1590 | 1605 | 528592 | CTCTAGGTCAATCTTG | e-e-e-$d_{(10)}$-k-k-k | 33 | 804 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1592 | 1607 | 528593 | GTCTCTAGGTCAATCT | e-e-e-$d_{(10)}$-k-k-k | 30 | 805 |
| 1594 | 1609 | 528594 | GGGTCTCTAGGTCAAT | e-e-e-$d_{(10)}$-k-k-k | 25 | 806 |
| 1595 | 1610 | 528595 | TGGGTCTCTAGGTCAA | e-e-e-$d_{(10)}$-k-k-k | 28 | 807 |
| 1596 | 1611 | 528596 | GTGGGTCTCTAGGTCA | e-e-e-$d_{(10)}$-k-k-k | 34 | 808 |
| 1597 | 1612 | 528597 | AGTGGGTCTCTAGGTC | e-e-e-$d_{(10)}$-k-k-k | 19 | 809 |
| 1599 | 1614 | 528598 | GGAGTGGGTCTCTAGG | e-e-e-$d_{(10)}$-k-k-k | 31 | 114 |
| 1600 | 1615 | 528599 | AGGAGTGGGTCTCTAG | e-e-e-$d_{(10)}$-k-k-k | 10 | 810 |
| 1601 | 1616 | 528600 | AAGGAGTGGGTCTCTA | e-e-e-$d_{(10)}$-k-k-k | 14 | 811 |
| 1602 | 1617 | 528601 | CAAGGAGTGGGTCTCT | e-e-e-$d_{(10)}$-k-k-k | 11 | 812 |
| 1609 | 1624 | 528602 | CAACTGGCAAGGAGTG | e-e-e-$d_{(10)}$-k-k-k | 17 | 813 |
| 1629 | 1644 | 528603 | ACAGATGTTGGAGATC | e-e-e-$d_{(10)}$-k-k-k | 8 | 814 |
| 1632 | 1647 | 528604 | CTGACAGATGTTGGAG | e-e-e-$d_{(10)}$-k-k-k | 11 | 815 |
| 1633 | 1648 | 528605 | TCTGACAGATGTTGGA | e-e-e-$d_{(10)}$-k-k-k | 25 | 119 |
| 1650 | 1665 | 528606 | CGCCCAGGCATTTGGC | e-e-e-$d_{(10)}$-k-k-k | 18 | 816 |
| 1651 | 1666 | 528607 | ACGCCCAGGCATTTGG | e-e-e-$d_{(10)}$-k-k-k | 36 | 817 |
| 1677 | 1692 | 528608 | GGTCAGCATGTTGTAC | e-e-e-$d_{(10)}$-k-k-k | 11 | 818 |
| 1678 | 1693 | 528609 | TGGTCAGCATGTTGTA | e-e-e-$d_{(10)}$-k-k-k | 9 | 819 |
| 1680 | 1695 | 528610 | GTTGGTCAGCATGTTG | e-e-e-$d_{(10)}$-k-k-k | 19 | 820 |
| 1682 | 1697 | 528611 | TTGTTGGTCAGCATGT | e-e-e-$d_{(10)}$-k-k-k | 27 | 821 |
| 1711 | 1726 | 528612 | GCTTGGTAAAAAAGTT | e-e-e-$d_{(10)}$-k-k-k | 0 | 822 |
| 1712 | 1727 | 528613 | GGCTTGGTAAAAAAGT | e-e-e-$d_{(10)}$-k-k-k | 0 | 823 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1713 | 1728 | 528614 | GGGCTTGGTAAAAAAG | e-e-e-$d_{(10)}$-k-k-k | 0 | 824 |
| 1736 | 1751 | 528615 | ACTTGATCCCAGGTTC | e-e-e-$d_{(10)}$-k-k-k | 26 | 825 |
| 1741 | 1756 | 528616 | CGGCCACTTGATCCCA | e-e-e-$d_{(10)}$-k-k-k | 41 | 826 |
| 1742 | 1757 | 528617 | TCGGCCACTTGATCCC | e-e-e-$d_{(10)}$-k-k-k | 40 | 827 |
| 1743 | 1758 | 528618 | CTCGGCCACTTGATCC | e-e-e-$d_{(10)}$-k-k-k | 27 | 828 |
| 1744 | 1759 | 528619 | CCTCGGCCACTTGATC | e-e-e-$d_{(10)}$-k-k-k | 10 | 829 |
| 1745 | 1760 | 528620 | ACCTCGGCCACTTGAT | e-e-e-$d_{(10)}$-k-k-k | 16 | 830 |
| 1746 | 1761 | 528621 | GACCTCGGCCACTTGA | e-e-e-$d_{(10)}$-k-k-k | 31 | 831 |
| 1747 | 1762 | 528622 | GGACCTCGGCCACTTG | e-e-e-$d_{(10)}$-k-k-k | 59 | 832 |
| 1748 | 1763 | 528623 | AGGACCTCGGCCACTT | e-e-e-$d_{(10)}$-k-k-k | 49 | 833 |
| 1749 | 1764 | 528624 | CAGGACCTCGGCCACT | e-e-e-$d_{(10)}$-k-k-k | 32 | 834 |
| 1753 | 1768 | 528625 | AGCTCAGGACCTCGGC | e-e-e-$d_{(10)}$-k-k-k | 28 | 835 |
| 1754 | 1769 | 528626 | CAGCTCAGGACCTCGG | e-e-e-$d_{(10)}$-k-k-k | 58 | 836 |
| 1755 | 1770 | 528627 | CCAGCTCAGGACCTCG | e-e-e-$d_{(10)}$-k-k-k | 56 | 837 |
| 1778 | 1793 | 528628 | CGCTTGGTGGTGGAGG | e-e-e-$d_{(10)}$-k-k-k | 15 | 838 |
| 1779 | 1794 | 528629 | TCGCTTGGTGGTGGAG | e-e-e-$d_{(10)}$-k-k-k | 9 | 839 |
| 1780 | 1795 | 528630 | CTCGCTTGGTGGTGGA | e-e-e-$d_{(10)}$-k-k-k | 14 | 127 |
| 1781 | 1796 | 528631 | CCTCGCTTGGTGGTGG | e-e-e-$d_{(10)}$-k-k-k | 26 | 840 |
| 1782 | 1797 | 528632 | TCCTCGCTTGGTGGTG | e-e-e-$d_{(10)}$-k-k-k | 24 | 841 |
| 1783 | 1798 | 528633 | GTCCTCGCTTGGTGGT | e-e-e-$d_{(10)}$-k-k-k | 40 | 842 |
| 1784 | 1799 | 528634 | AGTCCTCGCTTGGTGG | e-e-e-$d_{(10)}$-k-k-k | 38 | 843 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1785 | 1800 | 528635 | CAGTCCTCGCTTGGTG | e-e-e-$d_{(10)}$-k-k-k | 20 | 844 |
| 1786 | 1801 | 528636 | TCAGTCCTCGCTTGGT | e-e-e-$d_{(10)}$-k-k-k | 23 | 845 |
| 1787 | 1802 | 528637 | CTCAGTCCTCGCTTGG | e-e-e-$d_{(10)}$-k-k-k | 33 | 846 |
| 1788 | 1803 | 528638 | GCTCAGTCCTCGCTTG | e-e-e-$d_{(10)}$-k-k-k | 15 | 847 |
| 1789 | 1804 | 528639 | TGCTCAGTCCTCGCTT | e-e-e-$d_{(10)}$-k-k-k | 15 | 848 |
| 1791 | 1806 | 528640 | GATGCTCAGTCCTCGC | e-e-e-$d_{(10)}$-k-k-k | 43 | 849 |
| 1792 | 1807 | 528641 | CGATGCTCAGTCCTCG | e-e-e-$d_{(10)}$-k-k-k | 46 | 850 |
| 1793 | 1808 | 528642 | TCGATGCTCAGTCCTC | e-e-e-$d_{(10)}$-k-k-k | 39 | 851 |
| 1794 | 1809 | 528643 | CTCGATGCTCAGTCCT | e-e-e-$d_{(10)}$-k-k-k | 32 | 852 |
| 1795 | 1810 | 528644 | GCTCGATGCTCAGTCC | e-e-e-$d_{(10)}$-k-k-k | 43 | 129 |
| 1796 | 1811 | 528645 | TGCTCGATGCTCAGTC | e-e-e-$d_{(10)}$-k-k-k | 22 | 853 |
| 1797 | 1812 | 528646 | CTGCTCGATGCTCAGT | e-e-e-$d_{(10)}$-k-k-k | 38 | 854 |
| 1799 | 1814 | 528647 | AGCTGCTCGATGCTCA | e-e-e-$d_{(10)}$-k-k-k | 40 | 855 |
| 1800 | 1815 | 528648 | CAGCTGCTCGATGCTC | e-e-e-$d_{(10)}$-k-k-k | 39 | 856 |
| 1802 | 1817 | 528649 | GTCAGCTGCTCGATGC | e-e-e-$d_{(10)}$-k-k-k | 32 | 857 |
| 1803 | 1818 | 528650 | AGTCAGCTGCTCGATG | e-e-e-$d_{(10)}$-k-k-k | 10 | 858 |
| 1804 | 1819 | 528651 | TAGTCAGCTGCTCGAT | e-e-e-$d_{(10)}$-k-k-k | 4 | 859 |
| 1805 | 1820 | 528652 | GTAGTCAGCTGCTCGA | e-e-e-$d_{(10)}$-k-k-k | 17 | 860 |
| 1806 | 1821 | 528653 | TGTAGTCAGCTGCTCG | e-e-e-$d_{(10)}$-k-k-k | 28 | 861 |
| 1807 | 1822 | 528654 | GTGTAGTCAGCTGCTC | e-e-e-$d_{(10)}$-k-k-k | 31 | 862 |
| 1808 | 1823 | 528655 | AGTGTAGTCAGCTGCT | e-e-e-$d_{(10)}$-k-k-k | 30 | 863 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1809 | 1824 | 528656 | CAGTGTAGTCAGCTGC | e-e-e-$d_{(10)}$-k-k-k | 30 | 864 |
| 1810 | 1825 | 528657 | CCAGTGTAGTCAGCTG | e-e-e-$d_{(10)}$-k-k-k | 23 | 865 |
| 1811 | 1826 | 528658 | GCCAGTGTAGTCAGCT | e-e-e-$d_{(10)}$-k-k-k | 30 | 866 |
| 1832 | 1847 | 528659 | CCAGGTCCCAAGAGTT | e-e-e-$d_{(10)}$-k-k-k | 12 | 867 |
| 1852 | 1867 | 528660 | GACACCCTGAATAATT | e-e-e-$d_{(10)}$-k-k-k | 10 | 868 |
| 1853 | 1868 | 528661 | TGACACCCTGAATAAT | e-e-e-$d_{(10)}$-k-k-k | 10 | 869 |
| 1856 | 1871 | 528662 | ATCTGACACCCTGAAT | e-e-e-$d_{(10)}$-k-k-k | 12 | 870 |
| 1857 | 1872 | 528663 | GATCTGACACCCTGAA | e-e-e-$d_{(10)}$-k-k-k | 22 | 871 |
| 1859 | 1874 | 528664 | GTGATCTGACACCCTG | e-e-e-$d_{(10)}$-k-k-k | 61 | 872 |
| 1861 | 1876 | 528665 | ATGTGATCTGACACCC | e-e-e-$d_{(10)}$-k-k-k | 36 | 873 |
| 1865 | 1880 | 528666 | GCCCATGTGATCTGAC | e-e-e-$d_{(10)}$-k-k-k | 46 | 874 |
| 1866 | 1881 | 528667 | AGCCCATGTGATCTGA | e-e-e-$d_{(10)}$-k-k-k | 36 | 137 |
| 1867 | 1882 | 528668 | TAGCCCATGTGATCTG | e-e-e-$d_{(10)}$-k-k-k | 44 | 875 |
| 1869 | 1884 | 528669 | TTTAGCCCATGTGATC | e-e-e-$d_{(10)}$-k-k-k | 12 | 876 |
| 1907 | 1922 | 528670 | AAGGAGAAGCCCTTGC | e-e-e-$d_{(10)}$-k-k-k | 35 | 877 |
| 1925 | 1940 | 528671 | TTGTCCAGCCAGACCC | e-e-e-$d_{(10)}$-k-k-k | 40 | 878 |
| 1926 | 1941 | 528672 | ATTGTCCAGCCAGACC | e-e-e-$d_{(10)}$-k-k-k | 36 | 879 |
| 1927 | 1942 | 528673 | TATTGTCCAGCCAGAC | e-e-e-$d_{(10)}$-k-k-k | 23 | 880 |
| 1928 | 1943 | 528674 | ATATTGTCCAGCCAGA | e-e-e-$d_{(10)}$-k-k-k | 24 | 881 |
| 1929 | 1944 | 528675 | GATATTGTCCAGCCAG | e-e-e-$d_{(10)}$-k-k-k | 52 | 882 |
| 1931 | 1946 | 528676 | ATGATATTGTCCAGCC | e-e-e-$d_{(10)}$-k-k-k | 41 | 883 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1933 | 1948 | 528677 | CAATGATATTGTCCAG | e-e-e-$d_{(10)}$-k-k-k | 23 | 884 |
| 1935 | 1950 | 528678 | GTCAATGATATTGTCC | e-e-e-$d_{(10)}$-k-k-k | 32 | 885 |
| 1936 | 1951 | 528679 | GGTCAATGATATTGTC | e-e-e-$d_{(10)}$-k-k-k | 26 | 886 |
| 1941 | 1956 | 528680 | CACAAGGTCAATGATA | e-e-e-$d_{(10)}$-k-k-k | 5 | 887 |
| 1942 | 1957 | 528681 | TCACAAGGTCAATGAT | e-e-e-$d_{(10)}$-k-k-k | 9 | 888 |
| 1948 | 1963 | 518340 | ACTTTTTCACAAGGTC | e-e-e-$d_{(10)}$-k-k-k | 52 | 153 |
| 1950 | 1965 | 528682 | GTACTTTTTCACAAGG | e-e-e-$d_{(10)}$-k-k-k | 21 | 889 |
| 1954 | 1969 | 528683 | GGATGTACTTTTTCAC | e-e-e-$d_{(10)}$-k-k-k | 0 | 890 |
| 1958 | 1973 | 528684 | GCCAGGATGTACTTTT | e-e-e-$d_{(10)}$-k-k-k | 0 | 891 |
| 1962 | 1977 | 528685 | AAGGGCCAGGATGTAC | e-e-e-$d_{(10)}$-k-k-k | 0 | 892 |
| 1963 | 1978 | 528686 | AAAGGGCCAGGATGTA | e-e-e-$d_{(10)}$-k-k-k | 0 | 893 |
| 2004 | 2019 | 528687 | CCGCTCCTTACTGATA | e-e-e-$d_{(10)}$-k-k-k | 21 | 894 |
| 2010 | 2025 | 528688 | CCGCTCCCGCTCCTTA | e-e-e-$d_{(10)}$-k-k-k | 32 | 895 |
| 2014 | 2029 | 528689 | TGGCCCGCTCCCGCTC | e-e-e-$d_{(10)}$-k-k-k | 52 | 896 |
| 2015 | 2030 | 528690 | ATGGCCCGCTCCCGCT | e-e-e-$d_{(10)}$-k-k-k | 41 | 897 |
| 2017 | 2032 | 528691 | AGATGGCCCGCTCCCG | e-e-e-$d_{(10)}$-k-k-k | 51 | 898 |
| 2018 | 2033 | 528692 | AAGATGGCCCGCTCCC | e-e-e-$d_{(10)}$-k-k-k | 45 | 899 |
| 2019 | 2034 | 528693 | CAAGATGGCCCGCTCC | e-e-e-$d_{(10)}$-k-k-k | 46 | 900 |
| 2020 | 2035 | 528694 | TCAAGATGGCCCGCTC | e-e-e-$d_{(10)}$-k-k-k | 27 | 901 |
| 2022 | 2037 | 528695 | GCTCAAGATGGCCCGC | e-e-e-$d_{(10)}$-k-k-k | 54 | 902 |
| 2023 | 2038 | 528696 | TGCTCAAGATGGCCCG | e-e-e-$d_{(10)}$-k-k-k | 46 | 903 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2024 | 2039 | 528697 | GTGCTCAAGATGGCCC | e-e-e-$d_{(10)}$-k-k-k | 60 | 904 |
| 2041 | 2056 | 528698 | AGGTGCCTGGAGGCTT | e-e-e-$d_{(10)}$-k-k-k | 17 | 905 |
| 2093 | 2108 | 528699 | CAAGTGAAAGTGACGC | e-e-e-$d_{(10)}$-k-k-k | 2 | 161 |
| 2094 | 2109 | 528700 | CCAAGTGAAAGTGACG | e-e-e-$d_{(10)}$-k-k-k | 13 | 906 |
| 2095 | 2110 | 528701 | CCCAAGTGAAAGTGAC | e-e-e-$d_{(10)}$-k-k-k | 14 | 907 |
| 2128 | 2143 | 528702 | GGATCTGGGTCTTACC | e-e-e-$d_{(10)}$-k-k-k | 22 | 908 |
| 2129 | 2144 | 528703 | TGGATCTGGGTCTTAC | e-e-e-$d_{(10)}$-k-k-k | 22 | 909 |
| 2131 | 2146 | 528704 | ACTGGATCTGGGTCTT | e-e-e-$d_{(10)}$-k-k-k | 21 | 165 |
| 2133 | 2148 | 528705 | GGACTGGATCTGGGTC | e-e-e-$d_{(10)}$-k-k-k | 38 | 910 |
| 2138 | 2153 | 528706 | TCCACGGACTGGATCT | e-e-e-$d_{(10)}$-k-k-k | 13 | 911 |
| 2139 | 2154 | 528707 | TTCCACGGACTGGATC | e-e-e-$d_{(10)}$-k-k-k | 19 | 912 |
| 2140 | 2155 | 528708 | GTTCCACGGACTGGAT | e-e-e-$d_{(10)}$-k-k-k | 2 | 913 |
| 2141 | 2156 | 528709 | GGTTCCACGGACTGGA | e-e-e-$d_{(10)}$-k-k-k | 42 | 914 |
| 2142 | 2157 | 528710 | TGGTTCCACGGACTGG | e-e-e-$d_{(10)}$-k-k-k | 63 | 915 |
| 2143 | 2158 | 528711 | ATGGTTCCACGGACTG | e-e-e-$d_{(10)}$-k-k-k | 62 | 916 |
| 2144 | 2159 | 528712 | TATGGTTCCACGGACT | e-e-e-$d_{(10)}$-k-k-k | 35 | 917 |
| 2146 | 2161 | 528713 | TGTATGGTTCCACGGA | e-e-e-$d_{(10)}$-k-k-k | 40 | 918 |
| 2147 | 2162 | 528714 | GTGTATGGTTCCACGG | e-e-e-$d_{(10)}$-k-k-k | 48 | 919 |
| 2193 | 2208 | 528715 | GCCCATGATGATTTCA | e-e-e-$d_{(10)}$-k-k-k | 36 | 920 |
| 2194 | 2209 | 528716 | AGCCCATGATGATTTC | e-e-e-$d_{(10)}$-k-k-k | 25 | 921 |
| 2195 | 2210 | 528717 | TAGCCCATGATGATTT | e-e-e-$d_{(10)}$-k-k-k | 27 | 922 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2196 | 2211 | 528718 | ATAGCCCATGATGATT | e-e-e-$d_{(10)}$-k-k-k | 19 | 923 |
| 2197 | 2212 | 528719 | TATAGCCCATGATGAT | e-e-e-$d_{(10)}$-k-k-k | 14 | 924 |
| 2198 | 2213 | 528720 | TTATAGCCCATGATGA | e-e-e-$d_{(10)}$-k-k-k | 14 | 925 |
| 2199 | 2214 | 528721 | CTTATAGCCCATGATG | e-e-e-$d_{(10)}$-k-k-k | 21 | 926 |
| 2200 | 2215 | 528722 | TCTTATAGCCCATGAT | e-e-e-$d_{(10)}$-k-k-k | 0 | 927 |
| 2201 | 2216 | 528723 | ATCTTATAGCCCATGA | e-e-e-$d_{(10)}$-k-k-k | 17 | 928 |
| 2202 | 2217 | 528724 | GATCTTATAGCCCATG | e-e-e-$d_{(10)}$-k-k-k | 35 | 929 |
| 2203 | 2218 | 528725 | TGATCTTATAGCCCAT | e-e-e-$d_{(10)}$-k-k-k | 45 | 930 |
| 2204 | 2219 | 528726 | ATGATCTTATAGCCCA | e-e-e-$d_{(10)}$-k-k-k | 67 | 931 |
| 2205 | 2220 | 528727 | CATGATCTTATAGCCC | e-e-e-$d_{(10)}$-k-k-k | 45 | 932 |
| 2206 | 2221 | 528728 | CCATGATCTTATAGCC | e-e-e-$d_{(10)}$-k-k-k | 38 | 175 |
| 2207 | 2222 | 528729 | TCCATGATCTTATAGC | e-e-e-$d_{(10)}$-k-k-k | 0 | 933 |
| 2208 | 2223 | 528730 | ATCCATGATCTTATAG | e-e-e-$d_{(10)}$-k-k-k | 12 | 934 |
| 2213 | 2228 | 528731 | GTAGCATCCATGATCT | e-e-e-$d_{(10)}$-k-k-k | 14 | 935 |
| 2214 | 2229 | 528732 | GGTAGCATCCATGATC | e-e-e-$d_{(10)}$-k-k-k | 25 | 936 |
| 2217 | 2232 | 528733 | ATTGGTAGCATCCATG | e-e-e-$d_{(10)}$-k-k-k | 22 | 937 |
| 2218 | 2233 | 528734 | TATTGGTAGCATCCAT | e-e-e-$d_{(10)}$-k-k-k | 15 | 938 |
| 2219 | 2234 | 528735 | ATATTGGTAGCATCCA | e-e-e-$d_{(10)}$-k-k-k | 28 | 939 |
| 2264 | 2279 | 528736 | TCCTTGGGAATGTCAG | e-e-e-$d_{(10)}$-k-k-k | 30 | 940 |
| 2266 | 2281 | 528737 | CCTCCTTGGGAATGTC | e-e-e-$d_{(10)}$-k-k-k | 30 | 181 |
| 2275 | 2290 | 528738 | CGAATGCCTCCTCCTT | e-e-e-$d_{(10)}$-k-k-k | 29 | 186 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2277 | 2292 | 528739 | TCCGAATGCCTCCTCC | e-e-e-$d_{(10)}$-k-k-k | 33 | 941 |
| 2278 | 2293 | 528740 | TTCCGAATGCCTCCTC | e-e-e-$d_{(10)}$-k-k-k | 27 | 942 |
| 2279 | 2294 | 528741 | TTTCCGAATGCCTCCT | e-e-e-$d_{(10)}$-k-k-k | 20 | 943 |
| 2280 | 2295 | 528742 | CTTTCCGAATGCCTCC | e-e-e-$d_{(10)}$-k-k-k | 25 | 944 |
| 2281 | 2296 | 528743 | ACTTTCCGAATGCCTC | e-e-e-$d_{(10)}$-k-k-k | 39 | 945 |
| 2283 | 2298 | 528744 | ATACTTTCCGAATGCC | e-e-e-$d_{(10)}$-k-k-k | 44 | 946 |
| 2285 | 2300 | 528745 | CAATACTTTCCGAATG | e-e-e-$d_{(10)}$-k-k-k | 0 | 947 |
| 2286 | 2301 | 528746 | ACAATACTTTCCGAAT | e-e-e-$d_{(10)}$-k-k-k | 0 | 948 |
| 2288 | 2303 | 528747 | CGACAATACTTTCCGA | e-e-e-$d_{(10)}$-k-k-k | 11 | 949 |
| 2289 | 2304 | 528748 | CCGACAATACTTTCCG | e-e-e-$d_{(10)}$-k-k-k | 31 | 950 |
| 2290 | 2305 | 528749 | GCCGACAATACTTTCC | e-e-e-$d_{(10)}$-k-k-k | 18 | 951 |
| 2291 | 2306 | 528750 | GGCCGACAATACTTTC | e-e-e-$d_{(10)}$-k-k-k | 16 | 952 |
| 2293 | 2308 | 528751 | CTGGCCGACAATACTT | e-e-e-$d_{(10)}$-k-k-k | 18 | 953 |
| 2294 | 2309 | 528752 | TCTGGCCGACAATACT | e-e-e-$d_{(10)}$-k-k-k | 8 | 954 |
| 2295 | 2310 | 528753 | CTCTGGCCGACAATAC | e-e-e-$d_{(10)}$-k-k-k | 0 | 955 |
| 2296 | 2311 | 528754 | TCTCTGGCCGACAATA | e-e-e-$d_{(10)}$-k-k-k | 6 | 188 |
| 2297 | 2312 | 528755 | CTCTCTGGCCGACAAT | e-e-e-$d_{(10)}$-k-k-k | 18 | 956 |
| 2298 | 2313 | 528756 | GCTCTCTGGCCGACAA | e-e-e-$d_{(10)}$-k-k-k | 35 | 957 |
| 2299 | 2314 | 528757 | GGCTCTCTGGCCGACA | e-e-e-$d_{(10)}$-k-k-k | 57 | 958 |
| 2300 | 2315 | 528758 | TGGCTCTCTGGCCGAC | e-e-e-$d_{(10)}$-k-k-k | 64 | 959 |
| 2301 | 2316 | 528759 | CTGGCTCTCTGGCCGA | e-e-e-$d_{(10)}$-k-k-k | 12 | 960 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2326 | 2341 | 528760 | TACCTGGGTCAGCTTC | e-e-e-$d_{(10)}$-k-k-k | 21 | 961 |
| 2328 | 2343 | 528761 | GCTACCTGGGTCAGCT | e-e-e-$d_{(10)}$-k-k-k | 18 | 962 |
| 2329 | 2344 | 528762 | CGCTACCTGGGTCAGC | e-e-e-$d_{(10)}$-k-k-k | 28 | 963 |
| 2330 | 2345 | 528763 | GCGCTACCTGGGTCAG | e-e-e-$d_{(10)}$-k-k-k | 26 | 964 |
| 2349 | 2364 | 528764 | GGTCTTCAGGTATGGG | e-e-e-$d_{(10)}$-k-k-k | 38 | 965 |
| 2350 | 2365 | 528765 | TGGTCTTCAGGTATGG | e-e-e-$d_{(10)}$-k-k-k | 12 | 966 |
| 2352 | 2367 | 528766 | CTTGGTCTTCAGGTAT | e-e-e-$d_{(10)}$-k-k-k | 0 | 967 |
| 2353 | 2368 | 528767 | ACTTGGTCTTCAGGTA | e-e-e-$d_{(10)}$-k-k-k | 10 | 190 |
| 2358 | 2373 | 528768 | GATAAACTTGGTCTTC | e-e-e-$d_{(10)}$-k-k-k | 9 | 968 |
| 2360 | 2375 | 528769 | CAGATAAACTTGGTCT | e-e-e-$d_{(10)}$-k-k-k | 15 | 969 |
| 2361 | 2376 | 528770 | ACAGATAAACTTGGTC | e-e-e-$d_{(10)}$-k-k-k | 7 | 970 |
| 2369 | 2384 | 528771 | GGTGTCACACAGATAA | e-e-e-$d_{(10)}$-k-k-k | 35 | 971 |
| 2373 | 2388 | 528772 | CGTTGGTGTCACACAG | e-e-e-$d_{(10)}$-k-k-k | 52 | 972 |
| 2387 | 2402 | 528773 | GTATTGCTGCAGGTCG | e-e-e-$d_{(10)}$-k-k-k | 49 | 194 |
| 2388 | 2403 | 528774 | GGTATTGCTGCAGGTC | e-e-e-$d_{(10)}$-k-k-k | 48 | 973 |
| 2389 | 2404 | 528775 | TGGTATTGCTGCAGGT | e-e-e-$d_{(10)}$-k-k-k | 35 | 974 |
| 2390 | 2405 | 528776 | ATGGTATTGCTGCAGG | e-e-e-$d_{(10)}$-k-k-k | 20 | 975 |
| 2392 | 2407 | 528777 | CAATGGTATTGCTGCA | e-e-e-$d_{(10)}$-k-k-k | 24 | 976 |
| 2393 | 2408 | 528778 | TCAATGGTATTGCTGC | e-e-e-$d_{(10)}$-k-k-k | 15 | 977 |
| 2394 | 2409 | 528779 | GTCAATGGTATTGCTG | e-e-e-$d_{(10)}$-k-k-k | 16 | 978 |
| 2395 | 2410 | 528780 | GGTCAATGGTATTGCT | e-e-e-$d_{(10)}$-k-k-k | 34 | 196 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2396 | 2411 | 528781 | AGGTCAATGGTATTGC | e-e-e-$d_{(10)}$-k-k-k | 26 | 979 |
| 2397 | 2412 | 528782 | CAGGTCAATGGTATTG | e-e-e-$d_{(10)}$-k-k-k | 16 | 980 |
| 2398 | 2413 | 528783 | GCAGGTCAATGGTATT | e-e-e-$d_{(10)}$-k-k-k | 10 | 981 |
| 2399 | 2414 | 528784 | GGCAGGTCAATGGTAT | e-e-e-$d_{(10)}$-k-k-k | 32 | 982 |
| 2400 | 2415 | 528785 | CGGCAGGTCAATGGTA | e-e-e-$d_{(10)}$-k-k-k | 39 | 983 |
| 2401 | 2416 | 528786 | TCGGCAGGTCAATGGT | e-e-e-$d_{(10)}$-k-k-k | 51 | 984 |
| 2403 | 2418 | 528787 | CATCGGCAGGTCAATG | e-e-e-$d_{(10)}$-k-k-k | 26 | 198 |
| 2404 | 2419 | 528788 | ACATCGGCAGGTCAAT | e-e-e-$d_{(10)}$-k-k-k | 20 | 985 |
| 2405 | 2420 | 528789 | GACATCGGCAGGTCAA | e-e-e-$d_{(10)}$-k-k-k | 42 | 986 |
| 2406 | 2421 | 528790 | GGACATCGGCAGGTCA | e-e-e-$d_{(10)}$-k-k-k | 58 | 987 |
| 2407 | 2422 | 528791 | GGGACATCGGCAGGTC | e-e-e-$d_{(10)}$-k-k-k | 68 | 988 |
| 2423 | 2438 | 528792 | GAATCTAAAGTGCGGG | e-e-e-$d_{(10)}$-k-k-k | 46 | 200 |
| 2424 | 2439 | 528793 | TGAATCTAAAGTGCGG | e-e-e-$d_{(10)}$-k-k-k | 43 | 989 |
| 2427 | 2442 | 528794 | CAATGAATCTAAAGTG | e-e-e-$d_{(10)}$-k-k-k | 20 | 990 |
| 2462 | 2477 | 528795 | GGTTCAGCACCTTCAC | e-e-e-$d_{(10)}$-k-k-k | 13 | 991 |
| 2463 | 2478 | 528796 | GGGTTCAGCACCTTCA | e-e-e-$d_{(10)}$-k-k-k | 24 | 992 |
| 2464 | 2479 | 528797 | AGGGTTCAGCACCTTC | e-e-e-$d_{(10)}$-k-k-k | 23 | 993 |
| 2465 | 2480 | 528798 | GAGGGTTCAGCACCTT | e-e-e-$d_{(10)}$-k-k-k | 18 | 994 |
| 2466 | 2481 | 528799 | TGAGGGTTCAGCACCT | e-e-e-$d_{(10)}$-k-k-k | 24 | 995 |
| 2490 | 2505 | 528800 | GAGGGACTCAAACTGC | e-e-e-$d_{(10)}$-k-k-k | 28 | 996 |
| 2492 | 2507 | 528801 | GTGAGGGACTCAAACT | e-e-e-$d_{(10)}$-k-k-k | 22 | 997 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2493 | 2508 | 528802 | GGTGAGGGACTCAAAC | e-e-e-$d_{(10)}$-k-k-k | 20 | 998 |
| 2494 | 2509 | 528803 | AGGTGAGGGACTCAAA | e-e-e-$d_{(10)}$-k-k-k | 13 | 999 |
| 2495 | 2510 | 528804 | AAGGTGAGGGACTCAA | e-e-e-$d_{(10)}$-k-k-k | 20 | 1000 |
| 2497 | 2512 | 528805 | CAAAGGTGAGGGACTC | e-e-e-$d_{(10)}$-k-k-k | 20 | 1001 |
| 2498 | 2513 | 528806 | TCAAAGGTGAGGGACT | e-e-e-$d_{(10)}$-k-k-k | 18 | 1002 |
| 2506 | 2521 | 528807 | ACTCCATGTCAAAGGT | e-e-e-$d_{(10)}$-k-k-k | 54 | 1003 |
| 2510 | 2525 | 528808 | GTCAACTCCATGTCAA | e-e-e-$d_{(10)}$-k-k-k | 39 | 1004 |
| 2511 | 2526 | 528809 | GGTCAACTCCATGTCA | e-e-e-$d_{(10)}$-k-k-k | 56 | 1005 |
| 2513 | 2528 | 528810 | GAGGTCAACTCCATGT | e-e-e-$d_{(10)}$-k-k-k | 41 | 1006 |
| 2514 | 2529 | 528811 | CGAGGTCAACTCCATG | e-e-e-$d_{(10)}$-k-k-k | 45 | 1007 |
| 2515 | 2530 | 528812 | CCGAGGTCAACTCCAT | e-e-e-$d_{(10)}$-k-k-k | 45 | 1008 |
| 2517 | 2532 | 528813 | CTCCGAGGTCAACTCC | e-e-e-$d_{(10)}$-k-k-k | 58 | 1009 |
| 2518 | 2533 | 528814 | ACTCCGAGGTCAACTC | e-e-e-$d_{(10)}$-k-k-k | 40 | 1010 |
| 2519 | 2534 | 528815 | CACTCCGAGGTCAACT | e-e-e-$d_{(10)}$-k-k-k | 30 | 1011 |
| 2551 | 2566 | 528816 | CGTTCTCAGCTCCTCA | e-e-e-$d_{(10)}$-k-k-k | 54 | 1012 |
| 2554 | 2569 | 528817 | TTCCGTTCTCAGCTCC | e-e-e-$d_{(10)}$-k-k-k | 53 | 1013 |
| 2555 | 2570 | 528818 | CTTCCGTTCTCAGCTC | e-e-e-$d_{(10)}$-k-k-k | 27 | 1014 |
| 2556 | 2571 | 528819 | GCTTCCGTTCTCAGCT | e-e-e-$d_{(10)}$-k-k-k | 35 | 1015 |
| 2557 | 2572 | 528820 | AGCTTCCGTTCTCAGC | e-e-e-$d_{(10)}$-k-k-k | 38 | 1016 |
| 2558 | 2573 | 528821 | CAGCTTCCGTTCTCAG | e-e-e-$d_{(10)}$-k-k-k | 53 | 1017 |
| 2559 | 2574 | 528822 | GCAGCTTCCGTTCTCA | e-e-e-$d_{(10)}$-k-k-k | 66 | 1018 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2614 | 2629 | 528823 | TTTGGCTGTGTGAGGG | e-e-e-$d_{(10)}$-k-k-k | 62 | 1019 |
| 2615 | 2630 | 528824 | GTTTGGCTGTGTGAGG | e-e-e-$d_{(10)}$-k-k-k | 50 | 1020 |
| 2616 | 2631 | 528825 | GGTTTGGCTGTGTGAG | e-e-e-$d_{(10)}$-k-k-k | 15 | 1021 |
| 2641 | 2656 | 528826 | AAGTTAGTAGTTTCAG | e-e-e-$d_{(10)}$-k-k-k | 20 | 1022 |
| 2677 | 2692 | 528827 | GCAGAAGTAGGAGATT | e-e-e-$d_{(10)}$-k-k-k | 28 | 1023 |
| 2690 | 2705 | 528828 | TTGCTCAAAGATAGCA | e-e-e-$d_{(10)}$-k-k-k | 39 | 1024 |
| 2691 | 2706 | 528829 | ATTGCTCAAAGATAGC | e-e-e-$d_{(10)}$-k-k-k | 37 | 1025 |
| 2692 | 2707 | 528830 | GATTGCTCAAAGATAG | e-e-e-$d_{(10)}$-k-k-k | 22 | 1026 |
| 2694 | 2709 | 528831 | CAGATTGCTCAAAGAT | e-e-e-$d_{(10)}$-k-k-k | 26 | 1027 |
| 2695 | 2710 | 528832 | CCAGATTGCTCAAAGA | e-e-e-$d_{(10)}$-k-k-k | 41 | 1028 |
| 2699 | 2714 | 528833 | GTGCCCAGATTGCTCA | e-e-e-$d_{(10)}$-k-k-k | 77 | 1029 |
| 2738 | 2753 | 528834 | GCAGATCACCCACATT | e-e-e-$d_{(10)}$-k-k-k | 49 | 1030 |
| 2743 | 2758 | 528835 | TAAAAGCAGATCACCC | e-e-e-$d_{(10)}$-k-k-k | 40 | 1031 |
| 2809 | 2824 | 528836 | CTAGCCACCCCCCGCC | e-e-e-$d_{(10)}$-k-k-k | 19 | 1032 |
| 2810 | 2825 | 528837 | TCTAGCCACCCCCCGC | e-e-e-$d_{(10)}$-k-k-k | 9 | 1033 |
| 2811 | 2826 | 528838 | CTCTAGCCACCCCCCG | e-e-e-$d_{(10)}$-k-k-k | 16 | 1034 |
| 2908 | 2923 | 528839 | GGAGGCACTTGTCTAA | e-e-e-$d_{(10)}$-k-k-k | 56 | 235 |
| 2909 | 2924 | 528840 | AGGAGGCACTTGTCTA | e-e-e-$d_{(10)}$-k-k-k | 62 | 1036 |
| 2910 | 2925 | 528841 | CAGGAGGCACTTGTCT | e-e-e-$d_{(10)}$-k-k-k | 52 | 1037 |
| 2911 | 2926 | 528842 | CCAGGAGGCACTTGTC | e-e-e-$d_{(10)}$-k-k-k | 59 | 1038 |
| 2932 | 2947 | 528843 | GGCAGAAGGATGCCGC | e-e-e-$d_{(10)}$-k-k-k | 35 | 1039 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2945 | 2960 | 528844 | GCTTACAGAAACAGGC | e-e-e-$d_{(10)}$-k-k-k | 62 | 1040 |
| 2980 | 2995 | 528845 | CAGGAGTATGTAGCTA | e-e-e-$d_{(10)}$-k-k-k | 65 | 1041 |
| 2981 | 2996 | 528846 | CCAGGAGTATGTAGCT | e-e-e-$d_{(10)}$-k-k-k | 80 | 1042 |
| 2982 | 2997 | 528847 | GCCAGGAGTATGTAGC | e-e-e-$d_{(10)}$-k-k-k | 72 | 1043 |
| 2983 | 2998 | 528848 | TGCCAGGAGTATGTAG | e-e-e-$d_{(10)}$-k-k-k | 46 | 1044 |
| 2984 | 2999 | 528849 | ATGCCAGGAGTATGTA | e-e-e-$d_{(10)}$-k-k-k | 59 | 241 |
| 3001 | 3016 | 528850 | CAAGGTTAAAAAGTGC | e-e-e-$d_{(10)}$-k-k-k | 10 | 243 |
| 3008 | 3023 | 528851 | ATGTCAGCAAGGTTAA | e-e-e-$d_{(10)}$-k-k-k | 61 | 1045 |
| 3010 | 3025 | 528852 | GGATGTCAGCAAGGTT | e-e-e-$d_{(10)}$-k-k-k | 88 | 1046 |
| 3012 | 3027 | 528853 | TTGGATGTCAGCAAGG | e-e-e-$d_{(10)}$-k-k-k | 91 | 1047 |
| 3016 | 3031 | 518349 | CTATTTGGATGTCAGC | e-e-e-$d_{(10)}$-k-k-k | 85 | 245 |
| 3030 | 3045 | 528854 | GATAGTCCTATCTTCT | e-e-e-$d_{(10)}$-k-k-k | 42 | 1048 |
| 3091 | 3106 | 528855 | ACAGTGTTTTTTGCCC | e-e-e-$d_{(10)}$-k-k-k | 59 | 1049 |
| 3108 | 3123 | 528856 | AGAAAGGCTATGCTGA | e-e-e-$d_{(10)}$-k-k-k | 56 | 1050 |
| 3452 | 3467 | 528857 | GAGGCTGTTAACTGAA | e-e-e-$d_{(10)}$-k-k-k | 40 | 1051 |
| 3458 | 3473 | 528858 | ACCAAGGAGGCTGTTA | e-e-e-$d_{(10)}$-k-k-k | 26 | 1052 |
| 3474 | 3489 | 528859 | GCTGAATGCTTAAAGC | e-e-e-$d_{(10)}$-k-k-k | 36 | 1053 |
| 4022 | 4037 | 518344 | GCCACTGGATATCACC | e-e-e-$d_{(10)}$-k-k-k | 55 | 317 |

**Example 12: Dose-dependent antisense inhibition of human STAT3 in HuVEC cells**

**[0279]** Gapmers from the study described in Example 11, above, exhibiting significant *in vitro* inhibition of STAT3 were tested at various doses in HuVEC cells. Cells were plated at a density of 20,000 cells per well and

transfected using electroporation with 23.4375 nM, 93.75 nM, 375.0 nM, and 1,500.0 nM concentrations of antisense oligonucleotide, as specified in Table 12. After a treatment period of approximately 16 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0280]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 12 and was calculated by plotting the concentrations of oligonucleotides used versus the percent inhibition of STAT3 mRNA expression achieved at each concentration, and noting the concentration of oligonucleotide at which 50% inhibition of STAT3 mRNA expression was achieved compared to the control. As illustrated in Table 12, STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 12**

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 23.4375 nM | 93.75 nM | 375.0 nM | 1500.0 nM | $IC_{50}$ (μM) |
| 518340 | 0 | 8 | 28 | 63 | 1.0 |
| 518349 | 13 | 30 | 68 | 90 | 0.2 |
| 528189 | 8 | 13 | 43 | 71 | 0.5 |
| 528204 | 4 | 24 | 53 | 79 | 0.3 |
| 528205 | 0 | 9 | 59 | 80 | 0.4 |
| 528208 | 0 | 19 | 56 | 84 | 0.3 |
| 528209 | 0 | 28 | 58 | 90 | 0.3 |
| 528210 | 0 | 16 | 49 | 87 | 0.3 |
| 528211 | 0 | 10 | 47 | 86 | 0.4 |
| 528212 | 0 | 16 | 42 | 83 | 0.4 |
| 528214 | 0 | 25 | 55 | 88 | 0.3 |
| 528215 | 3 | 16 | 53 | 82 | 0.3 |
| 528237 | 13 | 19 | 33 | 73 | 0.6 |
| 528245 | 3 | 16 | 53 | 78 | 0.4 |
| 528263 | 0 | 3 | 32 | 76 | 0.6 |
| 528264 | 9 | 0 | 19 | 50 | >1.5 |
| 528268 | 0 | 7 | 25 | 63 | 1.0 |
| 528269 | 0 | 11 | 39 | 77 | 0.5 |
| 528270 | 5 | 9 | 48 | 79 | 0.4 |
| 528271 | 0 | 14 | 37 | 81 | 0.5 |
| 528327 | 0 | 0 | 26 | 72 | 0.8 |
| 528347 | 0 | 2 | 25 | 69 | 0.9 |
| 528357 | 0 | 17 | 36 | 69 | 0.6 |
| 528389 | 0 | 3 | 19 | 82 | 0.7 |
| 528501 | 0 | 17 | 40 | 69 | 0.6 |
| 528502 | 0 | 10 | 35 | 76 | 0.6 |
| 528503 | 3 | 1 | 38 | 70 | 0.7 |
| 528504 | 0 | 19 | 45 | 72 | 0.5 |

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 23.4375 nM | 93.75 nM | 375.0 nM | 1500.0 nM | $IC_{50}$ (μM) |
| 528505 | 0 | 7 | 41 | 73 | 0.6 |
| 528518 | 0 | 24 | 51 | 81 | 0.3 |
| 528534 | 0 | 8 | 32 | 72 | 0.7 |
| 528539 | 0 | 7 | 39 | 73 | 0.6 |
| 528557 | 0 | 9 | 26 | 53 | >1.5 |
| 528565 | 4 | 12 | 31 | 57 | 1.3 |
| 528567 | 8 | 13 | 25 | 54 | >1.5 |
| 528569 | 9 | 19 | 37 | 60 | 0.8 |
| 528574 | 5 | 17 | 32 | 62 | 0.9 |
| 528622 | 10 | 4 | 29 | 68 | 0.9 |
| 528623 | 0 | 13 | 24 | 62 | 1.1 |
| 528626 | 1 | 0 | 34 | 68 | 0.8 |
| 528627 | 22 | 19 | 30 | 64 | 1.0 |
| 528664 | 0 | 14 | 37 | 74 | 0.5 |
| 528675 | 0 | 10 | 28 | 62 | 1.0 |
| 528689 | 0 | 16 | 33 | 65 | 0.7 |
| 528691 | 0 | 3 | 34 | 61 | 0.9 |
| 528695 | 1 | 4 | 36 | 66 | 0.8 |
| 528697 | 3 | 15 | 39 | 72 | 0.5 |
| 528710 | 13 | 16 | 28 | 63 | 1.0 |
| 528711 | 8 | 13 | 14 | 62 | >1.5 |
| 528726 | 0 | 8 | 36 | 72 | 0.6 |
| 528757 | 4 | 10 | 29 | 76 | 0.6 |
| 528758 | 1 | 5 | 28 | 62 | 1.1 |
| 528772 | 0 | 2 | 21 | 63 | 1.2 |
| 528773 | 9 | 8 | 28 | 70 | 0.8 |
| 528791 | 4 | 9 | 41 | 69 | 0.6 |
| 528822 | 0 | 0 | 40 | 46 | >1.5 |
| 528833 | 0 | 23 | 47 | 82 | 0.4 |
| 528846 | 10 | 19 | 49 | 85 | 0.3 |
| 528847 | 0 | 19 | 45 | 75 | 0.4 |
| 528852 | 5 | 33 | 66 | 93 | 0.2 |
| 528853 | 19 | 46 | 77 | 95 | 0.1 |

**Example 13: Antisense inhibition of human STAT3 in HuVEC cells**

**[0281]** Antisense oligonucleotides were designed targeting a human STAT3 nucleic acid and were tested for their effect on human STAT3 mRNA expression *in vitro*. The chimeric antisense oligonucleotides in Tables 13 and 14 are gapmers16 or 17 nucleotides in length having various chemical modifications. Each gapmer

comprises a central gap segment consisting of nine or ten 2'-deoxynucleosides and is flanked on both sides (in the 5' and 3' directions) by wings comprising 1, 2, 3, 4, or 5 nucleotides each. Each of the nucleotides in the wings comprise a 2'-MOE sugar modification or a cEt sugar modification. Gapmer motifs include 3-10-3, 4-9-3, 2-10-4, 1-10-5, and 3-10-4. The chemistry column of Tables 13 and 14 provides the sugar motif of each gapmer, wherein 'e' indicates a 2'-MOE nucleoside, 'k' indicates a constrained ethyl (cEt) nucleoside, and 'd' indicates a 2'- deoxynucleoside. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines.

**[0282]** Potency of the chimeric antisense oligonucleotides was compared to ISIS 481464, ISIS 518344, and ISIS 518349 (described previously herein).

**[0283]** Cultured HuVEC 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 STAT3 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0284]** "Human Target start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Human Target stop site" indicates the 3'-most nucleoside to which the gapmer is targeted in the human gene sequence. Each gapmer listed in Table 13 is targeted to human STAT3 mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_139276.2). Each gapmer listed in Table 14 is targeted to human STAT3 genomic sequence, designated herein as SEQ ID NO: 2 (the complement of GENBANK Accession No. NT_010755.14 truncated from nucleotides 4185000 to 4264000).

**Table 13**

Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1

| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
|---|---|---|---|---|---|---|
| 728 | 743 | 530423 | AGATTCTCTACCACTT | k-d(10)-k-e-k-e-e | 70 | 1054 |
| 729 | 745 | 530053 | GGAGATTCTCTACCACT | e-e-k-d(10)-k-e-k-e | 84 | 1055 |
| 729 | 744 | 530373 | GAGATTCTCTACCACT | e-k-d(10)-k-e-k-e | 85 | 1056 |
| 730 | 745 | 530121 | GGAGATTCTCTACCAC | e-k-k-d(10)-k-k-e | 77 | 53 |
| 730 | 745 | 530168 | GGAGATTCTCTACCAC | e-e-k-d(10)-k-k-e | 75 | 53 |
| 730 | 745 | 530218 | GGAGATTCTCTACCAC | e-d-k-d(10)-k-k-e | 61 | 53 |
| 730 | 745 | 530268 | GGAGATTCTCTACCAC | e-d-d-k-d(9)-k-k-e | 76 | 53 |
| 730 | 745 | 530318 | GGAGATTCTCTACCAC | e-e-e-e-d(9)-k-k-e | 27 | 53 |
| 786 | 801 | 530424 | ATCTTGCATGTCTCCT | k-d(10)-k-e-k-e-e | 42 | 1057 |
| 787 | 803 | 530058 | AGATCTTGCATGTCTCC | e-e-k-d(10)-k-e-k-e | 73 | 1058 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 787 | 802 | 530374 | GATCTTGCATGTCTCC | e-k-d(10)-k-e-k-e | 71 | 647 |
| 788 | 803 | 530122 | AGATCTTGCATGTCTC | e-k-k-d(10)-k-k-e | 80 | 57 |
| 788 | 803 | 530169 | AGATCTTGCATGTCTC | e-e-k-d(10)-k-k-e | 72 | 57 |
| 788 | 803 | 530219 | AGATCTTGCATGTCTC | e-d-k-d(10)-k-k-e | 55 | 57 |
| 788 | 803 | 530269 | AGATCTTGCATGTCTC | e-d-d-k-d(9)-k-k-e | 76 | 57 |
| 788 | 803 | 530319 | AGATCTTGCATGTCTC | e-e-e-e-d(9)-k-k-e | 30 | 57 |
| 892 | 907 | 528400 | CCGCCAGCTCACTCAC | e-e-e-d(10)-k-k-k | 57 | 66 |
| 893 | 908 | 528401 | CCCGCCAGCTCACTCA | e-e-e-d(10)-k-k-k | 57 | 1059 |
| 894 | 909 | 528402 | CCCCGCCAGCTCACTC | e-e-e-d(10)-k-k-k | 42 | 1060 |
| 897 | 912 | 528403 | AAGCCCCGCCAGCTCA | e-e-e-d(10)-k-k-k | 72 | 1061 |
| 898 | 913 | 528404 | AAAGCCCCGCCAGCTC | e-e-e-d(10)-k-k-k | 52 | 1062 |
| 899 | 914 | 528405 | AAAAGCCCCGCCAGCT | e-e-e-d(10)-k-k-k | 27 | 1063 |
| 900 | 915 | 528406 | CAAAAGCCCCGCCAGC | e-e-e-d(10)-k-k-k | 29 | 1064 |
| 901 | 916 | 528407 | ACAAAAGCCCCGCCAG | e-e-e-d(10)-k-k-k | 9 | 1065 |
| 903 | 918 | 528408 | TGACAAAAGCCCCGCC | e-e-e-d(10)-k-k-k | 10 | 1066 |
| 904 | 919 | 528409 | CTGACAAAAGCCCCGC | e-e-e-d(10)-k-k-k | 31 | 1067 |
| 905 | 920 | 528410 | GCTGACAAAAGCCCCG | e-e-e-d(10)-k-k-k | 39 | 1068 |
| 906 | 921 | 528411 | CGCTGACAAAAGCCCC | e-e-e-d(10)-k-k-k | 49 | 1069 |
| 907 | 922 | 528412 | TCGCTGACAAAAGCCC | e-e-e-d(10)-k-k-k | 39 | 1070 |
| 908 | 923 | 528413 | ATCGCTGACAAAAGCC | e-e-e-d(10)-k-k-k | 20 | 1071 |
| 909 | 924 | 528414 | CATCGCTGACAAAAGC | e-e-e-d(10)-k-k-k | 10 | 1072 |
| 911 | 926 | 528415 | TCCATCGCTGACAAAA | e-e-e-d(10)-k-k-k | 11 | 1073 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 912 | 927 | 528416 | CTCCATCGCTGACAAA | e-e-e-d(10)-k-k-k | 15 | 1074 |
| 913 | 928 | 528417 | ACTCCATCGCTGACAA | e-e-e-d(10)-k-k-k | 22 | 1075 |
| 914 | 929 | 528418 | TACTCCATCGCTGACA | e-e-e-d(10)-k-k-k | 19 | 1076 |
| 915 | 930 | 528419 | GTACTCCATCGCTGAC | e-e-e-d(10)-k-k-k | 37 | 1077 |
| 916 | 931 | 528420 | CGTACTCCATCGCTGA | e-e-e-d(10)-k-k-k | 35 | 1078 |
| 930 | 945 | 528421 | GAGAGTTTTCTGCACG | e-e-e-d(10)-k-k-k | 36 | 1079 |
| 932 | 947 | 528422 | GTGAGAGTTTTCTGCA | e-e-e-d(10)-k-k-k | 22 | 1080 |
| 951 | 966 | 528423 | GTCAGCCAGCTCCTCG | e-e-e-d(10)-k-k-k | 49 | 1081 |
| 962 | 977 | 528424 | CGCCTCTTCCAGTCAG | e-e-e-d(10)-k-k-k | 42 | 1082 |
| 964 | 979 | 528425 | GCCGCCTCTTCCAGTC | e-e-e-d(10)-k-k-k | 44 | 1083 |
| 965 | 980 | 528426 | TGCCGCCTCTTCCAGT | e-e-e-d(10)-k-k-k | 15 | 1084 |
| 970 | 985 | 528427 | TCTGTTGCCGCCTCTT | e-e-e-d(10)-k-k-k | 9 | 1085 |
| 971 | 986 | 528428 | ATCTGTTGCCGCCTCT | e-e-e-d(10)-k-k-k | 30 | 1086 |
| 972 | 987 | 528429 | AATCTGTTGCCGCCTC | e-e-e-d(10)-k-k-k | 23 | 1087 |
| 973 | 988 | 528430 | CAATCTGTTGCCGCCT | e-e-e-d(10)-k-k-k | 12 | 1088 |
| 974 | 989 | 528431 | GCAATCTGTTGCCGCC | e-e-e-d(10)-k-k-k | 48 | 1089 |
| 975 | 990 | 528432 | GGCAATCTGTTGCCGC | e-e-e-d(10)-k-k-k | 18 | 1090 |
| 976 | 991 | 528433 | AGGCAATCTGTTGCCG | e-e-e-d(10)-k-k-k | 0 | 1091 |
| 977 | 992 | 528434 | CAGGCAATCTGTTGCC | e-e-e-d(10)-k-k-k | 8 | 1092 |
| 978 | 993 | 528435 | GCAGGCAATCTGTTGC | e-e-e-d(10)-k-k-k | 13 | 1093 |
| 982 | 997 | 528436 | CAATGCAGGCAATCTG | e-e-e-d(10)-k-k-k | 9 | 1094 |
| 983 | 998 | 528437 | CCAATGCAGGCAATCT | e-e-e-d(10)-k-k-k | 26 | 1095 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 984 | 999 | 528438 | TCCAATGCAGGCAATC | e-e-e-d(10)-k-k-k | 10 | 1096 |
| 985 | 1000 | 528439 | CTCCAATGCAGGCAAT | e-e-e-d(10)-k-k-k | 2 | 1097 |
| 986 | 1001 | 528440 | CCTCCAATGCAGGCAA | e-e-e-d(10)-k-k-k | 28 | 1098 |
| 1003 | 1018 | 528441 | GGCAGATGTTGGGCGG | e-e-e-d(10)-k-k-k | 8 | 1099 |
| 1004 | 1019 | 528442 | AGGCAGATGTTGGGCG | e-e-e-d(10)-k-k-k | 0 | 1100 |
| 1005 | 1020 | 528443 | TAGGCAGATGTTGGGC | e-e-e-d(10)-k-k-k | 1 | 1101 |
| 1006 | 1021 | 528444 | CTAGGCAGATGTTGGG | e-e-e-d(10)-k-k-k | 0 | 1102 |
| 1007 | 1022 | 528445 | TCTAGGCAGATGTTGG | e-e-e-d(10)-k-k-k | 7 | 1103 |
| 1008 | 1023 | 528446 | ATCTAGGCAGATGTTG | e-e-e-d(10)-k-k-k | 3 | 1104 |
| 1010 | 1025 | 528447 | CGATCTAGGCAGATGT | e-e-e-d(10)-k-k-k | 9 | 72 |
| 1011 | 1026 | 528448 | CCGATCTAGGCAGATG | e-e-e-d(10)-k-k-k | 13 | 1105 |
| 1013 | 1028 | 528449 | AGCCGATCTAGGCAGA | e-e-e-d(10)-k-k-k | 4 | 1106 |
| 1014 | 1029 | 528450 | TAGCCGATCTAGGCAG | e-e-e-d(10)-k-k-k | 11 | 1107 |
| 1015 | 1030 | 528451 | CTAGCCGATCTAGGCA | e-e-e-d(10)-k-k-k | 5 | 1108 |
| 1016 | 1031 | 528452 | TCTAGCCGATCTAGGC | e-e-e-d(10)-k-k-k | 5 | 1109 |
| 1017 | 1032 | 528453 | TTCTAGCCGATCTAGG | e-e-e-d(10)-k-k-k | 24 | 1110 |
| 1018 | 1033 | 528454 | TTTCTAGCCGATCTAG | e-e-e-d(10)-k-k-k | 29 | 1111 |
| 1019 | 1034 | 528455 | TTTTCTAGCCGATCTA | e-e-e-d(10)-k-k-k | 28 | 1112 |
| 1020 | 1035 | 528456 | GTTTTCTAGCCGATCT | e-e-e-d(10)-k-k-k | 42 | 1113 |
| 1022 | 1037 | 528457 | CAGTTTTCTAGCCGAT | e-e-e-d(10)-k-k-k | 50 | 1114 |
| 1023 | 1038 | 528458 | CCAGTTTTCTAGCCGA | e-e-e-d(10)-k-k-k | 70 | 1115 |
| 1024 | 1039 | 528459 | TCCAGTTTTCTAGCCG | e-e-e-d(10)-k-k-k | 56 | 1116 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1025 | 1040 | 528460 | ATCCAGTTTTCTAGCC | e-e-e-d(10)-k-k-k | 42 | 1117 |
| 1029 | 1044 | 528461 | CGTTATCCAGTTTTCT | e-e-e-d(10)-k-k-k | 47 | 1118 |
| 1043 | 1058 | 528462 | GATTCTGCTAATGACG | e-e-e-d(10)-k-k-k | 42 | 1119 |
| 1044 | 1059 | 528463 | AGATTCTGCTAATGAC | e-e-e-d(10)-k-k-k | 38 | 1120 |
| 1048 | 1063 | 528464 | GTTGAGATTCTGCTAA | e-e-e-d(10)-k-k-k | 30 | 1121 |
| 1049 | 1064 | 528465 | AGTTGAGATTCTGCTA | e-e-e-d(10)-k-k-k | 48 | 1122 |
| 1056 | 1071 | 528466 | GGTCTGAAGTTGAGAT | e-e-e-d(10)-k-k-k | 27 | 1123 |
| 1058 | 1073 | 528467 | CGGGTCTGAAGTTGAG | e-e-e-d(10)-k-k-k | 44 | 1124 |
| 1059 | 1074 | 528468 | ACGGGTCTGAAGTTGA | e-e-e-d(10)-k-k-k | 41 | 1125 |
| 1060 | 1075 | 528469 | GACGGGTCTGAAGTTG | e-e-e-d(10)-k-k-k | 45 | 1126 |
| 1061 | 1076 | 528470 | TGACGGGTCTGAAGTT | e-e-e-d(10)-k-k-k | 34 | 1127 |
| 1062 | 1077 | 528471 | TTGACGGGTCTGAAGT | e-e-e-d(10)-k-k-k | 19 | 1128 |
| 1063 | 1078 | 528472 | GTTGACGGGTCTGAAG | e-e-e-d(10)-k-k-k | 21 | 1129 |
| 1064 | 1079 | 528473 | TGTTGACGGGTCTGAA | e-e-e-d(10)-k-k-k | 37 | 1130 |
| 1065 | 1080 | 528474 | TTGTTGACGGGTCTGA | e-e-e-d(10)-k-k-k | 55 | 1131 |
| 1066 | 1081 | 528475 | TTTGTTGACGGGTCTG | e-e-e-d(10)-k-k-k | 63 | 1132 |
| 1067 | 1082 | 528476 | ATTTGTTGACGGGTCT | e-e-e-d(10)-k-k-k | 65 | 1133 |
| 1899 | 1914 | 530425 | GCCCTTGCCAGCCATG | k-d(10)-k-e-k-e-e | 73 | 1134 |
| 1900 | 1916 | 530054 | AAGCCCTTGCCAGCCAT | e-e-k-d(10)-k-e-k-e | 75 | 1135 |
| 1900 | 1915 | 530375 | AGCCCTTGCCAGCCAT | e-k-d(10)-k-e-k-e | 77 | 1136 |
| 1901 | 1916 | 530123 | AAGCCCTTGCCAGCCA | e-k-k-d(10)-k-k-e | 86 | 144 |
| 1901 | 1916 | 530170 | AAGCCCTTGCCAGCCA | e-e-k-d(10)-k-k-e | 87 | 144 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1901 | 1916 | 530220 | AAGCCCTTGCCAGCCA | e-d-k-d(10)-k-k-e | 74 | 144 |
| 1901 | 1916 | 530270 | AAGCCCTTGCCAGCCA | e-d-d-k-d(9)-k-k-e | 87 | 144 |
| 1901 | 1916 | 530320 | AAGCCCTTGCCAGCCA | e-e-e-e-d(9)-k-k-e | 17 | 144 |
| 1946 | 1961 | 530426 | TTTTTCACAAGGTCAA | k-d(10)-k-e-k-e-e | 55 | 1137 |
| 1947 | 1963 | 530059 | ACTTTTTCACAAGGTCA | e-e-k-d(10)-k-e-k-e | 73 | 1138 |
| 1947 | 1962 | 530376 | CTTTTTCACAAGGTCA | e-k-d(10)-k-e-k-e | 77 | 1139 |
| 1948 | 1963 | 530124 | ACTTTTTCACAAGGTC | e-k-k-d(10)-k-k-e | 79 | 153 |
| 1948 | 1963 | 530171 | ACTTTTTCACAAGGTC | e-e-k-d(10)-k-k-e | 69 | 153 |
| 1948 | 1963 | 530221 | ACTTTTTCACAAGGTC | e-d-k-d(10)-k-k-e | 64 | 153 |
| 1948 | 1963 | 530271 | ACTTTTTCACAAGGTC | e-d-d-k-d(9)-k-k-e | 73 | 153 |
| 1948 | 1963 | 530321 | ACTTTTTCACAAGGTC | e-e-e-e-d(9)-k-k-e | 44 | 153 |
| 2204 | 2219 | 530427 | ATGATCTTATAGCCCA | k-d(10)-k-e-k-e-e | 43 | 931 |
| 2205 | 2221 | 530060 | CCATGATCTTATAGCCC | e-e-k-d(10)-k-e-k-e | 77 | 1140 |
| 2205 | 2220 | 530377 | CATGATCTTATAGCCC | e-k-d(10)-k-e-k-e | 66 | 932 |
| 2206 | 2221 | 530125 | CCATGATCTTATAGCC | e-k-k-d(10)-k-k-e | 65 | 175 |
| 2206 | 2221 | 530172 | CCATGATCTTATAGCC | e-e-k-d(10)-k-k-e | 59 | 175 |
| 2206 | 2221 | 530222 | CCATGATCTTATAGCC | e-d-k-d(10)-k-k-e | 48 | 175 |
| 2206 | 2221 | 530272 | CCATGATCTTATAGCC | e-d-d-k-d(9)-k-k-e | 63 | 175 |
| 2206 | 2221 | 530322 | CCATGATCTTATAGCC | e-e-e-e-d(9)-k-k-e | 55 | 175 |
| 2679 | 2694 | 530428 | TAGCAGAAGTAGGAGA | k-d(10)-k-e-k-e-e | 49 | 1141 |
| 2680 | 2696 | 530061 | GATAGCAGAAGTAGGAG | e-e-k-d(10)-k-e-k-e | 49 | 1142 |
| 2680 | 2695 | 530378 | ATAGCAGAAGTAGGAG | e-k-d(10)-k-e-k-e | 48 | 1143 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2681 | 2696 | 530126 | GATAGCAGAAGTAGGA | e-k-k-d(10)-k-k-e | 70 | 223 |
| 2681 | 2696 | 530173 | GATAGCAGAAGTAGGA | e-e-k-d(10)-k-k-e | 62 | 223 |
| 2681 | 2696 | 530223 | GATAGCAGAAGTAGGA | e-d-k-d(10)-k-k-e | 44 | 223 |
| 2681 | 2696 | 530273 | GATAGCAGAAGTAGGA | e-d-d-k-d(9)-k-k-e | 63 | 223 |
| 2681 | 2696 | 530323 | GATAGCAGAAGTAGGA | e-e-e-e-d(9)-k-k-e | 63 | 223 |
| 3012 | 3027 | 530513 | TTGGATGTCAGCAAGG | k-d(10)-k-e-k-e-e | 88 | 1047 |
| 3013 | 3028 | 530507 | TTTGGATGTCAGCAAG | e-k-d(10)-k-e-k-e | 86 | 1144 |
| 3013 | 3028 | 530514 | TTTGGATGTCAGCAAG | k-d(10)-k-e-k-e-e | 80 | 1144 |
| 3014 | 3029 | 530430 | ATTTGGATGTCAGCAA | k-d(10)-k-e-k-e-e | 87 | 1145 |
| 3014 | 3029 | 530468 | ATTTGGATGTCAGCAA | e-k-k-d(10)-k-k-e | 81 | 1145 |
| 3014 | 3029 | 530476 | ATTTGGATGTCAGCAA | e-e-k-d(10)-k-k-e | 82 | 1145 |
| 3014 | 3029 | 530484 | ATTTGGATGTCAGCAA | e-d-k-d(10)-k-k-e | 74 | 1145 |
| 3014 | 3029 | 530492 | ATTTGGATGTCAGCAA | e-d-d-k-d(9)-k-k-e | 83 | 1145 |
| 3014 | 3029 | 530500 | ATTTGGATGTCAGCAA | e-e-e-e-d(9)-k-k-e | 56 | 1145 |
| 3014 | 3029 | 530508 | ATTTGGATGTCAGCAA | e-k-d(10)-k-e-k-e | 83 | 1145 |
| 3015 | 3031 | 530062 | CTATTTGGATGTCAGCA | e-e-k-d(10)-k-e-k-e | 94 | 1146 |
| 3015 | 3030 | 530380 | TATTTGGATGTCAGCA | e-k-d(10)-k-e-k-e | 94 | 1147 |
| 3015 | 3030 | 530469 | TATTTGGATGTCAGCA | e-k-k-d(10)-k-k-e | 91 | 1147 |
| 3015 | 3030 | 530477 | TATTTGGATGTCAGCA | e-e-k-d(10)-k-k-e | 87 | 1147 |
| 3015 | 3030 | 530485 | TATTTGGATGTCAGCA | e-d-k-d(10)-k-k-e | 87 | 1147 |
| 3015 | 3030 | 530493 | TATTTGGATGTCAGCA | e-d-d-k-d(9)-k-k-e | 81 | 1147 |
| 3015 | 3030 | 530501 | TATTTGGATGTCAGCA | e-e-e-e-d(9)-k-k-e | 74 | 1147 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 3015 | 3030 | 530515 | TATTTGGATGTCAGCA | k-d(10)-k-e-k-e-e | 87 | 1147 |
| 3016 | 3031 | 481464 | CTATTTGGATGTCAGC | k-k-k-d(10)-k-k-k | 93 | 245 |
| 3016 | 3031 | 518349 | CTATTTGGATGTCAGC | e-e-e-d(10)-k-k-k | 58 | 245 |
| 3016 | 3031 | 519637 | CTATTTGGATGTCAGC | e-k-k-d(10)-k-k-e | 96 | 245 |
| 3016 | 3031 | 530175 | CTATTTGGATGTCAGC | e-e-k-d(10)-k-k-e | 93 | 245 |
| 3016 | 3031 | 530225 | CTATTTGGATGTCAGC | e-d-k-d(10)-k-k-e | 85 | 245 |
| 3016 | 3031 | 530275 | CTATTTGGATGTCAGC | e-d-d-k-d(9)-k-k-e | 91 | 245 |
| 3016 | 3031 | 530325 | CTATTTGGATGTCAGC | e-e-e-e-d(9)-k-k-e | 91 | 245 |
| 3017 | 3032 | 530470 | TCTATTTGGATGTCAG | e-k-k-d(10)-k-k-e | 91 | 1148 |
| 3017 | 3032 | 530478 | TCTATTTGGATGTCAG | e-e-k-d(10)-k-k-e | 87 | 1148 |
| 3017 | 3032 | 530486 | TCTATTTGGATGTCAG | e-d-k-d(10)-k-k-e | 84 | 1148 |
| 3017 | 3032 | 530494 | TCTATTTGGATGTCAG | e-d-d-k-d(9)-k-k-e | 60 | 1148 |
| 3017 | 3032 | 530502 | TCTATTTGGATGTCAG | e-e-e-e-d(9)-k-k-e | 64 | 1148 |
| 3017 | 3032 | 530509 | TCTATTTGGATGTCAG | e-k-d(10)-k-e-k-e | 80 | 1148 |
| 3018 | 3033 | 530471 | TTCTATTTGGATGTCA | e-k-k-d(10)-k-k-e | 83 | 1149 |
| 3018 | 3033 | 530479 | TTCTATTTGGATGTCA | e-e-k-d(10)-k-k-e | 74 | 1149 |
| 3018 | 3033 | 530487 | TTCTATTTGGATGTCA | e-d-k-d(10)-k-k-e | 71 | 1149 |
| 3018 | 3033 | 530495 | TTCTATTTGGATGTCA | e-d-d-k-d(9)-k-k-e | 68 | 1149 |
| 3018 | 3033 | 530503 | TTCTATTTGGATGTCA | e-e-e-e-d(9)-k-k-e | 53 | 1149 |
| 3459 | 3474 | 530431 | CACCAAGGAGGCTGTT | k-d(10)-k-e-k-e-e | 44 | 1150 |
| 3460 | 3476 | 530055 | AGCACCAAGGAGGCTGT | e-e-k-d(10)-k-e-k-e | 45 | 1151 |
| 3460 | 3475 | 530381 | GCACCAAGGAGGCTGT | e-k-d(10)-k-e-k-e | 74 | 1152 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 3461 | 3476 | 530128 | AGCACCAAGGAGGCTG | e-k-k-d(10)-k-k-e | 52 | 257 |
| 3461 | 3476 | 530176 | AGCACCAAGGAGGCTG | e-e-k-d(10)-k-k-e | 66 | 257 |
| 3461 | 3476 | 530226 | AGCACCAAGGAGGCTG | e-d-k-d(10)-k-k-e | 51 | 257 |
| 3461 | 3476 | 530276 | AGCACCAAGGAGGCTG | e-d-d-k-d(9)-k-k-e | 70 | 257 |
| 3461 | 3476 | 530326 | AGCACCAAGGAGGCTG | e-e-e-e-d(9)-k-k-e | 52 | 257 |
| 3527 | 3542 | 528860 | GGTTTGACCTGAAGCC | e-e-e-d(10)-k-k-k | 58 | 1153 |
| 3528 | 3543 | 528861 | GGGTTTGACCTGAAGC | e-e-e-d(10)-k-k-k | 42 | 1154 |
| 3529 | 3544 | 528862 | AGGGTTTGACCTGAAG | e-e-e-d(10)-k-k-k | 57 | 1155 |
| 3530 | 3545 | 528863 | AAGGGTTTGACCTGAA | e-e-e-d(10)-k-k-k | 43 | 1156 |
| 3531 | 3546 | 528864 | TAAGGGTTTGACCTGA | e-e-e-d(10)-k-k-k | 50 | 1157 |
| 3532 | 3547 | 528865 | TTAAGGGTTTGACCTG | e-e-e-d(10)-k-k-k | 32 | 1158 |
| 3547 | 3562 | 528866 | GCAGCTTCAGATGTCT | e-e-e-d(10)-k-k-k | 60 | 1159 |
| 3548 | 3563 | 528867 | TGCAGCTTCAGATGTC | e-e-e-d(10)-k-k-k | 47 | 1160 |
| 3583 | 3598 | 530388 | CTTAAACCTTCCTATT | k-d(10)-k-e-k-e-e | 14 | 1161 |
| 3584 | 3599 | 530338 | CCTTAAACCTTCCTAT | e-k-d(10)-k-e-k-e | 47 | 1162 |
| 3585 | 3600 | 530086 | TCCTTAAACCTTCCTA | e-k-k-d(10)-k-k-e | 58 | 273 |
| 3585 | 3600 | 530133 | TCCTTAAACCTTCCTA | e-e-k-d(10)-k-k-e | 53 | 273 |
| 3585 | 3600 | 530183 | TCCTTAAACCTTCCTA | e-d-k-d(10)-k-k-e | 52 | 273 |
| 3585 | 3600 | 530233 | TCCTTAAACCTTCCTA | e-d-d-k-d(9)-k-k-e | 29 | 273 |
| 3585 | 3600 | 530283 | TCCTTAAACCTTCCTA | e-e-e-e-d(9)-k-k-e | 32 | 273 |
| 3590 | 3605 | 528868 | GATTCTCCTTAAACCT | e-e-e-d(10)-k-k-k | 45 | 1163 |
| 3591 | 3606 | 530389 | AGATTCTCCTTAAACC | k-d(10)-k-e-k-e-e | 44 | 1164 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 3592 | 3607 | 530339 | TAGATTCTCCTTAAAC | e-k-d(10)-k-e-k-e | 41 | 1165 |
| 3593 | 3608 | 530087 | TTAGATTCTCCTTAAA | e-k-k-d(10)-k-k-e | 43 | 1166 |
| 3593 | 3608 | 530134 | TTAGATTCTCCTTAAA | e-e-k-d(10)-k-k-e | 28 | 1166 |
| 3593 | 3608 | 530184 | TTAGATTCTCCTTAAA | e-d-k-d(10)-k-k-e | 13 | 1166 |
| 3593 | 3608 | 530234 | TTAGATTCTCCTTAAA | e-d-d-k-d(9)-k-k-e | 15 | 1166 |
| 3593 | 3608 | 530284 | TTAGATTCTCCTTAAA | e-e-e-e-d(9)-k-k-e | 14 | 1166 |
| 3595 | 3610 | 530390 | GCTTAGATTCTCCTTA | k-d(10)-k-e-k-e-e | 83 | 1167 |
| 3596 | 3611 | 530340 | TGCTTAGATTCTCCTT | e-k-d(10)-k-e-k-e | 89 | 1168 |
| 3597 | 3612 | 528869 | ATGCTTAGATTCTCCT | e-e-e-d(10)-k-k-k | 83 | 1169 |
| 3597 | 3612 | 530088 | ATGCTTAGATTCTCCT | e-k-k-d(10)-k-k-e | 90 | 1169 |
| 3597 | 3612 | 530135 | ATGCTTAGATTCTCCT | e-e-k-d(10)-k-k-e | 91 | 1169 |
| 3597 | 3612 | 530185 | ATGCTTAGATTCTCCT | e-d-k-d(10)-k-k-e | 85 | 1169 |
| 3597 | 3612 | 530235 | ATGCTTAGATTCTCCT | e-d-d-k-d(9)-k-k-e | 28 | 1169 |
| 3597 | 3612 | 530285 | ATGCTTAGATTCTCCT | e-e-e-e-d(9)-k-k-e | 86 | 1169 |
| 3597 | 3612 | 530391 | ATGCTTAGATTCTCCT | k-d(10)-k-e-k-e-e | 79 | 1169 |
| 3598 | 3614 | 530021 | AAATGCTTAGATTCTCC | e-e-k-d(10)-k-e-k-e | 87 | 1170 |
| 3598 | 3613 | 530341 | AATGCTTAGATTCTCC | e-k-d(10)-k-e-k-e | 88 | 1171 |
| 3599 | 3614 | 530089 | AAATGCTTAGATTCTC | e-k-k-d(10)-k-k-e | 71 | 1172 |
| 3599 | 3614 | 530136 | AAATGCTTAGATTCTC | e-e-k-d(10)-k-k-e | 66 | 1172 |
| 3599 | 3614 | 530186 | AAATGCTTAGATTCTC | e-d-k-d(10)-k-k-e | 51 | 1172 |
| 3599 | 3614 | 530236 | AAATGCTTAGATTCTC | e-d-d-k-d(9)-k-k-e | 74 | 1172 |
| 3599 | 3614 | 530286 | AAATGCTTAGATTCTC | e-e-e-e-d(9)-k-k-e | 56 | 1172 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 3682 | 3697 | 528870 | GTAAGCACCCTCTGCC | e-e-e-d(10)-k-k-k | 26 | 1173 |
| 3684 | 3699 | 528871 | TTGTAAGCACCCTCTG | e-e-e-d(10)-k-k-k | 14 | 1174 |
| 3686 | 3701 | 528872 | GGTTGTAAGCACCCTC | e-e-e-d(10)-k-k-k | 47 | 1175 |
| 3687 | 3702 | 528873 | AGGTTGTAAGCACCCT | e-e-e-d(10)-k-k-k | 40 | 1176 |
| 3688 | 3703 | 528874 | AAGGTTGTAAGCACCC | e-e-e-d(10)-k-k-k | 54 | 1177 |
| 3690 | 3705 | 528875 | TCAAGGTTGTAAGCAC | e-e-e-d(10)-k-k-k | 15 | 1178 |
| 3691 | 3706 | 528876 | GTCAAGGTTGTAAGCA | e-e-e-d(10)-k-k-k | 28 | 1179 |
| 3692 | 3707 | 528877 | AGTCAAGGTTGTAAGC | e-e-e-d(10)-k-k-k | 28 | 1180 |
| 3694 | 3709 | 528878 | GGAGTCAAGGTTGTAA | e-e-e-d(10)-k-k-k | 6 | 1181 |
| 3695 | 3710 | 528879 | GGGAGTCAAGGTTGTA | e-e-e-d(10)-k-k-k | 22 | 1182 |
| 3714 | 3729 | 530392 | GATCAAGTCCAGGGAG | k-d(10)-k-e-k-e-e | 47 | 1183 |
| 3715 | 3731 | 530022 | CAGATCAAGTCCAGGGA | e-e-k-d(10)-k-e-k-e | 80 | 1184 |
| 3715 | 3730 | 530342 | AGATCAAGTCCAGGGA | e-k-d(10)-k-e-k-e | 70 | 1185 |
| 3715 | 3730 | 530393 | AGATCAAGTCCAGGGA | k-d(10)-k-e-k-e-e | 46 | 1185 |
| 3716 | 3732 | 530023 | GCAGATCAAGTCCAGGG | e-e-k-d(10)-k-e-k-e | 74 | 1186 |
| 3716 | 3731 | 530090 | CAGATCAAGTCCAGGG | e-k-k-d(10)-k-k-e | 78 | 1187 |
| 3716 | 3731 | 530137 | CAGATCAAGTCCAGGG | e-e-k-d(10)-k-k-e | 76 | 1187 |
| 3716 | 3731 | 530187 | CAGATCAAGTCCAGGG | e-d-k-d(10)-k-k-e | 68 | 1187 |
| 3716 | 3731 | 530237 | CAGATCAAGTCCAGGG | e-d-d-k-d(9)-k-k-e | 36 | 1187 |
| 3716 | 3731 | 530287 | CAGATCAAGTCCAGGG | e-e-e-e-d(9)-k-k-e | 56 | 1187 |
| 3716 | 3731 | 530343 | CAGATCAAGTCCAGGG | e-k-d(10)-k-e-k-e | 68 | 1187 |
| 3716 | 3731 | 530394 | CAGATCAAGTCCAGGG | k-d(10)-k-e-k-e-e | 49 | 1187 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 3717 | 3732 | 518343 | GCAGATCAAGTCCAGG | e-e-e-d(10)-k-k-k | 5 | 1188 |
| 3717 | 3733 | 530024 | AGCAGATCAAGTCCAGG | e-e-k-d(10)-k-e-k-e | 79 | 1189 |
| 3717 | 3732 | 530091 | GCAGATCAAGTCCAGG | e-k-k-d(10)-k-k-e | 81 | 1188 |
| 3717 | 3732 | 530138 | GCAGATCAAGTCCAGG | e-e-k-d(10)-k-k-e | 81 | 1188 |
| 3717 | 3732 | 530188 | GCAGATCAAGTCCAGG | e-d-k-d(10)-k-k-e | 78 | 1188 |
| 3717 | 3732 | 530238 | GCAGATCAAGTCCAGG | e-d-d-k-d(9)-k-k-e | 29 | 1188 |
| 3717 | 3732 | 530288 | GCAGATCAAGTCCAGG | e-e-e-e-d(9)-k-k-e | 69 | 1188 |
| 3717 | 3732 | 530344 | GCAGATCAAGTCCAGG | e-k-d(10)-k-e-k-e | 85 | 1188 |
| 3718 | 3733 | 530092 | AGCAGATCAAGTCCAG | e-k-k-d(10)-k-k-e | 85 | 1190 |
| 3718 | 3733 | 530139 | AGCAGATCAAGTCCAG | e-e-k-d(10)-k-k-e | 79 | 1190 |
| 3718 | 3733 | 530189 | AGCAGATCAAGTCCAG | e-d-k-d(10)-k-k-e | 77 | 1190 |
| 3718 | 3733 | 530239 | AGCAGATCAAGTCCAG | e-d-d-k-d(9)-k-k-e | 61 | 1190 |
| 3718 | 3733 | 530289 | AGCAGATCAAGTCCAG | e-e-e-e-d(9)-k-k-e | 75 | 1190 |
| 3720 | 3735 | 528880 | ACAGCAGATCAAGTCC | e-e-e-d(10)-k-k-k | 65 | 1191 |
| 3721 | 3736 | 528881 | AACAGCAGATCAAGTC | e-e-e-d(10)-k-k-k | 44 | 1192 |
| 3737 | 3752 | 528882 | ACAACCTAGCCTCTGA | e-e-e-d(10)-k-k-k | 39 | 1193 |
| 3738 | 3753 | 528883 | AACAACCTAGCCTCTG | e-e-e-d(10)-k-k-k | 46 | 1194 |
| 3740 | 3755 | 528884 | GAAACAACCTAGCCTC | e-e-e-d(10)-k-k-k | 37 | 1195 |
| 3741 | 3756 | 528885 | AGAAACAACCTAGCCT | e-e-e-d(10)-k-k-k | 20 | 1196 |
| 3742 | 3757 | 528886 | CAGAAACAACCTAGCC | e-e-e-d(10)-k-k-k | 21 | 1197 |
| 3755 | 3770 | 528887 | GATAAGGCACCCACAG | e-e-e-d(10)-k-k-k | 25 | 1198 |
| 3756 | 3771 | 528888 | TGATAAGGCACCCACA | e-e-e-d(10)-k-k-k | 12 | 1199 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 3757 | 3772 | 528889 | CTGATAAGGCACCCAC | e-e-e-d(10)-k-k-k | 25 | 1200 |
| 3759 | 3774 | 528890 | CCCTGATAAGGCACCC | e-e-e-d(10)-k-k-k | 42 | 1201 |
| 3760 | 3775 | 528891 | GCCCTGATAAGGCACC | e-e-e-d(10)-k-k-k | 49 | 1202 |
| 3765 | 3780 | 528892 | TCCCAGCCCTGATAAG | e-e-e-d(10)-k-k-k | 0 | 1203 |
| 3767 | 3782 | 528893 | TATCCCAGCCCTGATA | e-e-e-d(10)-k-k-k | 0 | 1204 |
| 3770 | 3785 | 528894 | AAGTATCCCAGCCCTG | e-e-e-d(10)-k-k-k | 25 | 1205 |
| 3771 | 3786 | 528895 | GAAGTATCCCAGCCCT | e-e-e-d(10)-k-k-k | 39 | 1206 |
| 3772 | 3787 | 528896 | AGAAGTATCCCAGCCC | e-e-e-d(10)-k-k-k | 22 | 1207 |
| 3773 | 3788 | 528897 | CAGAAGTATCCCAGCC | e-e-e-d(10)-k-k-k | 36 | 1208 |
| 3892 | 3907 | 528898 | TGAGACCAGGATTCCT | e-e-e-d(10)-k-k-k | 41 | 1209 |
| 3896 | 3911 | 528899 | GTCCTGAGACCAGGAT | e-e-e-d(10)-k-k-k | 19 | 1210 |
| 3977 | 3992 | 528900 | AGCTCAACCAGACACG | e-e-e-d(10)-k-k-k | 54 | 311 |
| 3979 | 3994 | 528901 | TGAGCTCAACCAGACA | e-e-e-d(10)-k-k-k | 40 | 1211 |
| 3984 | 3999 | 528902 | TTCCCTGAGCTCAACC | e-e-e-d(10)-k-k-k | 32 | 1212 |
| 3992 | 4007 | 528903 | GAACCATATTCCCTGA | e-e-e-d(10)-k-k-k | 30 | 313 |
| 3995 | 4010 | 528904 | TAAGAACCATATTCCC | e-e-e-d(10)-k-k-k | 27 | 1213 |
| 4022 | 4037 | 518344 | GCCACTGGATATCACC | e-e-e-d(10)-k-k-k | 89 | 317 |
| 4067 | 4082 | 528905 | TAAGCCTTTGCCCTGC | e-e-e-d(10)-k-k-k | 64 | 1214 |
| 4068 | 4083 | 528906 | GTAAGCCTTTGCCCTG | e-e-e-d(10)-k-k-k | 53 | 1215 |
| 4069 | 4084 | 528907 | AGTAAGCCTTTGCCCT | e-e-e-d(10)-k-k-k | 45 | 1216 |
| 4070 | 4085 | 528908 | CAGTAAGCCTTTGCCC | e-e-e-d(10)-k-k-k | 40 | 1217 |
| 4072 | 4087 | 528909 | ATCAGTAAGCCTTTGC | e-e-e-d(10)-k-k-k | 53 | 1218 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4073 | 4088 | 528910 | TATCAGTAAGCCTTTG | e-e-e-d(10)-k-k-k | 47 | 1219 |
| 4077 | 4092 | 528911 | AGTTTATCAGTAAGCC | e-e-e-d(10)-k-k-k | 58 | 1220 |
| 4083 | 4098 | 528912 | GACTCAAGTTTATCAG | e-e-e-d(10)-k-k-k | 37 | 1221 |
| 4085 | 4100 | 528913 | CAGACTCAAGTTTATC | e-e-e-d(10)-k-k-k | 39 | 1222 |
| 4086 | 4101 | 528914 | GCAGACTCAAGTTTAT | e-e-e-d(10)-k-k-k | 0 | 1223 |
| 4087 | 4102 | 528915 | GGCAGACTCAAGTTTA | e-e-e-d(10)-k-k-k | 1 | 1224 |
| 4088 | 4103 | 528916 | GGGCAGACTCAAGTTT | e-e-e-d(10)-k-k-k | 0 | 1225 |
| 4089 | 4104 | 528917 | AGGGCAGACTCAAGTT | e-e-e-d(10)-k-k-k | 9 | 1226 |
| 4091 | 4106 | 528918 | CGAGGGCAGACTCAAG | e-e-e-d(10)-k-k-k | 2 | 1227 |
| 4093 | 4108 | 528919 | TACGAGGGCAGACTCA | e-e-e-d(10)-k-k-k | 20 | 324 |
| 4094 | 4109 | 528920 | ATACGAGGGCAGACTC | e-e-e-d(10)-k-k-k | 14 | 1228 |
| 4095 | 4110 | 528921 | CATACGAGGGCAGACT | e-e-e-d(10)-k-k-k | 0 | 1229 |
| 4096 | 4111 | 528922 | TCATACGAGGGCAGAC | e-e-e-d(10)-k-k-k | 8 | 1230 |
| 4098 | 4113 | 528923 | CCTCATACGAGGGCAG | e-e-e-d(10)-k-k-k | 2 | 1231 |
| 4099 | 4114 | 528924 | CCCTCATACGAGGGCA | e-e-e-d(10)-k-k-k | 2 | 1232 |
| 4100 | 4115 | 528925 | ACCCTCATACGAGGGC | e-e-e-d(10)-k-k-k | 0 | 1233 |
| 4225 | 4240 | 528926 | TACGCACAGGAGAGGC | e-e-e-d(10)-k-k-k | 20 | 1233 |
| 4226 | 4241 | 528927 | ATACGCACAGGAGAGG | e-e-e-d(10)-k-k-k | 0 | 1234 |
| 4227 | 4242 | 528928 | CATACGCACAGGAGAG | e-e-e-d(10)-k-k-k | 6 | 1235 |
| 4228 | 4243 | 528929 | CCATACGCACAGGAGA | e-e-e-d(10)-k-k-k | 4 | 1236 |
| 4229 | 4244 | 528930 | CCCATACGCACAGGAG | e-e-e-d(10)-k-k-k | 36 | 1237 |
| 4230 | 4245 | 528931 | TCCCATACGCACAGGA | e-e-e-d(10)-k-k-k | 22 | 1238 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4231 | 4246 | 528932 | TTCCCATACGCACAGG | e-e-e-d(10)-k-k-k | 32 | 1239 |
| 4232 | 4247 | 528933 | GTTCCCATACGCACAG | e-e-e-d(10)-k-k-k | 45 | 1240 |
| 4233 | 4248 | 528934 | TGTTCCCATACGCACA | e-e-e-d(10)-k-k-k | 36 | 1241 |
| 4234 | 4249 | 528935 | GTGTTCCCATACGCAC | e-e-e-d(10)-k-k-k | 20 | 1242 |
| 4234 | 4249 | 530395 | GTGTTCCCATACGCAC | k-d(10)-k-e-k-e-e | 71 | 1242 |
| 4235 | 4250 | 528936 | GGTGTTCCCATACGCA | e-e-e-d(10)-k-k-k | 71 | 1243 |
| 4235 | 4251 | 530025 | AGGTGTTCCCATACGCA | e-e-k-d(10)-k-e-k-e | 90 | 1244 |
| 4235 | 4250 | 530345 | GGTGTTCCCATACGCA | e-k-d(10)-k-e-k-e | 93 | 1243 |
| 4235 | 4250 | 530396 | GGTGTTCCCATACGCA | k-d(10)-k-e-k-e-e | 71 | 1243 |
| 4236 | 4251 | 528937 | AGGTGTTCCCATACGC | e-e-e-d(10)-k-k-k | 73 | 1245 |
| 4236 | 4252 | 530026 | TAGGTGTTCCCATACGC | e-e-k-d(10)-k-e-k-e | 87 | 1246 |
| 4236 | 4251 | 530093 | AGGTGTTCCCATACGC | e-k-k-d(10)-k-k-e | 95 | 1245 |
| 4236 | 4251 | 530140 | AGGTGTTCCCATACGC | e-e-k-d(10)-k-k-e | 89 | 1245 |
| 4236 | 4251 | 530190 | AGGTGTTCCCATACGC | e-d-k-d(10)-k-k-e | 82 | 1245 |
| 4236 | 4251 | 530240 | AGGTGTTCCCATACGC | e-d-d-k-d(9)-k-k-e | 50 | 1245 |
| 4236 | 4251 | 530290 | AGGTGTTCCCATACGC | e-e-e-e-d(9)-k-k-e | 69 | 1245 |
| 4236 | 4251 | 530346 | AGGTGTTCCCATACGC | e-k-d(10)-k-e-k-e | 89 | 1245 |
| 4237 | 4252 | 528938 | TAGGTGTTCCCATACG | e-e-e-d(10)-k-k-k | 72 | 336 |
| 4237 | 4252 | 530094 | TAGGTGTTCCCATACG | e-k-k-d(10)-k-k-e | 88 | 336 |
| 4237 | 4252 | 530141 | TAGGTGTTCCCATACG | e-e-k-d(10)-k-k-e | 80 | 336 |
| 4237 | 4252 | 530191 | TAGGTGTTCCCATACG | e-d-k-d(10)-k-k-e | 74 | 336 |
| 4237 | 4252 | 530241 | TAGGTGTTCCCATACG | e-d-d-k-d(9)-k-k-e | 53 | 336 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4237 | 4252 | 530291 | TAGGTGTTCCCATACG | e-e-e-e-d(9)-k-k-e | 68 | 336 |
| 4238 | 4253 | 528939 | CTAGGTGTTCCCATAC | e-e-e-d(10)-k-k-k | 39 | 1247 |
| 4239 | 4254 | 528940 | GCTAGGTGTTCCCATA | e-e-e-d(10)-k-k-k | 62 | 1248 |
| 4240 | 4255 | 528941 | TGCTAGGTGTTCCCAT | e-e-e-d(10)-k-k-k | 49 | 1249 |
| 4242 | 4257 | 528942 | CGTGCTAGGTGTTCCC | e-e-e-d(10)-k-k-k | 77 | 1250 |
| 4304 | 4319 | 528943 | CAAGGTGGTTTTGAGT | e-e-e-d(10)-k-k-k | 25 | 1251 |
| 4305 | 4320 | 528944 | GCAAGGTGGTTTTGAG | e-e-e-d(10)-k-k-k | 28 | 344 |
| 4320 | 4335 | 528945 | CTCTGATCAGCTGAGG | e-e-e-d(10)-k-k-k | 74 | 1252 |
| 4321 | 4336 | 528946 | ACTCTGATCAGCTGAG | e-e-e-d(10)-k-k-k | 56 | 1253 |
| 4362 | 4377 | 528947 | GAGACCAGCTAATTTG | e-e-e-d(10)-k-k-k | 36 | 1254 |
| 4395 | 4410 | 528948 | CATCTTAGAGAAGGTC | e-e-e-d(10)-k-k-k | 59 | 1255 |
| 4435 | 4450 | 528949 | TCAACTGTCTCCAGGC | e-e-e-d(10)-k-k-k | 67 | 1256 |
| 4435 | 4450 | 530397 | TCAACTGTCTCCAGGC | k-d(10)-k-e-k-e-e | 60 | 1256 |
| 4436 | 4451 | 528950 | ATCAACTGTCTCCAGG | e-e-e-d(10)-k-k-k | 57 | 1257 |
| 4436 | 4452 | 530027 | CATCAACTGTCTCCAGG | e-e-k-d(10)-k-e-k-e | 56 | 1258 |
| 4436 | 4451 | 530347 | ATCAACTGTCTCCAGG | e-k-d(10)-k-e-k-e | 49 | 1257 |
| 4437 | 4452 | 530095 | CATCAACTGTCTCCAG | e-k-k-d(10)-k-k-e | 40 | 354 |
| 4437 | 4452 | 530142 | CATCAACTGTCTCCAG | e-e-k-d(10)-k-k-e | 43 | 354 |
| 4437 | 4452 | 530192 | CATCAACTGTCTCCAG | e-d-k-d(10)-k-k-e | 42 | 354 |
| 4437 | 4452 | 530242 | CATCAACTGTCTCCAG | e-d-d-k-d(9)-k-k-e | 0 | 354 |
| 4437 | 4452 | 530292 | CATCAACTGTCTCCAG | e-e-e-e-d(9)-k-k-e | 36 | 354 |
| 4437 | 4452 | 530398 | CATCAACTGTCTCCAG | k-d(10)-k-e-k-e-e | 28 | 354 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4438 | 4454 | 530028 | CACATCAACTGTCTCCA | e-e-k-d(10)-k-e-k-e | 57 | 1259 |
| 4438 | 4453 | 530348 | ACATCAACTGTCTCCA | e-k-d(10)-k-e-k-e | 58 | 1260 |
| 4439 | 4454 | 530096 | CACATCAACTGTCTCC | e-k-k-d(10)-k-k-e | 72 | 356 |
| 4439 | 4454 | 530143 | CACATCAACTGTCTCC | e-e-k-d(10)-k-k-e | 74 | 356 |
| 4439 | 4454 | 530193 | CACATCAACTGTCTCC | e-d-k-d(10)-k-k-e | 62 | 356 |
| 4439 | 4454 | 530243 | CACATCAACTGTCTCC | e-d-d-k-d(9)-k-k-e | 34 | 356 |
| 4439 | 4454 | 530293 | CACATCAACTGTCTCC | e-e-e-e-d(9)-k-k-e | 59 | 356 |
| 4441 | 4456 | 528951 | GACACATCAACTGTCT | e-e-e-d(10)-k-k-k | 16 | 1261 |
| 4475 | 4490 | 528952 | GAAGAGTGTTGCTGGA | e-e-e-d(10)-k-k-k | 57 | 1262 |
| 4477 | 4492 | 528953 | CTGAAGAGTGTTGCTG | e-e-e-d(10)-k-k-k | 46 | 1263 |
| 4479 | 4494 | 528954 | TACTGAAGAGTGTTGC | e-e-e-d(10)-k-k-k | 42 | 1264 |
| 4485 | 4500 | 530510 | ATTATGTACTGAAGAG | k-d(10)-k-e-k-e-e | 53 | 1265 |
| 4486 | 4501 | 530504 | TATTATGTACTGAAGA | e-k-d(10)-k-e-k-e | 25 | 1266 |
| 4486 | 4501 | 530511 | TATTATGTACTGAAGA | k-d(10)-k-e-k-e-e | 31 | 1266 |
| 4487 | 4502 | 530432 | TTATTATGTACTGAAG | k-d(10)-k-e-k-e-e | 15 | 1267 |
| 4487 | 4502 | 530463 | TTATTATGTACTGAAG | e-k-k-d(10)-k-k-e | 20 | 1267 |
| 4487 | 4502 | 530472 | TTATTATGTACTGAAG | e-e-k-d(10)-k-k-e | 17 | 1267 |
| 4487 | 4502 | 530480 | TTATTATGTACTGAAG | e-d-k-d(10)-k-k-e | 4 | 1267 |
| 4487 | 4502 | 530488 | TTATTATGTACTGAAG | e-d-d-k-d(9)-k-k-e | 13 | 1267 |
| 4487 | 4502 | 530496 | TTATTATGTACTGAAG | e-e-e-e-d(9)-k-k-e | 0 | 1267 |
| 4487 | 4502 | 530505 | TTATTATGTACTGAAG | e-k-d(10)-k-e-k-e | 37 | 1267 |
| 4488 | 4504 | 530063 | GCTTATTATGTACTGAA | e-e-k-d(10)-k-e-k-e | 74 | 1268 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4488 | 4503 | 530382 | CTTATTATGTACTGAA | e-k-d(10)-k-e-k-e | 17 | 1269 |
| 4488 | 4503 | 530465 | CTTATTATGTACTGAA | e-k-k-d(10)-k-k-e | 63 | 1269 |
| 4488 | 4503 | 530473 | CTTATTATGTACTGAA | e-e-k-d(10)-k-k-e | 45 | 1269 |
| 4488 | 4503 | 530481 | CTTATTATGTACTGAA | e-d-k-d(10)-k-k-e | 14 | 1269 |
| 4488 | 4503 | 530489 | CTTATTATGTACTGAA | e-d-d-k-d(9)-k-k-e | 13 | 1269 |
| 4488 | 4503 | 530497 | CTTATTATGTACTGAA | e-e-e-e-d(9)-k-k-e | 7 | 1269 |
| 4488 | 4503 | 530512 | CTTATTATGTACTGAA | k-d(10)-k-e-k-e-e | 21 | 1269 |
| 4489 | 4504 | 519638 | GCTTATTATGTACTGA | e-k-k-d(10)-k-k-e | 86 | 362 |
| 4489 | 4504 | 530177 | GCTTATTATGTACTGA | e-e-k-d(10)-k-k-e | 71 | 362 |
| 4489 | 4504 | 530227 | GCTTATTATGTACTGA | e-d-k-d(10)-k-k-e | 51 | 362 |
| 4489 | 4504 | 530277 | GCTTATTATGTACTGA | e-d-d-k-d(9)-k-k-e | 70 | 362 |
| 4489 | 4504 | 530327 | GCTTATTATGTACTGA | e-e-e-e-d(9)-k-k-e | 61 | 362 |
| 4490 | 4505 | 530466 | AGCTTATTATGTACTG | e-k-k-d(10)-k-k-e | 82 | 1270 |
| 4490 | 4505 | 530474 | AGCTTATTATGTACTG | e-e-k-d(10)-k-k-e | 62 | 1270 |
| 4490 | 4505 | 530482 | AGCTTATTATGTACTG | e-d-k-d(10)-k-k-e | 53 | 1270 |
| 4490 | 4505 | 530490 | AGCTTATTATGTACTG | e-d-d-k-d(9)-k-k-e | 42 | 1270 |
| 4490 | 4505 | 530498 | AGCTTATTATGTACTG | e-e-e-e-d(9)-k-k-e | 45 | 1270 |
| 4490 | 4505 | 530506 | AGCTTATTATGTACTG | e-k-d(10)-k-e-k-e | 70 | 1270 |
| 4491 | 4506 | 530467 | AAGCTTATTATGTACT | e-k-k-d(10)-k-k-e | 50 | 1271 |
| 4491 | 4506 | 530475 | AAGCTTATTATGTACT | e-e-k-d(10)-k-k-e | 26 | 1271 |
| 4491 | 4506 | 530483 | AAGCTTATTATGTACT | e-d-k-d(10)-k-k-e | 19 | 1271 |
| 4491 | 4506 | 530491 | AAGCTTATTATGTACT | e-d-d-k-d(9)-k-k-e | 13 | 1271 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4491 | 4506 | 530499 | AAGCTTATTATGTACT | e-e-e-e-d(9)-k-k-e | 15 | 1271 |
| 4492 | 4507 | 528955 | TAAGCTTATTATGTAC | e-e-e-d(10)-k-k-k | 0 | 1272 |
| 4499 | 4514 | 528956 | TATCAGTTAAGCTTAT | e-e-e-d(10)-k-k-k | 0 | 1273 |
| 4502 | 4517 | 528957 | GTTTATCAGTTAAGCT | e-e-e-d(10)-k-k-k | 31 | 1274 |
| 4539 | 4554 | 530433 | CAATGGTAAGCCCAAG | k-d(10)-k-e-k-e-e | 62 | 1275 |
| 4540 | 4555 | 528958 | CCAATGGTAAGCCCAA | e-e-e-d(10)-k-k-k | 66 | 1276 |
| 4540 | 4556 | 530056 | CCCAATGGTAAGCCCAA | e-e-k-d(10)-k-e-k-e | 73 | 1277 |
| 4540 | 4555 | 530383 | CCAATGGTAAGCCCAA | e-k-d(10)-k-e-k-e | 64 | 1276 |
| 4541 | 4556 | 518345 | CCCAATGGTAAGCCCA | e-e-e-d(10)-k-k-k | 80 | 366 |
| 4541 | 4556 | 519636 | CCCAATGGTAAGCCCA | e-k-k-d(10)-k-k-e | 90 | 366 |
| 4541 | 4556 | 530178 | CCCAATGGTAAGCCCA | e-e-k-d(10)-k-k-e | 86 | 366 |
| 4541 | 4556 | 530228 | CCCAATGGTAAGCCCA | e-d-k-d(10)-k-k-e | 77 | 366 |
| 4541 | 4556 | 530278 | CCCAATGGTAAGCCCA | e-d-d-k-d(9)-k-k-e | 86 | 366 |
| 4541 | 4556 | 530328 | CCCAATGGTAAGCCCA | e-e-e-e-d(9)-k-k-e | 80 | 366 |
| 4542 | 4557 | 528959 | ACCCAATGGTAAGCCC | e-e-e-d(10)-k-k-k | 73 | 1277 |
| 4544 | 4559 | 528960 | AAACCCAATGGTAAGC | e-e-e-d(10)-k-k-k | 43 | 1278 |
| 4545 | 4560 | 528961 | TAAACCCAATGGTAAG | e-e-e-d(10)-k-k-k | 18 | 1279 |
| 4546 | 4561 | 528962 | TTAAACCCAATGGTAA | e-e-e-d(10)-k-k-k | 13 | 1280 |
| 4547 | 4562 | 528963 | TTTAAACCCAATGGTA | e-e-e-d(10)-k-k-k | 2 | 1281 |
| 4554 | 4569 | 528964 | CCTATGATTTAAACCC | e-e-e-d(10)-k-k-k | 17 | 1282 |
| 4558 | 4573 | 528965 | GGTCCCTATGATTTAA | e-e-e-d(10)-k-k-k | 31 | 1283 |
| 4559 | 4574 | 528966 | AGGTCCCTATGATTTA | e-e-e-d(10)-k-k-k | 22 | 1284 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4615 | 4630 | 528967 | CCTAAGGCCATGAACT | e-e-e-d(10)-k-k-k | 19 | 374 |
| 4616 | 4631 | 528968 | ACCTAAGGCCATGAAC | e-e-e-d(10)-k-k-k | 25 | 1285 |
| 4617 | 4632 | 528969 | TACCTAAGGCCATGAA | e-e-e-d(10)-k-k-k | 41 | 1286 |
| 4618 | 4633 | 528970 | CTACCTAAGGCCATGA | e-e-e-d(10)-k-k-k | 55 | 1287 |
| 4619 | 4634 | 528971 | GCTACCTAAGGCCATG | e-e-e-d(10)-k-k-k | 66 | 1288 |
| 4620 | 4635 | 528972 | TGCTACCTAAGGCCAT | e-e-e-d(10)-k-k-k | 56 | 1289 |
| 4621 | 4636 | 528973 | ATGCTACCTAAGGCCA | e-e-e-d(10)-k-k-k | 71 | 1290 |
| 4622 | 4637 | 528974 | CATGCTACCTAAGGCC | e-e-e-d(10)-k-k-k | 58 | 1291 |
| 4623 | 4638 | 528975 | ACATGCTACCTAAGGC | e-e-e-d(10)-k-k-k | 34 | 1292 |
| 4636 | 4651 | 528976 | GTTAAGACCAGATACA | e-e-e-d(10)-k-k-k | 45 | 1293 |
| 4637 | 4652 | 528977 | AGTTAAGACCAGATAC | e-e-e-d(10)-k-k-k | 40 | 1294 |
| 4638 | 4653 | 528978 | GAGTTAAGACCAGATA | e-e-e-d(10)-k-k-k | 40 | 1295 |
| 4639 | 4654 | 528979 | AGAGTTAAGACCAGAT | e-e-e-d(10)-k-k-k | 62 | 1296 |
| 4644 | 4659 | 530399 | CAATCAGAGTTAAGAC | k-d(10)-k-e-k-e-e | 36 | 1297 |
| 4645 | 4661 | 530029 | TACAATCAGAGTTAAGA | e-e-k-d(10)-k-e-k-e | 29 | 1298 |
| 4645 | 4660 | 530349 | ACAATCAGAGTTAAGA | e-k-d(10)-k-e-k-e | 33 | 1299 |
| 4646 | 4661 | 528980 | TACAATCAGAGTTAAG | e-e-e-d(10)-k-k-k | 0 | 378 |
| 4646 | 4661 | 530097 | TACAATCAGAGTTAAG | e-k-k-d(10)-k-k-e | 41 | 378 |
| 4646 | 4661 | 530144 | TACAATCAGAGTTAAG | e-e-k-d(10)-k-k-e | 16 | 378 |
| 4646 | 4661 | 530194 | TACAATCAGAGTTAAG | e-d-k-d(10)-k-k-e | 28 | 378 |
| 4646 | 4661 | 530244 | TACAATCAGAGTTAAG | e-d-d-k-d(9)-k-k-e | 0 | 378 |
| 4646 | 4661 | 530294 | TACAATCAGAGTTAAG | e-e-e-e-d(9)-k-k-e | 7 | 378 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4648 | 4663 | 528981 | GCTACAATCAGAGTTA | e-e-e-d(10)-k-k-k | 52 | 1300 |
| 4649 | 4664 | 528982 | TGCTACAATCAGAGTT | e-e-e-d(10)-k-k-k | 47 | 1301 |
| 4650 | 4665 | 528983 | TTGCTACAATCAGAGT | e-e-e-d(10)-k-k-k | 44 | 1302 |
| 4662 | 4677 | 530400 | CTCTCAGAACTTTTGC | k-d(10)-k-e-k-e-e | 65 | 1303 |
| 4663 | 4679 | 530030 | TCCTCTCAGAACTTTTG | e-e-k-d(10)-k-e-k-e | 47 | 1304 |
| 4663 | 4678 | 530350 | CCTCTCAGAACTTTTG | e-k-d(10)-k-e-k-e | 54 | 1305 |
| 4664 | 4679 | 530098 | TCCTCTCAGAACTTTT | e-k-k-d(10)-k-k-e | 42 | 380 |
| 4664 | 4679 | 530145 | TCCTCTCAGAACTTTT | e-e-k-d(10)-k-k-e | 38 | 380 |
| 4664 | 4679 | 530195 | TCCTCTCAGAACTTTT | e-d-k-d(10)-k-k-e | 43 | 380 |
| 4664 | 4679 | 530245 | TCCTCTCAGAACTTTT | e-d-d-k-d(9)-k-k-e | 28 | 380 |
| 4664 | 4679 | 530295 | TCCTCTCAGAACTTTT | e-e-e-e-d(9)-k-k-e | 39 | 380 |
| 4770 | 4785 | 528984 | CCCACGGGATTCCCTC | e-e-e-d(10)-k-k-k | 39 | 1306 |
| 4771 | 4786 | 528985 | ACCCACGGGATTCCCT | e-e-e-d(10)-k-k-k | 36 | 1307 |
| 4772 | 4787 | 528986 | AACCCACGGGATTCCC | e-e-e-d(10)-k-k-k | 47 | 1308 |
| 4773 | 4788 | 528987 | CAACCCACGGGATTCC | e-e-e-d(10)-k-k-k | 39 | 1309 |
| 4774 | 4789 | 528988 | GCAACCCACGGGATTC | e-e-e-d(10)-k-k-k | 48 | 1310 |
| 4775 | 4790 | 528989 | AGCAACCCACGGGATT | e-e-e-d(10)-k-k-k | 40 | 1311 |
| 4777 | 4792 | 528990 | TAAGCAACCCACGGGA | e-e-e-d(10)-k-k-k | 27 | 1312 |
| 4778 | 4793 | 528991 | GTAAGCAACCCACGGG | e-e-e-d(10)-k-k-k | 47 | 1313 |
| 4779 | 4794 | 528992 | GGTAAGCAACCCACGG | e-e-e-d(10)-k-k-k | 42 | 1314 |
| 4780 | 4795 | 528993 | AGGTAAGCAACCCACG | e-e-e-d(10)-k-k-k | 54 | 1315 |
| 4780 | 4795 | 530434 | AGGTAAGCAACCCACG | k-d(10)-k-e-k-e-e | 51 | 1315 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4781 | 4796 | 528994 | TAGGTAAGCAACCCAC | e-e-e-d(10)-k-k-k | 53 | 1316 |
| 4781 | 4797 | 530064 | GTAGGTAAGCAACCCAC | e-e-k-d(10)-k-e-k-e | 53 | 1317 |
| 4781 | 4796 | 530384 | TAGGTAAGCAACCCAC | e-k-d(10)-k-e-k-e | 48 | 1316 |
| 4782 | 4797 | 528995 | GTAGGTAAGCAACCCA | e-e-e-d(10)-k-k-k | 64 | 388 |
| 4782 | 4797 | 530129 | GTAGGTAAGCAACCCA | e-k-k-d(10)-k-k-e | 79 | 388 |
| 4782 | 4797 | 530179 | GTAGGTAAGCAACCCA | e-e-k-d(10)-k-k-e | 74 | 388 |
| 4782 | 4797 | 530229 | GTAGGTAAGCAACCCA | e-d-k-d(10)-k-k-e | 64 | 388 |
| 4782 | 4797 | 530279 | GTAGGTAAGCAACCCA | e-d-d-k-d(9)-k-k-e | 55 | 388 |
| 4782 | 4797 | 530329 | GTAGGTAAGCAACCCA | e-e-e-e-d(9)-k-k-e | 61 | 388 |
| 4784 | 4799 | 528996 | AGGTAGGTAAGCAACC | e-e-e-d(10)-k-k-k | 21 | 1318 |
| 4788 | 4803 | 528997 | TTATAGGTAGGTAAGC | e-e-e-d(10)-k-k-k | 10 | 1319 |
| 4792 | 4807 | 528998 | CACCTTATAGGTAGGT | e-e-e-d(10)-k-k-k | 22 | 1320 |
| 4794 | 4809 | 528999 | ACCACCTTATAGGTAG | e-e-e-d(10)-k-k-k | 15 | 1321 |
| 4797 | 4812 | 529000 | TAAACCACCTTATAGG | e-e-e-d(10)-k-k-k | 0 | 1322 |
| 4798 | 4813 | 529001 | ATAAACCACCTTATAG | e-e-e-d(10)-k-k-k | 7 | 1323 |
| 4810 | 4825 | 529002 | GGACAGCAGCTTATAA | e-e-e-d(10)-k-k-k | 12 | 1324 |
| 4811 | 4826 | 529003 | AGGACAGCAGCTTATA | e-e-e-d(10)-k-k-k | 40 | 1325 |
| 4811 | 4826 | 530401 | AGGACAGCAGCTTATA | k-d(10)-k-e-k-e-e | 41 | 1325 |
| 4812 | 4827 | 529004 | CAGGACAGCAGCTTAT | e-e-e-d(10)-k-k-k | 38 | 1326 |
| 4812 | 4828 | 530031 | CCAGGACAGCAGCTTAT | e-e-k-d(10)-k-e-k-e | 58 | 1327 |
| 4812 | 4827 | 530351 | CAGGACAGCAGCTTAT | e-k-d(10)-k-e-k-e | 58 | 1326 |
| 4812 | 4827 | 530402 | CAGGACAGCAGCTTAT | k-d(10)-k-e-k-e-e | 60 | 1326 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4813 | 4829 | 530032 | GCCAGGACAGCAGCTTA | e-e-k-d(10)-k-e-k-e | 74 | 1328 |
| 4813 | 4828 | 530099 | CCAGGACAGCAGCTTA | e-k-k-d(10)-k-k-e | 73 | 1329 |
| 4813 | 4828 | 530146 | CCAGGACAGCAGCTTA | e-e-k-d(10)-k-k-e | 70 | 1329 |
| 4813 | 4828 | 530196 | CCAGGACAGCAGCTTA | e-d-k-d(10)-k-k-e | 67 | 1329 |
| 4813 | 4828 | 530246 | CCAGGACAGCAGCTTA | e-d-d-k-d(9)-k-k-e | 39 | 1329 |
| 4813 | 4828 | 530296 | CCAGGACAGCAGCTTA | e-e-e-e-d(9)-k-k-e | 67 | 1329 |
| 4813 | 4828 | 530352 | CCAGGACAGCAGCTTA | e-k-d(10)-k-e-k-e | 67 | 1329 |
| 4814 | 4829 | 530100 | GCCAGGACAGCAGCTT | e-k-k-d(10)-k-k-e | 77 | 1330 |
| 4814 | 4829 | 530147 | GCCAGGACAGCAGCTT | e-e-k-d(10)-k-k-e | 84 | 1330 |
| 4814 | 4829 | 530197 | GCCAGGACAGCAGCTT | e-d-k-d(10)-k-k-e | 71 | 1330 |
| 4814 | 4829 | 530247 | GCCAGGACAGCAGCTT | e-d-d-k-d(9)-k-k-e | 53 | 1330 |
| 4814 | 4829 | 530297 | GCCAGGACAGCAGCTT | e-e-e-e-d(9)-k-k-e | 75 | 1330 |
| 4814 | 4829 | 530403 | GCCAGGACAGCAGCTT | k-d(10)-k-e-k-e-e | 77 | 1330 |
| 4815 | 4831 | 530033 | TGGCCAGGACAGCAGCT | e-e-k-d(10)-k-e-k-e | 65 | 1331 |
| 4815 | 4830 | 530353 | GGCCAGGACAGCAGCT | e-k-d(10)-k-e-k-e | 83 | 1332 |
| 4816 | 4831 | 530101 | TGGCCAGGACAGCAGC | e-k-k-d(10)-k-k-e | 59 | 1333 |
| 4816 | 4831 | 530148 | TGGCCAGGACAGCAGC | e-e-k-d(10)-k-k-e | 79 | 1333 |
| 4816 | 4831 | 530198 | TGGCCAGGACAGCAGC | e-d-k-d(10)-k-k-e | 54 | 1333 |
| 4816 | 4831 | 530248 | TGGCCAGGACAGCAGC | e-d-d-k-d(9)-k-k-e | 32 | 1333 |
| 4816 | 4831 | 530298 | TGGCCAGGACAGCAGC | e-e-e-e-d(9)-k-k-e | 73 | 1333 |
| 4827 | 4842 | 530404 | TTTGAATGCAGTGGCC | k-d(10)-k-e-k-e-e | 67 | 1334 |
| 4828 | 4844 | 530034 | AATTTGAATGCAGTGGC | e-e-k-d(10)-k-e-k-e | 69 | 1335 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4828 | 4843 | 530354 | ATTTGAATGCAGTGGC | e-k-d(10)-k-e-k-e | 85 | 1336 |
| 4828 | 4843 | 530405 | ATTTGAATGCAGTGGC | k-d(10)-k-e-k-e-e | 55 | 1336 |
| 4829 | 4845 | 530035 | GAATTTGAATGCAGTGG | e-e-k-d(10)-k-e-k-e | 69 | 1337 |
| 4829 | 4844 | 530102 | AATTTGAATGCAGTGG | e-k-k-d(10)-k-k-e | 71 | 1338 |
| 4829 | 4844 | 530149 | AATTTGAATGCAGTGG | e-e-k-d(10)-k-k-e | 70 | 1338 |
| 4829 | 4844 | 530199 | AATTTGAATGCAGTGG | e-d-k-d(10)-k-k-e | 58 | 1338 |
| 4829 | 4844 | 530249 | AATTTGAATGCAGTGG | e-d-d-k-d(9)-k-k-e | 47 | 1338 |
| 4829 | 4844 | 530299 | AATTTGAATGCAGTGG | e-e-e-e-d(9)-k-k-e | 47 | 1338 |
| 4829 | 4844 | 530355 | AATTTGAATGCAGTGG | e-k-d(10)-k-e-k-e | 72 | 1338 |
| 4830 | 4845 | 530103 | GAATTTGAATGCAGTG | e-k-k-d(10)-k-k-e | 77 | 390 |
| 4830 | 4845 | 530150 | GAATTTGAATGCAGTG | e-e-k-d(10)-k-k-e | 73 | 390 |
| 4830 | 4845 | 530200 | GAATTTGAATGCAGTG | e-d-k-d(10)-k-k-e | 63 | 390 |
| 4830 | 4845 | 530250 | GAATTTGAATGCAGTG | e-d-d-k-d(9)-k-k-e | 59 | 390 |
| 4830 | 4845 | 530300 | GAATTTGAATGCAGTG | e-e-e-e-d(9)-k-k-e | 65 | 390 |
| 4842 | 4857 | 530435 | AAGTACACATTGGAAT | k-d(10)-k-e-k-e-e | 62 | 1339 |
| 4843 | 4859 | 530057 | TGAAGTACACATTGGAA | e-e-k-d(10)-k-e-k-e | 69 | 1340 |
| 4843 | 4858 | 530385 | GAAGTACACATTGGAA | e-k-d(10)-k-e-k-e | 70 | 1341 |
| 4844 | 4859 | 529005 | TGAAGTACACATTGGA | e-e-e-d(10)-k-k-k | 64 | 392 |
| 4844 | 4859 | 530130 | TGAAGTACACATTGGA | e-k-k-d(10)-k-k-e | 85 | 392 |
| 4844 | 4859 | 530180 | TGAAGTACACATTGGA | e-e-k-d(10)-k-k-e | 82 | 392 |
| 4844 | 4859 | 530230 | TGAAGTACACATTGGA | e-d-k-d(10)-k-k-e | 65 | 392 |
| 4844 | 4859 | 530280 | TGAAGTACACATTGGA | e-d-d-k-d(9)-k-k-e | 75 | 392 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 4844 | 4859 | 530330 | TGAAGTACACATTGGA | e-e-e-e-d(9)-k-k-e | 52 | 392 |
| 4852 | 4867 | 529006 | TTACACTATGAAGTAC | e-e-e-d(10)-k-k-k | 16 | 1342 |
| 4929 | 4944 | 529007 | AGTTAAAGTAGATACA | e-e-e-d(10)-k-k-k | 0 | 1343 |
| 4934 | 4949 | 529008 | CTGGAAGTTAAAGTAG | e-e-e-d(10)-k-k-k | 30 | 397 |
| 4943 | 4958 | 529009 | CGTTTATTTCTGGAAG | e-e-e-d(10)-k-k-k | 52 | 1344 |
| 4957 | 4972 | 529010 | CGGTTCCTATATAACG | e-e-e-d(10)-k-k-k | 21 | 1345 |
| 4958 | 4973 | 529011 | ACGGTTCCTATATAAC | e-e-e-d(10)-k-k-k | 10 | 1346 |

**Table 14**

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1359 | 1374 | 529012 | GTCATCCCGAAGAGTC | e-e-e-d(10)-k-k-k | 34 | 1347 |
| 1386 | 1401 | 529013 | CCCGAGTCCCTTCCGA | e-e-e-d(10)-k-k-k | 18 | 1348 |
| 1390 | 1405 | 529014 | GCGCCCCGAGTCCCTT | e-e-e-d(10)-k-k-k | 53 | 1349 |
| 1412 | 1427 | 529015 | CGAAGAACGAAACTTC | e-e-e-d(10)-k-k-k | 8 | 1350 |
| 1418 | 1433 | 529016 | TTTCTCCGAAGAACGA | e-e-e-d(10)-k-k-k | 31 | 1351 |
| 1461 | 1476 | 529017 | CGAGTGCGCCCTCGCC | e-e-e-d(10)-k-k-k | 52 | 1352 |
| 1548 | 1563 | 529018 | GTGACAGTCGCTCCGG | e-e-e-d(10)-k-k-k | 30 | 1353 |
| 1549 | 1564 | 529019 | CGTGACAGTCGCTCCG | e-e-e-d(10)-k-k-k | 31 | 1354 |
| 1590 | 1605 | 529020 | GCGCTTTCCGACCCCC | e-e-e-d(10)-k-k-k | 45 | 1355 |
| 1790 | 1805 | 529021 | GTACCGGTCTGTCAAT | e-e-e-d(10)-k-k-k | 23 | 1356 |
| 1794 | 1809 | 529022 | AAGAGTACCGGTCTGT | e-e-e-d(10)-k-k-k | 69 | 1357 |
| 1796 | 1811 | 529023 | GAAAGAGTACCGGTCT | e-e-e-d(10)-k-k-k | 72 | 1358 |
| 1906 | 1921 | 529024 | CTGGCTTGACGGGTTG | e-e-e-d(10)-k-k-k | 64 | 1359 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 1907 | 1922 | 529025 | GCTGGCTTGACGGGTT | e-e-e-d(10)-k-k-k | 73 | 1360 |
| 1966 | 1981 | 529026 | CCGACTTTACCAGGTA | e-e-e-d(10)-k-k-k | 78 | 1361 |
| 1968 | 1983 | 529027 | GGCCGACTTTACCAGG | e-e-e-d(10)-k-k-k | 92 | 1362 |
| 1972 | 1987 | 529028 | TTCTGGCCGACTTTAC | e-e-e-d(10)-k-k-k | 13 | 1363 |
| 2031 | 2046 | 529029 | CGTCCTATGCAATTAA | e-e-e-d(10)-k-k-k | 24 | 1364 |
| 2039 | 2054 | 529030 | GTTCATTCCGTCCTAT | e-e-e-d(10)-k-k-k | 41 | 1365 |
| 2198 | 2213 | 529031 | GACGGTTTGAATCTTG | e-e-e-d(10)-k-k-k | 40 | 1366 |
| 2201 | 2216 | 529032 | GGCGACGGTTTGAATC | e-e-e-d(10)-k-k-k | 37 | 1367 |
| 2204 | 2219 | 529033 | TTGGGCGACGGTTTGA | e-e-e-d(10)-k-k-k | 31 | 1368 |
| 2207 | 2222 | 529034 | AACTTGGGCGACGGTT | e-e-e-d(10)-k-k-k | 54 | 1369 |
| 2253 | 2268 | 529035 | CGACCTGATATGGCAC | e-e-e-d(10)-k-k-k | 56 | 1370 |
| 2255 | 2270 | 529036 | AACGACCTGATATGGC | e-e-e-d(10)-k-k-k | 52 | 1371 |
| 2257 | 2272 | 529037 | ACAACGACCTGATATG | e-e-e-d(10)-k-k-k | 24 | 1372 |
| 2338 | 2353 | 530406 | ATACAGTAAGACCAGC | k-d(10)-k-e-k-e-e | 65 | 1373 |
| 2339 | 2355 | 530036 | ACATACAGTAAGACCAG | e-e-k-d(10)-k-e-k-e | 58 | 1374 |
| 2339 | 2354 | 530356 | CATACAGTAAGACCAG | e-k-d(10)-k-e-k-e | 65 | 1375 |
| 2340 | 2355 | 530104 | ACATACAGTAAGACCA | e-k-k-d(10)-k-k-e | 67 | 1376 |
| 2340 | 2355 | 530151 | ACATACAGTAAGACCA | e-e-k-d(10)-k-k-e | 64 | 1376 |
| 2340 | 2355 | 530201 | ACATACAGTAAGACCA | e-d-k-d(10)-k-k-e | 42 | 1376 |
| 2340 | 2355 | 530251 | ACATACAGTAAGACCA | e-d-d-k-d(9)-k-k-e | 58 | 1376 |
| 2340 | 2355 | 530301 | ACATACAGTAAGACCA | e-e-e-e-d(9)-k-k-e | 56 | 1376 |
| 2383 | 2398 | 530407 | AAAATTTACAACCCAT | k-d(10)-k-e-k-e-e | 9 | 1377 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2384 | 2400 | 530037 | CAAAAATTTACAACCCA | e-e-k-d(10)-k-e-k-e | 42 | 1378 |
| 2384 | 2399 | 530357 | AAAAATTTACAACCCA | e-k-d(10)-k-e-k-e | 34 | 1379 |
| 2385 | 2400 | 530105 | CAAAAATTTACAACCC | e-k-k-d(10)-k-k-e | 40 | 1380 |
| 2385 | 2400 | 530152 | CAAAAATTTACAACCC | e-e-k-d(10)-k-k-e | 33 | 1380 |
| 2385 | 2400 | 530202 | CAAAAATTTACAACCC | e-d-k-d(10)-k-k-e | 10 | 1380 |
| 2385 | 2400 | 530252 | CAAAAATTTACAACCC | e-d-d-k-d(9)-k-k-e | 29 | 1380 |
| 2385 | 2400 | 530302 | CAAAAATTTACAACCC | e-e-e-e-d(9)-k-k-e | 14 | 1380 |
| 2408 | 2423 | 530408 | AATGCTTTATCAGCAC | k-d(10)-k-e-k-e-e | 36 | 1381 |
| 2409 | 2425 | 530038 | CCAATGCTTTATCAGCA | e-e-k-d(10)-k-e-k-e | 71 | 1382 |
| 2409 | 2424 | 530358 | CAATGCTTTATCAGCA | e-k-d(10)-k-e-k-e | 46 | 1383 |
| 2410 | 2425 | 530106 | CCAATGCTTTATCAGC | e-k-k-d(10)-k-k-e | 70 | 1384 |
| 2410 | 2425 | 530153 | CCAATGCTTTATCAGC | e-e-k-d(10)-k-k-e | 50 | 1384 |
| 2410 | 2425 | 530203 | CCAATGCTTTATCAGC | e-d-k-d(10)-k-k-e | 43 | 1384 |
| 2410 | 2425 | 530253 | CCAATGCTTTATCAGC | e-d-d-k-d(9)-k-k-e | 33 | 1384 |
| 2410 | 2425 | 530303 | CCAATGCTTTATCAGC | e-e-e-e-d(9)-k-k-e | 40 | 1384 |
| 2669 | 2684 | 530409 | ACTAAAATCAAGGCTC | k-d(10)-k-e-k-e-e | 42 | 1385 |
| 2670 | 2686 | 530039 | AGACTAAAATCAAGGCT | e-e-k-d(10)-k-e-k-e | 73 | 1386 |
| 2670 | 2685 | 530359 | GACTAAAATCAAGGCT | e-k-d(10)-k-e-k-e | 82 | 1387 |
| 2671 | 2686 | 530107 | AGACTAAAATCAAGGC | e-k-k-d(10)-k-k-e | 77 | 1388 |
| 2671 | 2686 | 530154 | AGACTAAAATCAAGGC | e-e-k-d(10)-k-k-e | 57 | 1388 |
| 2671 | 2686 | 530204 | AGACTAAAATCAAGGC | e-d-k-d(10)-k-k-e | 28 | 1388 |
| 2671 | 2686 | 530254 | AGACTAAAATCAAGGC | e-d-d-k-d(9)-k-k-e | 3 | 1388 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 2671 | 2686 | 530304 | AGACTAAAATCAAGGC | e-e-e-e-d(9)-k-k-e | 22 | 1388 |
| 2703 | 2718 | 530429 | AATGGTTCTTTGTGAT | k-d(10)-k-e-k-e-e | 60 | 1389 |
| 2704 | 2720 | 530065 | CTAATGGTTCTTTGTGA | e-e-k-d(10)-k-e-k-e | 70 | 1390 |
| 2704 | 2719 | 530379 | TAATGGTTCTTTGTGA | e-k-d(10)-k-e-k-e | 54 | 1391 |
| 2705 | 2720 | 530127 | CTAATGGTTCTTTGTG | e-k-k-d(10)-k-k-e | 80 | 411 |
| 2705 | 2720 | 530174 | CTAATGGTTCTTTGTG | e-e-k-d(10)-k-k-e | 69 | 411 |
| 2705 | 2720 | 530224 | CTAATGGTTCTTTGTG | e-d-k-d(10)-k-k-e | 32 | 411 |
| 2705 | 2720 | 530274 | CTAATGGTTCTTTGTG | e-d-d-k-d(9)-k-k-e | 38 | 411 |
| 2705 | 2720 | 530324 | CTAATGGTTCTTTGTG | e-e-e-e-d(9)-k-k-e | 32 | 411 |
| 5000 | 5015 | 530410 | CTGAAATTCCTTGGTC | k-d(10)-k-e-k-e-e | 53 | 1392 |
| 5001 | 5017 | 530040 | AACTGAAATTCCTTGGT | e-e-k-d(10)-k-e-k-e | 67 | 1393 |
| 5001 | 5016 | 530360 | ACTGAAATTCCTTGGT | e-k-d(10)-k-e-k-e | 70 | 1394 |
| 5002 | 5017 | 530108 | AACTGAAATTCCTTGG | e-k-k-d(10)-k-k-e | 70 | 1395 |
| 5002 | 5017 | 530155 | AACTGAAATTCCTTGG | e-e-k-d(10)-k-k-e | 53 | 1395 |
| 5002 | 5017 | 530205 | AACTGAAATTCCTTGG | e-d-k-d(10)-k-k-e | 44 | 1395 |
| 5002 | 5017 | 530255 | AACTGAAATTCCTTGG | e-d-d-k-d(9)-k-k-e | 33 | 1395 |
| 5002 | 5017 | 530305 | AACTGAAATTCCTTGG | e-e-e-e-d(9)-k-k-e | 22 | 1395 |
| 5699 | 5714 | 530411 | ACTCTTTCAGTGGTTT | k-d(10)-k-e-k-e-e | 91 | 1396 |
| 5700 | 5716 | 530041 | GTACTCTTTCAGTGGTT | e-e-k-d(10)-k-e-k-e | 89 | 1397 |
| 5700 | 5715 | 530361 | TACTCTTTCAGTGGTT | e-k-d(10)-k-e-k-e | 88 | 1398 |
| 5701 | 5716 | 530109 | GTACTCTTTCAGTGGT | e-k-k-d(10)-k-k-e | 89 | 1399 |
| 5701 | 5716 | 530156 | GTACTCTTTCAGTGGT | e-e-k-d(10)-k-k-e | 91 | 1399 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 5701 | 5716 | 530206 | GTACTCTTTCAGTGGT | e-d-k-d(10)-k-k-e | 89 | 1399 |
| 5701 | 5716 | 530256 | GTACTCTTTCAGTGGT | e-d-d-k-d(9)-k-k-e | 33 | 1399 |
| 5701 | 5716 | 530306 | GTACTCTTTCAGTGGT | e-e-e-e-d(9)-k-k-e | 83 | 1399 |
| 5883 | 5898 | 529038 | CTACACTTTACGCTTA | e-e-e-d(10)-k-k-k | 9 | 1400 |
| 6474 | 6489 | 530436 | AATTCATTCTTCCATA | k-d(10)-k-e-k-e-e | 49 | 1401 |
| 6475 | 6491 | 530066 | GAAATTCATTCTTCCAT | e-e-k-d(10)-k-e-k-e | 82 | 1402 |
| 6475 | 6490 | 530386 | AAATTCATTCTTCCAT | e-k-d(10)-k-e-k-e | 53 | 1403 |
| 6476 | 6491 | 530131 | GAAATTCATTCTTCCA | e-k-k-d(10)-k-k-e | 97 | 413 |
| 6476 | 6491 | 530181 | GAAATTCATTCTTCCA | e-e-k-d(10)-k-k-e | 82 | 413 |
| 6476 | 6491 | 530231 | GAAATTCATTCTTCCA | e-d-k-d(10)-k-k-e | 75 | 413 |
| 6476 | 6491 | 530281 | GAAATTCATTCTTCCA | e-d-d-k-d(9)-k-k-e | 69 | 413 |
| 6476 | 6491 | 530331 | GAAATTCATTCTTCCA | e-e-e-e-d(9)-k-k-e | 53 | 413 |
| 6846 | 6861 | 529039 | TTAAAGAGTTGCGGTA | e-e-e-d(10)-k-k-k | 31 | 1404 |
| 6847 | 6862 | 529040 | ATTAAAGAGTTGCGGT | e-e-e-d(10)-k-k-k | 34 | 1405 |
| 8078 | 8093 | 530412 | AGATTTACCTTCCTTA | k-d(10)-k-e-k-e-e | 50 | 1406 |
| 8079 | 8095 | 530042 | GCAGATTTACCTTCCTT | e-e-k-d(10)-k-e-k-e | 78 | 1407 |
| 8079 | 8094 | 530362 | CAGATTTACCTTCCTT | e-k-d(10)-k-e-k-e | 76 | 1408 |
| 8080 | 8095 | 530110 | GCAGATTTACCTTCCT | e-k-k-d(10)-k-k-e | 84 | 1409 |
| 8080 | 8095 | 530157 | GCAGATTTACCTTCCT | e-e-k-d(10)-k-k-e | 69 | 1409 |
| 8080 | 8095 | 530207 | GCAGATTTACCTTCCT | e-d-k-d(10)-k-k-e | 55 | 1409 |
| 8080 | 8095 | 530257 | GCAGATTTACCTTCCT | e-d-d-k-d(9)-k-k-e | 39 | 1409 |
| 8080 | 8095 | 530307 | GCAGATTTACCTTCCT | e-e-e-e-d(9)-k-k-e | 77 | 1409 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 9123 | 9138 | 530413 | GCCCCTATGTATAAGC | k-d(10)-k-e-k-e-e | 73 | 1410 |
| 9124 | 9140 | 530043 | CTGCCCCTATGTATAAG | e-e-k-d(10)-k-e-k-e | 42 | 1411 |
| 9124 | 9139 | 530363 | TGCCCCTATGTATAAG | e-k-d(10)-k-e-k-e | 25 | 1412 |
| 9125 | 9140 | 530111 | CTGCCCCTATGTATAA | e-k-k-d(10)-k-k-e | 35 | 1413 |
| 9125 | 9140 | 530158 | CTGCCCCTATGTATAA | e-e-k-d(10)-k-k-e | 36 | 1413 |
| 9125 | 9140 | 530208 | CTGCCCCTATGTATAA | e-d-k-d(10)-k-k-e | 14 | 1413 |
| 9125 | 9140 | 530258 | CTGCCCCTATGTATAA | e-d-d-k-d(9)-k-k-e | 5 | 1413 |
| 9125 | 9140 | 530308 | CTGCCCCTATGTATAA | e-e-e-e-d(9)-k-k-e | 25 | 1413 |
| 9862 | 9877 | 530414 | TTCTTCCTGAGACACA | k-d(10)-k-e-k-e-e | 61 | 1414 |
| 9863 | 9879 | 530044 | GCTTCTTCCTGAGACAC | e-e-k-d(10)-k-e-k-e | 78 | 1415 |
| 9863 | 9878 | 530364 | CTTCTTCCTGAGACAC | e-k-d(10)-k-e-k-e | 59 | 1416 |
| 9864 | 9879 | 530112 | GCTTCTTCCTGAGACA | e-k-k-d(10)-k-k-e | 84 | 1417 |
| 9864 | 9879 | 530159 | GCTTCTTCCTGAGACA | e-e-k-d(10)-k-k-e | 69 | 1417 |
| 9864 | 9879 | 530209 | GCTTCTTCCTGAGACA | e-d-k-d(10)-k-k-e | 54 | 1417 |
| 9864 | 9879 | 530259 | GCTTCTTCCTGAGACA | e-d-d-k-d(9)-k-k-e | 57 | 1417 |
| 9864 | 9879 | 530309 | GCTTCTTCCTGAGACA | e-e-e-e-d(9)-k-k-e | 46 | 1417 |
| 9864 | 9879 | 530415 | GCTTCTTCCTGAGACA | k-d(10)-k-e-k-e-e | 51 | 1417 |
| 9865 | 9881 | 530045 | TGGCTTCTTCCTGAGAC | e-e-k-d(10)-k-e-k-e | 73 | 1418 |
| 9865 | 9880 | 530365 | GGCTTCTTCCTGAGAC | e-k-d(10)-k-e-k-e | 78 | 1419 |
| 9866 | 9881 | 530113 | TGGCTTCTTCCTGAGA | e-k-k-d(10)-k-k-e | 60 | 1420 |
| 9866 | 9881 | 530160 | TGGCTTCTTCCTGAGA | e-e-k-d(10)-k-k-e | 54 | 1420 |
| 9866 | 9881 | 530210 | TGGCTTCTTCCTGAGA | e-d-k-d(10)-k-k-e | 28 | 1420 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 9866 | 9881 | 530260 | TGGCTTCTTCCTGAGA | e-d-d-k-d(9)-k-k-e | 0 | 1420 |
| 9866 | 9881 | 530310 | TGGCTTCTTCCTGAGA | e-e-e-e-d(9)-k-k-e | 26 | 1420 |
| 9873 | 9888 | 530416 | CTCCTGTTGGCTTCTT | k-d(10)-k-e-k-e-e | 57 | 1421 |
| 9874 | 9890 | 530046 | TCCTCCTGTTGGCTTCT | e-e-k-d(10)-k-e-k-e | 76 | 1422 |
| 9874 | 9889 | 530366 | CCTCCTGTTGGCTTCT | e-k-d(10)-k-e-k-e | 75 | 1423 |
| 9874 | 9889 | 530417 | CCTCCTGTTGGCTTCT | k-d(10)-k-e-k-e-e | 66 | 1423 |
| 9875 | 9891 | 530047 | TTCCTCCTGTTGGCTTC | e-e-k-d(10)-k-e-k-e | 75 | 1424 |
| 9875 | 9890 | 530114 | TCCTCCTGTTGGCTTC | e-k-k-d(10)-k-k-e | 80 | 1425 |
| 9875 | 9890 | 530161 | TCCTCCTGTTGGCTTC | e-e-k-d(10)-k-k-e | 81 | 1425 |
| 9875 | 9890 | 530211 | TCCTCCTGTTGGCTTC | e-d-k-d(10)-k-k-e | 73 | 1425 |
| 9875 | 9890 | 530261 | TCCTCCTGTTGGCTTC | e-d-d-k-d(9)-k-k-e | 78 | 1425 |
| 9875 | 9890 | 530311 | TCCTCCTGTTGGCTTC | e-e-e-e-d(9)-k-k-e | 82 | 1425 |
| 9875 | 9890 | 530367 | TCCTCCTGTTGGCTTC | e-k-d(10)-k-e-k-e | 80 | 1425 |
| 9876 | 9891 | 530115 | TTCCTCCTGTTGGCTT | e-k-k-d(10)-k-k-e | 74 | 1426 |
| 9876 | 9891 | 530162 | TTCCTCCTGTTGGCTT | e-e-k-d(10)-k-k-e | 68 | 1426 |
| 9876 | 9891 | 530212 | TTCCTCCTGTTGGCTT | e-d-k-d(10)-k-k-e | 58 | 1426 |
| 9876 | 9891 | 530262 | TTCCTCCTGTTGGCTT | e-d-d-k-d(9)-k-k-e | 23 | 1426 |
| 9876 | 9891 | 530312 | TTCCTCCTGTTGGCTT | e-e-e-e-d(9)-k-k-e | 52 | 1426 |
| 9876 | 9891 | 530418 | TTCCTCCTGTTGGCTT | k-d(10)-k-e-k-e-e | 59 | 1426 |
| 9877 | 9893 | 530048 | GGTTCCTCCTGTTGGCT | e-e-k-d(10)-k-e-k-e | 82 | 1427 |
| 9877 | 9892 | 530368 | GTTCCTCCTGTTGGCT | e-k-d(10)-k-e-k-e | 85 | 1428 |
| 9878 | 9893 | 530116 | GGTTCCTCCTGTTGGC | e-k-k-d(10)-k-k-e | 90 | 1429 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 9878 | 9893 | 530163 | GGTTCCTCCTGTTGGC | e-e-k-d(10)-k-k-e | 79 | 1429 |
| 9878 | 9893 | 530213 | GGTTCCTCCTGTTGGC | e-d-k-d(10)-k-k-e | 72 | 1429 |
| 9878 | 9893 | 530263 | GGTTCCTCCTGTTGGC | e-d-d-k-d(9)-k-k-e | 73 | 1429 |
| 9878 | 9893 | 530313 | GGTTCCTCCTGTTGGC | e-e-e-e-d(9)-k-k-e | 61 | 1429 |
| 9964 | 9979 | 529041 | GTAATGTGCAGCAATC | e-e-e-d(10)-k-k-k | 53 | 1430 |
| 9991 | 10006 | 530711 | ATGTGAGGGCACATTT | e-e-e-d(10)-k-k-k | 25 | 1431 |
| 10286 | 10301 | 529042 | CCAAGCCGTTTATTTC | e-e-e-d(10)-k-k-k | 44 | 1432 |
| 10291 | 10306 | 529043 | GGAAGCCAAGCCGTTT | e-e-e-d(10)-k-k-k | 39 | 1433 |
| 11261 | 11276 | 530413 | GCCCCTATGTATAAGC | k-d(10)-k-e-k-e-e | 73 | 1410 |
| 11262 | 11278 | 530043 | CTGCCCCTATGTATAAG | e-e-k-d(10)-k-e-k-e | 42 | 1411 |
| 11262 | 11277 | 530363 | TGCCCCTATGTATAAG | e-k-d(10)-k-e-k-e | 25 | 1412 |
| 11263 | 11278 | 530111 | CTGCCCCTATGTATAA | e-k-k-d(10)-k-k-e | 35 | 1413 |
| 11263 | 11278 | 530158 | CTGCCCCTATGTATAA | e-e-k-d(10)-k-k-e | 36 | 1413 |
| 11263 | 11278 | 530208 | CTGCCCCTATGTATAA | e-d-k-d(10)-k-k-e | 14 | 1413 |
| 11263 | 11278 | 530258 | CTGCCCCTATGTATAA | e-d-d-k-d(9)-k-k-e | 5 | 1413 |
| 11263 | 11278 | 530308 | CTGCCCCTATGTATAA | e-e-e-e-d(9)-k-k-e | 25 | 1413 |
| 12345 | 12360 | 530414 | TTCTTCCTGAGACACA | k-d(10)-k-e-k-e-e | 61 | 1414 |
| 12346 | 12362 | 530044 | GCTTCTTCCTGAGACAC | e-e-k-d(10)-k-e-k-e | 78 | 1415 |
| 12346 | 12361 | 530364 | CTTCTTCCTGAGACAC | e-k-d(10)-k-e-k-e | 59 | 1416 |
| 12347 | 12362 | 530112 | GCTTCTTCCTGAGACA | e-k-k-d(10)-k-k-e | 84 | 1417 |
| 12347 | 12362 | 530159 | GCTTCTTCCTGAGACA | e-e-k-d(10)-k-k-e | 69 | 1417 |
| 12347 | 12362 | 530209 | GCTTCTTCCTGAGACA | e-d-k-d(10)-k-k-e | 54 | 1417 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 12347 | 12362 | 530259 | GCTTCTTCCTGAGACA | e-d-d-k-d(9)-k-k-e | 57 | 1417 |
| 12347 | 12362 | 530309 | GCTTCTTCCTGAGACA | e-e-e-e-d(9)-k-k-e | 46 | 1417 |
| 12347 | 12362 | 530415 | GCTTCTTCCTGAGACA | k-d(10)-k-e-k-e-e | 51 | 1417 |
| 12348 | 12364 | 530045 | TGGCTTCTTCCTGAGAC | e-e-k-d(10)-k-e-k-e | 73 | 1418 |
| 12348 | 12363 | 530365 | GGCTTCTTCCTGAGAC | e-k-d(10)-k-e-k-e | 78 | 1419 |
| 12349 | 12364 | 530113 | TGGCTTCTTCCTGAGA | e-k-k-d(10)-k-k-e | 60 | 1420 |
| 12349 | 12364 | 530160 | TGGCTTCTTCCTGAGA | e-e-k-d(10)-k-k-e | 54 | 1420 |
| 12349 | 12364 | 530210 | TGGCTTCTTCCTGAGA | e-d-k-d(10)-k-k-e | 28 | 1420 |
| 12349 | 12364 | 530260 | TGGCTTCTTCCTGAGA | e-d-d-k-d(9)-k-k-e | 0 | 1420 |
| 12349 | 12364 | 530310 | TGGCTTCTTCCTGAGA | e-e-e-e-d(9)-k-k-e | 26 | 1420 |
| 12356 | 12371 | 530416 | CTCCTGTTGGCTTCTT | k-d(10)-k-e-k-e-e | 57 | 1421 |
| 12357 | 12373 | 530046 | TCCTCCTGTTGGCTTCT | e-e-k-d(10)-k-e-k-e | 76 | 1422 |
| 12357 | 12372 | 530366 | CCTCCTGTTGGCTTCT | e-k-d(10)-k-e-k-e | 75 | 1423 |
| 12357 | 12372 | 530417 | CCTCCTGTTGGCTTCT | k-d(10)-k-e-k-e-e | 66 | 1423 |
| 12358 | 12374 | 530047 | TTCCTCCTGTTGGCTTC | e-e-k-d(10)-k-e-k-e | 75 | 1424 |
| 12358 | 12373 | 530114 | TCCTCCTGTTGGCTTC | e-k-k-d(10)-k-k-e | 80 | 1425 |
| 12358 | 12373 | 530161 | TCCTCCTGTTGGCTTC | e-e-k-d(10)-k-k-e | 81 | 1425 |
| 12358 | 12373 | 530211 | TCCTCCTGTTGGCTTC | e-d-k-d(10)-k-k-e | 73 | 1425 |
| 12358 | 12373 | 530261 | TCCTCCTGTTGGCTTC | e-d-d-k-d(9)-k-k-e | 78 | 1425 |
| 12358 | 12373 | 530311 | TCCTCCTGTTGGCTTC | e-e-e-e-d(9)-k-k-e | 82 | 1425 |
| 12358 | 12373 | 530367 | TCCTCCTGTTGGCTTC | e-k-d(10)-k-e-k-e | 80 | 1425 |
| 12359 | 12374 | 530115 | TTCCTCCTGTTGGCTT | e-k-k-d(10)-k-k-e | 74 | 1426 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 12359 | 12374 | 530162 | TTCCTCCTGTTGGCTT | e-e-k-d(10)-k-k-e | 68 | 1426 |
| 12359 | 12374 | 530212 | TTCCTCCTGTTGGCTT | e-d-k-d(10)-k-k-e | 58 | 1426 |
| 12359 | 12374 | 530262 | TTCCTCCTGTTGGCTT | e-d-d-k-d(9)-k-k-e | 23 | 1426 |
| 12359 | 12374 | 530312 | TTCCTCCTGTTGGCTT | e-e-e-e-d(9)-k-k-e | 52 | 1426 |
| 12359 | 12374 | 530418 | TTCCTCCTGTTGGCTT | k-d(10)-k-e-k-e-e | 59 | 1426 |
| 12360 | 12376 | 530048 | GGTTCCTCCTGTTGGCT | e-e-k-d(10)-k-e-k-e | 82 | 1427 |
| 12360 | 12375 | 530368 | GTTCCTCCTGTTGGCT | e-k-d(10)-k-e-k-e | 85 | 1428 |
| 12361 | 12376 | 530116 | GGTTCCTCCTGTTGGC | e-k-k-d(10)-k-k-e | 90 | 1429 |
| 12361 | 12376 | 530163 | GGTTCCTCCTGTTGGC | e-e-k-d(10)-k-k-e | 79 | 1429 |
| 12361 | 12376 | 530213 | GGTTCCTCCTGTTGGC | e-d-k-d(10)-k-k-e | 72 | 1429 |
| 12361 | 12376 | 530263 | GGTTCCTCCTGTTGGC | e-d-d-k-d(9)-k-k-e | 73 | 1429 |
| 12361 | 12376 | 530313 | GGTTCCTCCTGTTGGC | e-e-e-e-d(9)-k-k-e | 61 | 1429 |
| 12586 | 12601 | 530710 | TACAATTCCTGCCTGT | e-e-e-d(10)-k-k-k | 18 | 1434 |
| 15467 | 15482 | 530437 | AGCTTTTCTATGAAAA | k-d(10)-k-e-k-e-e | 5 | 1435 |
| 15468 | 15484 | 530067 | CAAGCTTTTCTATGAAA | e-e-k-d(10)-k-e-k-e | 53 | 1436 |
| 15468 | 15483 | 530387 | AAGCTTTTCTATGAAA | e-k-d(10)-k-e-k-e | 24 | 1437 |
| 15469 | 15484 | 530132 | CAAGCTTTTCTATGAA | e-k-k-d(10)-k-k-e | 74 | 423 |
| 15469 | 15484 | 530182 | CAAGCTTTTCTATGAA | e-e-k-d(10)-k-k-e | 48 | 423 |
| 15469 | 15484 | 530232 | CAAGCTTTTCTATGAA | e-d-k-d(10)-k-k-e | 21 | 423 |
| 15469 | 15484 | 530282 | CAAGCTTTTCTATGAA | e-d-d-k-d(9)-k-k-e | 19 | 423 |
| 15469 | 15484 | 530332 | CAAGCTTTTCTATGAA | e-e-e-e-d(9)-k-k-e | 20 | 423 |
| 16863 | 16878 | 530419 | TAATTGTGTACTGGCA | k-d(10)-k-e-k-e-e | 75 | 1438 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 16864 | 16880 | 530049 | TATAATTGTGTACTGGC | e-e-k-d(10)-k-e-k-e | 88 | 1439 |
| 16864 | 16879 | 530369 | ATAATTGTGTACTGGC | e-k-d(10)-k-e-k-e | 92 | 1440 |
| 16865 | 16880 | 530117 | TATAATTGTGTACTGG | e-k-k-d(10)-k-k-e | 73 | 1441 |
| 16865 | 16880 | 530164 | TATAATTGTGTACTGG | e-e-k-d(10)-k-k-e | 65 | 1441 |
| 16865 | 16880 | 530214 | TATAATTGTGTACTGG | e-d-k-d(10)-k-k-e | 37 | 1441 |
| 16865 | 16880 | 530264 | TATAATTGTGTACTGG | e-d-d-k-d(9)-k-k-e | 48 | 1441 |
| 16865 | 16880 | 530314 | TATAATTGTGTACTGG | e-e-e-e-d(9)-k-k-e | 42 | 1441 |
| 17385 | 17400 | 530709 | TGGAGTAACAGGAACT | e-e-e-d(10)-k-k-k | 25 | 1442 |
| 21456 | 21471 | 530720 | AAAGTTTCCCAATAGA | e-e-e-d(10)-k-k-k | 17 | 1443 |
| 22061 | 22076 | 529044 | AGTCCTACCACGGCCC | e-e-e-d(10)-k-k-k | 27 | 1444 |
| 24514 | 24529 | 529045 | TGACGATGCTTGGATA | e-e-e-d(10)-k-k-k | 37 | 1445 |
| 24515 | 24530 | 529046 | CTGACGATGCTTGGAT | e-e-e-d(10)-k-k-k | 8 | 1446 |
| 24579 | 24594 | 529047 | TCACTTTCCCTATACG | e-e-e-d(10)-k-k-k | 18 | 1447 |
| 25105 | 25120 | 530717 | GTAGGTTGAGCAAGCA | e-e-e-d(10)-k-k-k | 77 | 1448 |
| 26061 | 26076 | 530420 | ACTTTAGCCCCTTCCA | k-d(10)-k-e-k-e-e | 44 | 1449 |
| 26062 | 26078 | 530050 | CAACTTTAGCCCCTTCC | e-e-k-d(10)-k-e-k-e | 64 | 1450 |
| 26062 | 26077 | 530370 | AACTTTAGCCCCTTCC | e-k-d(10)-k-e-k-e | 55 | 1451 |
| 26063 | 26078 | 530118 | CAACTTTAGCCCCTTC | e-k-k-d(10)-k-k-e | 58 | 1452 |
| 26063 | 26078 | 530165 | CAACTTTAGCCCCTTC | e-e-k-d(10)-k-k-e | 38 | 1452 |
| 26063 | 26078 | 530215 | CAACTTTAGCCCCTTC | e-d-k-d(10)-k-k-e | 29 | 1452 |
| 26063 | 26078 | 530265 | CAACTTTAGCCCCTTC | e-d-d-k-d(9)-k-k-e | 3 | 1452 |
| 26063 | 26078 | 530315 | CAACTTTAGCCCCTTC | e-e-e-e-d(9)-k-k-e | 30 | 1452 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 26767 | 26782 | 529048 | AATTCATCGAGCTAAT | e-e-e-d(10)-k-k-k | 0 | 1453 |
| 37758 | 37773 | 529049 | TGCCCCAATTAGGCCA | e-e-e-d(10)-k-k-k | 32 | 1454 |
| 37759 | 37774 | 529050 | TTGCCCCAATTAGGCC | e-e-e-d(10)-k-k-k | 21 | 1455 |
| 41484 | 41499 | 530714 | CCCTGTGGCTCCTTCC | e-e-e-d(10)-k-k-k | 27 | 1456 |
| 41760 | 41775 | 529051 | TACTGTCCTCGAGACA | e-e-e-d(10)-k-k-k | 2 | 1457 |
| 42754 | 42769 | 530719 | AGGAAAAGGAAGAATG | e-e-e-d(10)-k-k-k | 2 | 1458 |
| 42766 | 42781 | 529052 | CGCATATGCCCTAGGA | e-e-e-d(10)-k-k-k | 7 | 1459 |
| 42768 | 42783 | 529053 | GCCGCATATGCCCTAG | e-e-e-d(10)-k-k-k | 41 | 1460 |
| 42769 | 42784 | 529054 | GGCCGCATATGCCCTA | e-e-e-d(10)-k-k-k | 51 | 1461 |
| 43072 | 43087 | 529055 | CGGGTAAGTATACAGA | e-e-e-d(10)-k-k-k | 18 | 1462 |
| 43074 | 43089 | 529056 | CACGGGTAAGTATACA | e-e-e-d(10)-k-k-k | 4 | 1463 |
| 43075 | 43090 | 529057 | TCACGGGTAAGTATAC | e-e-e-d(10)-k-k-k | 5 | 1464 |
| 43077 | 43092 | 529058 | GCTCACGGGTAAGTAT | e-e-e-d(10)-k-k-k | 15 | 1465 |
| 45633 | 45648 | 529059 | GTATACAATGGCCTTT | e-e-e-d(10)-k-k-k | 59 | 1466 |
| 46633 | 46648 | 529060 | CGACCCAATCAGATGC | e-e-e-d(10)-k-k-k | 34 | 1467 |
| 47430 | 47445 | 530708 | GGATAAAATACAAAGG | e-e-e-d(10)-k-k-k | 14 | 1468 |
| 47617 | 47632 | 529061 | GTTCCGAAAAAACCTC | e-e-e-d(10)-k-k-k | 59 | 1469 |
| 47619 | 47634 | 529062 | GGGTTCCGAAAAAACC | e-e-e-d(10)-k-k-k | 16 | 1470 |
| 47752 | 47767 | 530712 | TGCAAACTTTTTCTCT | e-e-e-d(10)-k-k-k | 21 | 1471 |
| 48092 | 48107 | 529063 | ACCCGCTATCCACTCA | e-e-e-d(10)-k-k-k | 20 | 1472 |
| 48402 | 48417 | 530421 | CACTTTCCATTCTAGT | k-d(10)-k-e-k-e-e | 20 | 1473 |
| 48403 | 48419 | 530051 | CACACTTTCCATTCTAG | e-e-k-d(10)-k-e-k-e | 48 | 1474 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 48403 | 48418 | 530371 | ACACTTTCCATTCTAG | e-k-d(10)-k-e-k-e | 36 | 1475 |
| 48404 | 48419 | 530119 | CACACTTTCCATTCTA | e-k-k-d(10)-k-k-e | 47 | 1476 |
| 48404 | 48419 | 530166 | CACACTTTCCATTCTA | e-e-k-d(10)-k-k-e | 53 | 1476 |
| 48404 | 48419 | 530216 | CACACTTTCCATTCTA | e-d-k-d(10)-k-k-e | 34 | 1476 |
| 48404 | 48419 | 530266 | CACACTTTCCATTCTA | e-d-d-k-d(9)-k-k-e | 31 | 1476 |
| 48404 | 48419 | 530316 | CACACTTTCCATTCTA | e-e-e-e-d(9)-k-k-e | 34 | 1476 |
| 48429 | 48444 | 529064 | AGCCCCTATGGTTACC | e-e-e-d(10)-k-k-k | 32 | 1477 |
| 48567 | 48582 | 529065 | GTCTAGAGGCCTATCC | e-e-e-d(10)-k-k-k | 14 | 1478 |
| 48568 | 48583 | 529066 | GGTCTAGAGGCCTATC | e-e-e-d(10)-k-k-k | 17 | 1479 |
| 49762 | 49777 | 530718 | AGATGTTGGATGTCTA | e-e-e-d(10)-k-k-k | 46 | 1480 |
| 50692 | 50707 | 530423 | AGATTCTCTACCACTT | k-d(10)-k-e-k-e-e | 70 | 1054 |
| 50693 | 50709 | 530053 | GGAGATTCTCTACCACT | e-e-k-d(10)-k-e-k-e | 84 | 1055 |
| 50693 | 50708 | 530373 | GAGATTCTCTACCACT | e-k-d(10)-k-e-k-e | 85 | 1056 |
| 50694 | 50709 | 530121 | GGAGATTCTCTACCAC | e-k-k-d(10)-k-k-e | 77 | 53 |
| 50694 | 50709 | 530168 | GGAGATTCTCTACCAC | e-e-k-d(10)-k-k-e | 75 | 53 |
| 50694 | 50709 | 530218 | GGAGATTCTCTACCAC | e-d-k-d(10)-k-k-e | 61 | 53 |
| 50694 | 50709 | 530268 | GGAGATTCTCTACCAC | e-d-d-k-d(9)-k-k-e | 76 | 53 |
| 50694 | 50709 | 530318 | GGAGATTCTCTACCAC | e-e-e-e-d(9)-k-k-e | 73 | 53 |
| 50838 | 50853 | 529067 | CCGCCTTAAGATCTAA | e-e-e-d(10)-k-k-k | 5 | 1481 |
| 51714 | 51729 | 529068 | CCCTTACTCTCCGCAT | e-e-e-d(10)-k-k-k | 15 | 1482 |
| 51734 | 51749 | 529069 | GGGAAGTGGTCCGACC | e-e-e-d(10)-k-k-k | 22 | 1483 |
| 51757 | 51772 | 529070 | CCGCAAGTGAGCGAGA | e-e-e-d(10)-k-k-k | 6 | 1484 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 51760 | 51775 | 529071 | ATCCCGCAAGTGAGCG | e-e-e-d(10)-k-k-k | 11 | 1485 |
| 51763 | 51778 | 529072 | GAAATCCCGCAAGTGA | e-e-e-d(10)-k-k-k | 0 | 1486 |
| 51905 | 51920 | 528400 | CCGCCAGCTCACTCAC | e-e-e-d(10)-k-k-k | 57 | 66 |
| 51906 | 51921 | 528401 | CCCGCCAGCTCACTCA | e-e-e-d(10)-k-k-k | 57 | 1059 |
| 51907 | 51922 | 528402 | CCCCGCCAGCTCACTC | e-e-e-d(10)-k-k-k | 42 | 1060 |
| 51910 | 51925 | 528403 | AAGCCCCGCCAGCTCA | e-e-e-d(10)-k-k-k | 72 | 1060 |
| 51911 | 51926 | 528404 | AAAGCCCCGCCAGCTC | e-e-e-d(10)-k-k-k | 52 | 1062 |
| 51912 | 51927 | 528405 | AAAAGCCCCGCCAGCT | e-e-e-d(10)-k-k-k | 27 | 1063 |
| 51913 | 51928 | 528406 | CAAAAGCCCCGCCAGC | e-e-e-d(10)-k-k-k | 29 | 1064 |
| 51914 | 51929 | 528407 | ACAAAAGCCCCGCCAG | e-e-e-d(10)-k-k-k | 9 | 1065 |
| 51916 | 51931 | 528408 | TGACAAAAGCCCCGCC | e-e-e-d(10)-k-k-k | 10 | 1066 |
| 51917 | 51932 | 528409 | CTGACAAAAGCCCCGC | e-e-e-d(10)-k-k-k | 31 | 1067 |
| 51918 | 51933 | 528410 | GCTGACAAAAGCCCCG | e-e-e-d(10)-k-k-k | 39 | 1068 |
| 51919 | 51934 | 528411 | CGCTGACAAAAGCCCC | e-e-e-d(10)-k-k-k | 49 | 1069 |
| 51920 | 51935 | 528412 | TCGCTGACAAAAGCCC | e-e-e-d(10)-k-k-k | 39 | 1070 |
| 51921 | 51936 | 528413 | ATCGCTGACAAAAGCC | e-e-e-d(10)-k-k-k | 20 | 1071 |
| 51922 | 51937 | 528414 | CATCGCTGACAAAAGC | e-e-e-d(10)-k-k-k | 10 | 1072 |
| 51924 | 51939 | 528415 | TCCATCGCTGACAAAA | e-e-e-d(10)-k-k-k | 11 | 1073 |
| 51925 | 51940 | 528416 | CTCCATCGCTGACAAA | e-e-e-d(10)-k-k-k | 15 | 1074 |
| 51926 | 51941 | 528417 | ACTCCATCGCTGACAA | e-e-e-d(10)-k-k-k | 22 | 1075 |
| 51927 | 51942 | 528418 | TACTCCATCGCTGACA | e-e-e-d(10)-k-k-k | 19 | 1076 |
| 51928 | 51943 | 528419 | GTACTCCATCGCTGAC | e-e-e-d(10)-k-k-k | 37 | 1077 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 51929 | 51944 | 528420 | CGTACTCCATCGCTGA | e-e-e-d(10)-k-k-k | 35 | 1078 |
| 51943 | 51958 | 528421 | GAGAGTTTTCTGCACG | e-e-e-d(10)-k-k-k | 36 | 1079 |
| 51945 | 51960 | 528422 | GTGAGAGTTTTCTGCA | e-e-e-d(10)-k-k-k | 22 | 1080 |
| 51964 | 51979 | 528423 | GTCAGCCAGCTCCTCG | e-e-e-d(10)-k-k-k | 49 | 1081 |
| 51975 | 51990 | 528424 | CGCCTCTTCCAGTCAG | e-e-e-d(10)-k-k-k | 42 | 1082 |
| 51977 | 51992 | 528425 | GCCGCCTCTTCCAGTC | e-e-e-d(10)-k-k-k | 44 | 1083 |
| 51978 | 51993 | 528426 | TGCCGCCTCTTCCAGT | e-e-e-d(10)-k-k-k | 15 | 1084 |
| 51983 | 51998 | 528427 | TCTGTTGCCGCCTCTT | e-e-e-d(10)-k-k-k | 9 | 1085 |
| 51984 | 51999 | 528428 | ATCTGTTGCCGCCTCT | e-e-e-d(10)-k-k-k | 30 | 1086 |
| 51985 | 52000 | 528429 | AATCTGTTGCCGCCTC | e-e-e-d(10)-k-k-k | 23 | 1087 |
| 51986 | 52001 | 528430 | CAATCTGTTGCCGCCT | e-e-e-d(10)-k-k-k | 12 | 1088 |
| 51987 | 52002 | 528431 | GCAATCTGTTGCCGCC | e-e-e-d(10)-k-k-k | 48 | 1089 |
| 51988 | 52003 | 528432 | GGCAATCTGTTGCCGC | e-e-e-d(10)-k-k-k | 18 | 1090 |
| 51989 | 52004 | 528433 | AGGCAATCTGTTGCCG | e-e-e-d(10)-k-k-k | 0 | 1091 |
| 51990 | 52005 | 528434 | CAGGCAATCTGTTGCC | e-e-e-d(10)-k-k-k | 8 | 1092 |
| 51991 | 52006 | 528435 | GCAGGCAATCTGTTGC | e-e-e-d(10)-k-k-k | 13 | 1093 |
| 51995 | 52010 | 528436 | CAATGCAGGCAATCTG | e-e-e-d(10)-k-k-k | 9 | 1094 |
| 51996 | 52011 | 528437 | CCAATGCAGGCAATCT | e-e-e-d(10)-k-k-k | 26 | 1095 |
| 51997 | 52012 | 528438 | TCCAATGCAGGCAATC | e-e-e-d(10)-k-k-k | 10 | 1096 |
| 51998 | 52013 | 528439 | CTCCAATGCAGGCAAT | e-e-e-d(10)-k-k-k | 2 | 1097 |
| 51999 | 52014 | 528440 | CCTCCAATGCAGGCAA | e-e-e-d(10)-k-k-k | 28 | 1098 |
| 52016 | 52031 | 528441 | GGCAGATGTTGGGCGG | e-e-e-d(10)-k-k-k | 8 | 1099 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 52017 | 52032 | 528442 | AGGCAGATGTTGGGCG | e-e-e-d(10)-k-k-k | 0 | 1100 |
| 52018 | 52033 | 528443 | TAGGCAGATGTTGGGC | e-e-e-d(10)-k-k-k | 1 | 1101 |
| 52019 | 52034 | 528444 | CTAGGCAGATGTTGGG | e-e-e-d(10)-k-k-k | 0 | 1102 |
| 52020 | 52035 | 528445 | TCTAGGCAGATGTTGG | e-e-e-d(10)-k-k-k | 7 | 1103 |
| 52021 | 52036 | 528446 | ATCTAGGCAGATGTTG | e-e-e-d(10)-k-k-k | 3 | 1104 |
| 52023 | 52038 | 528447 | CGATCTAGGCAGATGT | e-e-e-d(10)-k-k-k | 9 | 72 |
| 52024 | 52039 | 528448 | CCGATCTAGGCAGATG | e-e-e-d(10)-k-k-k | 13 | 1105 |
| 52026 | 52041 | 528449 | AGCCGATCTAGGCAGA | e-e-e-d(10)-k-k-k | 4 | 1106 |
| 52027 | 52042 | 528450 | TAGCCGATCTAGGCAG | e-e-e-d(10)-k-k-k | 11 | 1107 |
| 52028 | 52043 | 528451 | CTAGCCGATCTAGGCA | e-e-e-d(10)-k-k-k | 5 | 1108 |
| 52029 | 52044 | 528452 | TCTAGCCGATCTAGGC | e-e-e-d(10)-k-k-k | 5 | 1109 |
| 52030 | 52045 | 528453 | TTCTAGCCGATCTAGG | e-e-e-d(10)-k-k-k | 24 | 1110 |
| 52031 | 52046 | 528454 | TTTCTAGCCGATCTAG | e-e-e-d(10)-k-k-k | 29 | 1111 |
| 52032 | 52047 | 528455 | TTTTCTAGCCGATCTA | e-e-e-d(10)-k-k-k | 28 | 1112 |
| 52033 | 52048 | 528456 | GTTTTCTAGCCGATCT | e-e-e-d(10)-k-k-k | 42 | 1113 |
| 52035 | 52050 | 528457 | CAGTTTTCTAGCCGAT | e-e-e-d(10)-k-k-k | 50 | 1114 |
| 52036 | 52051 | 528458 | CCAGTTTTCTAGCCGA | e-e-e-d(10)-k-k-k | 70 | 1115 |
| 52083 | 52098 | 529073 | TCAATCTAGCTTTCGA | e-e-e-d(10)-k-k-k | 33 | 1487 |
| 52084 | 52099 | 529074 | TTCAATCTAGCTTTCG | e-e-e-d(10)-k-k-k | 36 | 1488 |
| 52119 | 52134 | 529075 | GTACCAATTCTGTGGG | e-e-e-d(10)-k-k-k | 33 | 1489 |
| 55441 | 55456 | 528462 | GATTCTGCTAATGACG | e-e-e-d(10)-k-k-k | 42 | 1119 |
| 55442 | 55457 | 528463 | AGATTCTGCTAATGAC | e-e-e-d(10)-k-k-k | 38 | 1120 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 55446 | 55461 | 528464 | GTTGAGATTCTGCTAA | e-e-e-d(10)-k-k-k | 30 | 1121 |
| 55447 | 55462 | 528465 | AGTTGAGATTCTGCTA | e-e-e-d(10)-k-k-k | 48 | 1122 |
| 55454 | 55469 | 528466 | GGTCTGAAGTTGAGAT | e-e-e-d(10)-k-k-k | 27 | 1123 |
| 55456 | 55471 | 528467 | CGGGTCTGAAGTTGAG | e-e-e-d(10)-k-k-k | 44 | 1124 |
| 55457 | 55472 | 528468 | ACGGGTCTGAAGTTGA | e-e-e-d(10)-k-k-k | 41 | 1125 |
| 55458 | 55473 | 528469 | GACGGGTCTGAAGTTG | e-e-e-d(10)-k-k-k | 45 | 1126 |
| 55459 | 55474 | 528470 | TGACGGGTCTGAAGTT | e-e-e-d(10)-k-k-k | 34 | 1127 |
| 55460 | 55475 | 528471 | TTGACGGGTCTGAAGT | e-e-e-d(10)-k-k-k | 19 | 1128 |
| 55461 | 55476 | 528472 | GTTGACGGGTCTGAAG | e-e-e-d(10)-k-k-k | 21 | 1129 |
| 55462 | 55477 | 528473 | TGTTGACGGGTCTGAA | e-e-e-d(10)-k-k-k | 37 | 1130 |
| 55463 | 55478 | 528474 | TTGTTGACGGGTCTGA | e-e-e-d(10)-k-k-k | 55 | 1131 |
| 55464 | 55479 | 528475 | TTTGTTGACGGGTCTG | e-e-e-d(10)-k-k-k | 63 | 1132 |
| 55465 | 55480 | 528476 | ATTTGTTGACGGGTCT | e-e-e-d(10)-k-k-k | 65 | 1133 |
| 56208 | 56223 | 529076 | GTAACACCTCACCCTA | e-e-e-d(10)-k-k-k | 14 | 1490 |
| 58396 | 58411 | 530715 | TCTGCCACCCAGGTTT | e-e-e-d(10)-k-k-k | 31 | 1491 |
| 59836 | 59851 | 529077 | TAAATTTCCGGGATCT | e-e-e-d(10)-k-k-k | 13 | 1492 |
| 64187 | 64202 | 529078 | CCGGTCCCTTGTAAAA | e-e-e-d(10)-k-k-k | 12 | 1493 |
| 64289 | 64304 | 529079 | GCCAACTCTAGGCGAG | e-e-e-d(10)-k-k-k | 16 | 1494 |
| 64551 | 64566 | 529080 | CGCAAGAGATCCCGGG | e-e-e-d(10)-k-k-k | 0 | 1495 |
| 64552 | 64567 | 529081 | TCGCAAGAGATCCCGG | e-e-e-d(10)-k-k-k | 16 | 1496 |
| 64959 | 64974 | 529082 | TGATCACCTCGACTGA | e-e-e-d(10)-k-k-k | 20 | 1497 |
| 66136 | 66151 | 530425 | GCCCTTGCCAGCCATG | k-d(10)-k-e-k-e-e | 73 | 1134 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 66137 | 66153 | 530054 | AAGCCCTTGCCAGCCAT | e-e-k-d(10)-k-e-k-e | 75 | 1135 |
| 66137 | 66152 | 530375 | AGCCCTTGCCAGCCAT | e-k-d(10)-k-e-k-e | 77 | 1136 |
| 66138 | 66153 | 530123 | AAGCCCTTGCCAGCCA | e-k-k-d(10)-k-k-e | 86 | 144 |
| 66138 | 66153 | 530170 | AAGCCCTTGCCAGCCA | e-e-k-d(10)-k-k-e | 87 | 144 |
| 66138 | 66153 | 530220 | AAGCCCTTGCCAGCCA | e-d-k-d(10)-k-k-e | 74 | 144 |
| 66138 | 66153 | 530270 | AAGCCCTTGCCAGCCA | e-d-d-k-d(9)-k-k-e | 87 | 144 |
| 66138 | 66153 | 530320 | AAGCCCTTGCCAGCCA | e-e-e-e-d(9)-k-k-e | 83 | 144 |
| 66183 | 66198 | 530426 | TTTTTCACAAGGTCAA | k-d(10)-k-e-k-e-e | 55 | 1137 |
| 66184 | 66200 | 530059 | ACTTTTTCACAAGGTCA | e-e-k-d(10)-k-e-k-e | 73 | 1138 |
| 66184 | 66199 | 530376 | CTTTTTCACAAGGTCA | e-k-d(10)-k-e-k-e | 77 | 1139 |
| 66185 | 66200 | 530124 | ACTTTTTCACAAGGTC | e-k-k-d(10)-k-k-e | 79 | 153 |
| 66185 | 66200 | 530171 | ACTTTTTCACAAGGTC | e-e-k-d(10)-k-k-e | 69 | 153 |
| 66185 | 66200 | 530221 | ACTTTTTCACAAGGTC | e-d-k-d(10)-k-k-e | 64 | 153 |
| 66185 | 66200 | 530271 | ACTTTTTCACAAGGTC | e-d-d-k-d(9)-k-k-e | 73 | 153 |
| 66185 | 66200 | 530321 | ACTTTTTCACAAGGTC | e-e-e-e-d(9)-k-k-e | 56 | 153 |
| 66875 | 66890 | 529083 | GCCACCCTAGTGTTGA | e-e-e-d(10)-k-k-k | 27 | 1498 |
| 67066 | 67081 | 530427 | ATGATCTTATAGCCCA | k-d(10)-k-e-k-e-e | 43 | 931 |
| 67067 | 67083 | 530060 | CCATGATCTTATAGCCC | e-e-k-d(10)-k-e-k-e | 77 | 1140 |
| 67067 | 67082 | 530377 | CATGATCTTATAGCCC | e-k-d(10)-k-e-k-e | 66 | 932 |
| 67068 | 67083 | 530125 | CCATGATCTTATAGCC | e-k-k-d(10)-k-k-e | 65 | 175 |
| 67068 | 67083 | 530172 | CCATGATCTTATAGCC | e-e-k-d(10)-k-k-e | 59 | 175 |
| 67068 | 67083 | 530222 | CCATGATCTTATAGCC | e-d-k-d(10)-k-k-e | 48 | 175 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 67068 | 67083 | 530272 | CCATGATCTTATAGCC | e-d-d-k-d(9)-k-k-e | 63 | 175 |
| 67068 | 67083 | 530322 | CCATGATCTTATAGCC | e-e-e-e-d(9)-k-k-e | 45 | 175 |
| 67270 | 67285 | 530716 | TTTGCCTATCTATCCT | e-e-e-d(10)-k-k-k | 11 | 1499 |
| 67346 | 67361 | 529084 | CGGTCACCCCAACAAA | e-e-e-d(10)-k-k-k | 33 | 1500 |
| 69470 | 69485 | 529085 | AAGGGCGATGGTAATG | e-e-e-d(10)-k-k-k | 4 | 1501 |
| 71614 | 71629 | 530422 | GTACAATTGCTTCAAC | k-d(10)-k-e-k-e-e | 46 | 1502 |
| 71615 | 71631 | 530052 | CAGTACAATTGCTTCAA | e-e-k-d(10)-k-e-k-e | 51 | 1503 |
| 71615 | 71630 | 530372 | AGTACAATTGCTTCAA | e-k-d(10)-k-e-k-e | 51 | 1504 |
| 71616 | 71631 | 530120 | CAGTACAATTGCTTCA | e-k-k-d(10)-k-k-e | 78 | 1505 |
| 71616 | 71631 | 530167 | CAGTACAATTGCTTCA | e-e-k-d(10)-k-k-e | 69 | 1505 |
| 71616 | 71631 | 530217 | CAGTACAATTGCTTCA | e-d-k-d(10)-k-k-e | 47 | 1505 |
| 71616 | 71631 | 530267 | CAGTACAATTGCTTCA | e-d-d-k-d(9)-k-k-e | 64 | 1505 |
| 71616 | 71631 | 530317 | CAGTACAATTGCTTCA | e-e-e-e-d(9)-k-k-e | 60 | 1505 |
| 72138 | 72153 | 530713 | CTCATGCCAAGATTGT | e-e-e-d(10)-k-k-k | 26 | 1506 |
| 72299 | 72314 | 529086 | AAGCCACTTACGGTGT | e-e-e-d(10)-k-k-k | 0 | 1507 |
| 72874 | 72889 | 529087 | CGTCTATTTCCAGTGT | e-e-e-d(10)-k-k-k | 22 | 1508 |
| 73648 | 73663 | 529088 | ACTAGTTCAGTTGTCC | e-e-e-d(10)-k-k-k | 0 | 1509 |
| 73866 | 73881 | 530428 | TAGCAGAAGTAGGAGA | k-d(10)-k-e-k-e-e | 49 | 1141 |
| 73867 | 73883 | 530061 | GATAGCAGAAGTAGGAG | e-e-k-d(10)-k-e-k-e | 49 | 1142 |
| 73867 | 73882 | 530378 | ATAGCAGAAGTAGGAG | e-k-d(10)-k-e-k-e | 48 | 1143 |
| 73868 | 73883 | 530126 | GATAGCAGAAGTAGGA | e-k-k-d(10)-k-k-e | 70 | 223 |
| 73868 | 73883 | 530173 | GATAGCAGAAGTAGGA | e-e-k-d(10)-k-k-e | 62 | 223 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 73868 | 73883 | 530223 | GATAGCAGAAGTAGGA | e-d-k-d(10)-k-k-e | 44 | 223 |
| 73868 | 73883 | 530273 | GATAGCAGAAGTAGGA | e-d-d-k-d(9)-k-k-e | 63 | 223 |
| 73868 | 73883 | 530323 | GATAGCAGAAGTAGGA | e-e-e-e-d(9)-k-k-e | 37 | 223 |
| 74199 | 74214 | 530513 | TTGGATGTCAGCAAGG | k-d(10)-k-e-k-e-e | 88 | 1047 |
| 74200 | 74215 | 530507 | TTTGGATGTCAGCAAG | e-k-d(10)-k-e-k-e | 86 | 1144 |
| 74200 | 74215 | 530514 | TTTGGATGTCAGCAAG | k-d(10)-k-e-k-e-e | 80 | 1144 |
| 74201 | 74216 | 530430 | ATTTGGATGTCAGCAA | k-d(10)-k-e-k-e-e | 87 | 1145 |
| 74201 | 74216 | 530468 | ATTTGGATGTCAGCAA | e-k-k-d(10)-k-k-e | 81 | 1145 |
| 74201 | 74216 | 530476 | ATTTGGATGTCAGCAA | e-e-k-d(10)-k-k-e | 82 | 1145 |
| 74201 | 74216 | 530484 | ATTTGGATGTCAGCAA | e-d-k-d(10)-k-k-e | 74 | 1145 |
| 74201 | 74216 | 530492 | ATTTGGATGTCAGCAA | e-d-d-k-d(9)-k-k-e | 83 | 1145 |
| 74201 | 74216 | 530500 | ATTTGGATGTCAGCAA | e-e-e-e-d(9)-k-k-e | 56 | 1145 |
| 74201 | 74216 | 530508 | ATTTGGATGTCAGCAA | e-k-d(10)-k-e-k-e | 83 | 1145 |
| 74202 | 74218 | 530062 | CTATTTGGATGTCAGCA | e-e-k-d(10)-k-e-k-e | 94 | 1146 |
| 74202 | 74217 | 530380 | TATTTGGATGTCAGCA | e-k-d(10)-k-e-k-e | 94 | 1147 |
| 74202 | 74217 | 530469 | TATTTGGATGTCAGCA | e-k-k-d(10)-k-k-e | 91 | 1147 |
| 74202 | 74217 | 530477 | TATTTGGATGTCAGCA | e-e-k-d(10)-k-k-e | 87 | 1147 |
| 74202 | 74217 | 530485 | TATTTGGATGTCAGCA | e-d-k-d(10)-k-k-e | 87 | 1147 |
| 74202 | 74217 | 530493 | TATTTGGATGTCAGCA | e-d-d-k-d(9)-k-k-e | 81 | 1147 |
| 74202 | 74217 | 530501 | TATTTGGATGTCAGCA | e-e-e-e-d(9)-k-k-e | 74 | 1147 |
| 74202 | 74217 | 530515 | TATTTGGATGTCAGCA | k-d(10)-k-e-k-e-e | 87 | 1147 |
| 74203 | 74218 | 481464 | CTATTTGGATGTCAGC | k-k-k-d(10)-k-k-k | 93 | 245 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74203 | 74218 | 518349 | CTATTTGGATGTCAGC | e-e-e-d(10)-k-k-k | 58 | 245 |
| 74203 | 74218 | 519637 | CTATTTGGATGTCAGC | e-k-k-d(10)-k-k-e | 96 | 245 |
| 74203 | 74218 | 530175 | CTATTTGGATGTCAGC | e-e-k-d(10)-k-k-e | 93 | 245 |
| 74203 | 74218 | 530225 | CTATTTGGATGTCAGC | e-d-k-d(10)-k-k-e | 85 | 245 |
| 74203 | 74218 | 530275 | CTATTTGGATGTCAGC | e-d-d-k-d(9)-k-k-e | 91 | 245 |
| 74203 | 74218 | 530325 | CTATTTGGATGTCAGC | e-e-e-e-d(9)-k-k-e | 91 | 245 |
| 74204 | 74219 | 530470 | TCTATTTGGATGTCAG | e-k-k-d(10)-k-k-e | 91 | 1148 |
| 74204 | 74219 | 530478 | TCTATTTGGATGTCAG | e-e-k-d(10)-k-k-e | 87 | 1148 |
| 74204 | 74219 | 530486 | TCTATTTGGATGTCAG | e-d-k-d(10)-k-k-e | 84 | 1148 |
| 74204 | 74219 | 530494 | TCTATTTGGATGTCAG | e-d-d-k-d(9)-k-k-e | 60 | 1148 |
| 74204 | 74219 | 530502 | TCTATTTGGATGTCAG | e-e-e-e-d(9)-k-k-e | 64 | 1148 |
| 74204 | 74219 | 530509 | TCTATTTGGATGTCAG | e-k-d(10)-k-e-k-e | 80 | 1148 |
| 74205 | 74220 | 530471 | TTCTATTTGGATGTCA | e-k-k-d(10)-k-k-e | 83 | 1149 |
| 74205 | 74220 | 530479 | TTCTATTTGGATGTCA | e-e-k-d(10)-k-k-e | 74 | 1149 |
| 74205 | 74220 | 530487 | TTCTATTTGGATGTCA | e-d-k-d(10)-k-k-e | 71 | 1149 |
| 74205 | 74220 | 530495 | TTCTATTTGGATGTCA | e-d-d-k-d(9)-k-k-e | 68 | 1149 |
| 74205 | 74220 | 530503 | TTCTATTTGGATGTCA | e-e-e-e-d(9)-k-k-e | 53 | 1149 |
| 74646 | 74661 | 530431 | CACCAAGGAGGCTGTT | k-d(10)-k-e-k-e-e | 44 | 1150 |
| 74647 | 74663 | 530055 | AGCACCAAGGAGGCTGT | e-e-k-d(10)-k-e-k-e | 45 | 1151 |
| 74647 | 74662 | 530381 | GCACCAAGGAGGCTGT | e-k-d(10)-k-e-k-e | 74 | 1152 |
| 74648 | 74663 | 530128 | AGCACCAAGGAGGCTG | e-k-k-d(10)-k-k-e | 52 | 257 |
| 74648 | 74663 | 530176 | AGCACCAAGGAGGCTG | e-e-k-d(10)-k-k-e | 66 | 257 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74648 | 74663 | 530226 | AGCACCAAGGAGGCTG | e-d-k-d(10)-k-k-e | 51 | 257 |
| 74648 | 74663 | 530276 | AGCACCAAGGAGGCTG | e-d-d-k-d(9)-k-k-e | 70 | 257 |
| 74648 | 74663 | 530326 | AGCACCAAGGAGGCTG | e-e-e-e-d(9)-k-k-e | 52 | 257 |
| 74714 | 74729 | 528860 | GGTTTGACCTGAAGCC | e-e-e-d(10)-k-k-k | 58 | 1153 |
| 74715 | 74730 | 528861 | GGGTTTGACCTGAAGC | e-e-e-d(10)-k-k-k | 42 | 1154 |
| 74716 | 74731 | 528862 | AGGGTTTGACCTGAAG | e-e-e-d(10)-k-k-k | 57 | 1155 |
| 74717 | 74732 | 528863 | AAGGGTTTGACCTGAA | e-e-e-d(10)-k-k-k | 43 | 1156 |
| 74718 | 74733 | 528864 | TAAGGGTTTGACCTGA | e-e-e-d(10)-k-k-k | 50 | 1157 |
| 74719 | 74734 | 528865 | TTAAGGGTTTGACCTG | e-e-e-d(10)-k-k-k | 32 | 1158 |
| 74734 | 74749 | 528866 | GCAGCTTCAGATGTCT | e-e-e-d(10)-k-k-k | 60 | 1159 |
| 74735 | 74750 | 528867 | TGCAGCTTCAGATGTC | e-e-e-d(10)-k-k-k | 47 | 1160 |
| 74770 | 74785 | 530388 | CTTAAACCTTCCTATT | k-d(10)-k-e-k-e-e | 14 | 1161 |
| 74771 | 74786 | 530338 | CCTTAAACCTTCCTAT | e-k-d(10)-k-e-k-e | 47 | 1162 |
| 74772 | 74787 | 530086 | TCCTTAAACCTTCCTA | e-k-k-d(10)-k-k-e | 58 | 273 |
| 74772 | 74787 | 530133 | TCCTTAAACCTTCCTA | e-e-k-d(10)-k-k-e | 53 | 273 |
| 74772 | 74787 | 530183 | TCCTTAAACCTTCCTA | e-d-k-d(10)-k-k-e | 52 | 273 |
| 74772 | 74787 | 530233 | TCCTTAAACCTTCCTA | e-d-d-k-d(9)-k-k-e | 29 | 273 |
| 74772 | 74787 | 530283 | TCCTTAAACCTTCCTA | e-e-e-e-d(9)-k-k-e | 32 | 273 |
| 74777 | 74792 | 528868 | GATTCTCCTTAAACCT | e-e-e-d(10)-k-k-k | 45 | 1163 |
| 74778 | 74793 | 530389 | AGATTCTCCTTAAACC | k-d(10)-k-e-k-e-e | 44 | 1164 |
| 74779 | 74794 | 530339 | TAGATTCTCCTTAAAC | e-k-d(10)-k-e-k-e | 41 | 1165 |
| 74780 | 74795 | 530087 | TTAGATTCTCCTTAAA | e-k-k-d(10)-k-k-e | 43 | 1166 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74780 | 74795 | 530134 | TTAGATTCTCCTTAAA | e-e-k-d(10)-k-k-e | 28 | 1166 |
| 74780 | 74795 | 530184 | TTAGATTCTCCTTAAA | e-d-k-d(10)-k-k-e | 13 | 1166 |
| 74780 | 74795 | 530234 | TTAGATTCTCCTTAAA | e-d-d-k-d(9)-k-k-e | 15 | 1166 |
| 74780 | 74795 | 530284 | TTAGATTCTCCTTAAA | e-e-e-e-d(9)-k-k-e | 14 | 1166 |
| 74782 | 74797 | 530390 | GCTTAGATTCTCCTTA | k-d(10)-k-e-k-e-e | 83 | 1167 |
| 74783 | 74798 | 530340 | TGCTTAGATTCTCCTT | e-k-d(10)-k-e-k-e | 89 | 1168 |
| 74784 | 74799 | 528869 | ATGCTTAGATTCTCCT | e-e-e-d(10)-k-k-k | 83 | 1169 |
| 74784 | 74799 | 530088 | ATGCTTAGATTCTCCT | e-k-k-d(10)-k-k-e | 90 | 1169 |
| 74784 | 74799 | 530135 | ATGCTTAGATTCTCCT | e-e-k-d(10)-k-k-e | 91 | 1169 |
| 74784 | 74799 | 530185 | ATGCTTAGATTCTCCT | e-d-k-d(10)-k-k-e | 85 | 1169 |
| 74784 | 74799 | 530235 | ATGCTTAGATTCTCCT | e-d-d-k-d(9)-k-k-e | 28 | 1169 |
| 74784 | 74799 | 530285 | ATGCTTAGATTCTCCT | e-e-e-e-d(9)-k-k-e | 86 | 1169 |
| 74784 | 74799 | 530391 | ATGCTTAGATTCTCCT | k-d(10)-k-e-k-e-e | 79 | 1169 |
| 74785 | 74801 | 530021 | AAATGCTTAGATTCTCC | e-e-k-d(10)-k-e-k-e | 87 | 1170 |
| 74785 | 74800 | 530341 | AATGCTTAGATTCTCC | e-k-d(10)-k-e-k-e | 88 | 1171 |
| 74786 | 74801 | 530089 | AAATGCTTAGATTCTC | e-k-k-d(10)-k-k-e | 71 | 1172 |
| 74786 | 74801 | 530136 | AAATGCTTAGATTCTC | e-e-k-d(10)-k-k-e | 66 | 1172 |
| 74786 | 74801 | 530186 | AAATGCTTAGATTCTC | e-d-k-d(10)-k-k-e | 51 | 1172 |
| 74786 | 74801 | 530236 | AAATGCTTAGATTCTC | e-d-d-k-d(9)-k-k-e | 74 | 1172 |
| 74786 | 74801 | 530286 | AAATGCTTAGATTCTC | e-e-e-e-d(9)-k-k-e | 56 | 1172 |
| 74869 | 74884 | 528870 | GTAAGCACCCTCTGCC | e-e-e-d(10)-k-k-k | 26 | 1173 |
| 74871 | 74886 | 528871 | TTGTAAGCACCCTCTG | e-e-e-d(10)-k-k-k | 14 | 1174 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74873 | 74888 | 528872 | GGTTGTAAGCACCCTC | e-e-e-d(10)-k-k-k | 47 | 1175 |
| 74874 | 74889 | 528873 | AGGTTGTAAGCACCCT | e-e-e-d(10)-k-k-k | 40 | 1176 |
| 74875 | 74890 | 528874 | AAGGTTGTAAGCACCC | e-e-e-d(10)-k-k-k | 54 | 1177 |
| 74877 | 74892 | 528875 | TCAAGGTTGTAAGCAC | e-e-e-d(10)-k-k-k | 15 | 1178 |
| 74878 | 74893 | 528876 | GTCAAGGTTGTAAGCA | e-e-e-d(10)-k-k-k | 28 | 1179 |
| 74879 | 74894 | 528877 | AGTCAAGGTTGTAAGC | e-e-e-d(10)-k-k-k | 28 | 1180 |
| 74881 | 74896 | 528878 | GGAGTCAAGGTTGTAA | e-e-e-d(10)-k-k-k | 6 | 1181 |
| 74882 | 74897 | 528879 | GGGAGTCAAGGTTGTA | e-e-e-d(10)-k-k-k | 22 | 1182 |
| 74901 | 74916 | 530392 | GATCAAGTCCAGGGAG | k-d(10)-k-e-k-e-e | 47 | 1183 |
| 74902 | 74918 | 530022 | CAGATCAAGTCCAGGGA | e-e-k-d(10)-k-e-k-e | 80 | 1184 |
| 74902 | 74917 | 530342 | AGATCAAGTCCAGGGA | e-k-d(10)-k-e-k-e | 70 | 1185 |
| 74902 | 74917 | 530393 | AGATCAAGTCCAGGGA | k-d(10)-k-e-k-e-e | 46 | 1185 |
| 74903 | 74919 | 530023 | GCAGATCAAGTCCAGGG | e-e-k-d(10)-k-e-k-e | 74 | 1186 |
| 74903 | 74918 | 530090 | CAGATCAAGTCCAGGG | e-k-k-d(10)-k-k-e | 78 | 1187 |
| 74903 | 74918 | 530137 | CAGATCAAGTCCAGGG | e-e-k-d(10)-k-k-e | 76 | 1187 |
| 74903 | 74918 | 530187 | CAGATCAAGTCCAGGG | e-d-k-d(10)-k-k-e | 68 | 1187 |
| 74903 | 74918 | 530237 | CAGATCAAGTCCAGGG | e-d-d-k-d(9)-k-k-e | 36 | 1187 |
| 74903 | 74918 | 530287 | CAGATCAAGTCCAGGG | e-e-e-e-d(9)-k-k-e | 56 | 1187 |
| 74903 | 74918 | 530343 | CAGATCAAGTCCAGGG | e-k-d(10)-k-e-k-e | 68 | 1187 |
| 74903 | 74918 | 530394 | CAGATCAAGTCCAGGG | k-d(10)-k-e-k-e-e | 49 | 1187 |
| 74904 | 74919 | 518343 | GCAGATCAAGTCCAGG | e-e-e-d(10)-k-k-k | 5 | 1188 |
| 74904 | 74920 | 530024 | AGCAGATCAAGTCCAGG | e-e-k-d(10)-k-e-k-e | 79 | 1189 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74904 | 74919 | 530091 | GCAGATCAAGTCCAGG | e-k-k-d(10)-k-k-e | 81 | 1188 |
| 74904 | 74919 | 530138 | GCAGATCAAGTCCAGG | e-e-k-d(10)-k-k-e | 81 | 1188 |
| 74904 | 74919 | 530188 | GCAGATCAAGTCCAGG | e-d-k-d(10)-k-k-e | 78 | 1188 |
| 74904 | 74919 | 530238 | GCAGATCAAGTCCAGG | e-d-d-k-d(9)-k-k-e | 29 | 1188 |
| 74904 | 74919 | 530288 | GCAGATCAAGTCCAGG | e-e-e-e-d(9)-k-k-e | 69 | 1188 |
| 74904 | 74919 | 530344 | GCAGATCAAGTCCAGG | e-k-d(10)-k-e-k-e | 85 | 1188 |
| 74905 | 74920 | 530092 | AGCAGATCAAGTCCAG | e-k-k-d(10)-k-k-e | 85 | 1190 |
| 74905 | 74920 | 530139 | AGCAGATCAAGTCCAG | e-e-k-d(10)-k-k-e | 79 | 1190 |
| 74905 | 74920 | 530189 | AGCAGATCAAGTCCAG | e-d-k-d(10)-k-k-e | 77 | 1190 |
| 74905 | 74920 | 530239 | AGCAGATCAAGTCCAG | e-d-d-k-d(9)-k-k-e | 61 | 1190 |
| 74905 | 74920 | 530289 | AGCAGATCAAGTCCAG | e-e-e-e-d(9)-k-k-e | 75 | 1190 |
| 74907 | 74922 | 528880 | ACAGCAGATCAAGTCC | e-e-e-d(10)-k-k-k | 65 | 1191 |
| 74908 | 74923 | 528881 | AACAGCAGATCAAGTC | e-e-e-d(10)-k-k-k | 44 | 1192 |
| 74924 | 74939 | 528882 | ACAACCTAGCCTCTGA | e-e-e-d(10)-k-k-k | 39 | 1193 |
| 74925 | 74940 | 528883 | AACAACCTAGCCTCTG | e-e-e-d(10)-k-k-k | 46 | 1194 |
| 74927 | 74942 | 528884 | GAAACAACCTAGCCTC | e-e-e-d(10)-k-k-k | 37 | 1195 |
| 74928 | 74943 | 528885 | AGAAACAACCTAGCCT | e-e-e-d(10)-k-k-k | 20 | 1196 |
| 74929 | 74944 | 528886 | CAGAAACAACCTAGCC | e-e-e-d(10)-k-k-k | 21 | 1197 |
| 74942 | 74957 | 528887 | GATAAGGCACCCACAG | e-e-e-d(10)-k-k-k | 25 | 1198 |
| 74943 | 74958 | 528888 | TGATAAGGCACCCACA | e-e-e-d(10)-k-k-k | 12 | 1199 |
| 74944 | 74959 | 528889 | CTGATAAGGCACCCAC | e-e-e-d(10)-k-k-k | 25 | 1200 |
| 74946 | 74961 | 528890 | CCCTGATAAGGCACCC | e-e-e-d(10)-k-k-k | 42 | 1201 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74947 | 74962 | 528891 | GCCCTGATAAGGCACC | e-e-e-d(10)-k-k-k | 49 | 1202 |
| 74952 | 74967 | 528892 | TCCCAGCCCTGATAAG | e-e-e-d(10)-k-k-k | 0 | 1203 |
| 74954 | 74969 | 528893 | TATCCCAGCCCTGATA | e-e-e-d(10)-k-k-k | 0 | 1204 |
| 74957 | 74972 | 528894 | AAGTATCCCAGCCCTG | e-e-e-d(10)-k-k-k | 25 | 1205 |
| 74958 | 74973 | 528895 | GAAGTATCCCAGCCCT | e-e-e-d(10)-k-k-k | 39 | 1206 |
| 74959 | 74974 | 528896 | AGAAGTATCCCAGCCC | e-e-e-d(10)-k-k-k | 22 | 1207 |
| 74960 | 74975 | 528897 | CAGAAGTATCCCAGCC | e-e-e-d(10)-k-k-k | 36 | 1208 |
| 75079 | 75094 | 528898 | TGAGACCAGGATTCCT | e-e-e-d(10)-k-k-k | 41 | 1209 |
| 75083 | 75098 | 528899 | GTCCTGAGACCAGGAT | e-e-e-d(10)-k-k-k | 19 | 1210 |
| 75164 | 75179 | 528900 | AGCTCAACCAGACACG | e-e-e-d(10)-k-k-k | 54 | 311 |
| 75166 | 75181 | 528901 | TGAGCTCAACCAGACA | e-e-e-d(10)-k-k-k | 40 | 1211 |
| 75171 | 75186 | 528902 | TTCCCTGAGCTCAACC | e-e-e-d(10)-k-k-k | 32 | 1212 |
| 75179 | 75194 | 528903 | GAACCATATTCCCTGA | e-e-e-d(10)-k-k-k | 30 | 313 |
| 75182 | 75197 | 528904 | TAAGAACCATATTCCC | e-e-e-d(10)-k-k-k | 27 | 1213 |
| 75209 | 75224 | 518344 | GCCACTGGATATCACC | e-e-e-d(10)-k-k-k | 89 | 317 |
| 75254 | 75269 | 528905 | TAAGCCTTTGCCCTGC | e-e-e-d(10)-k-k-k | 64 | 1214 |
| 75255 | 75270 | 528906 | GTAAGCCTTTGCCCTG | e-e-e-d(10)-k-k-k | 53 | 1215 |
| 75256 | 75271 | 528907 | AGTAAGCCTTTGCCCT | e-e-e-d(10)-k-k-k | 45 | 1216 |
| 75257 | 75272 | 528908 | CAGTAAGCCTTTGCCC | e-e-e-d(10)-k-k-k | 40 | 1217 |
| 75259 | 75274 | 528909 | ATCAGTAAGCCTTTGC | e-e-e-d(10)-k-k-k | 53 | 1218 |
| 75260 | 75275 | 528910 | TATCAGTAAGCCTTTG | e-e-e-d(10)-k-k-k | 47 | 1219 |
| 75264 | 75279 | 528911 | AGTTTATCAGTAAGCC | e-e-e-d(10)-k-k-k | 58 | 1220 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75270 | 75285 | 528912 | GACTCAAGTTTATCAG | e-e-e-d(10)-k-k-k | 37 | 1221 |
| 75272 | 75287 | 528913 | CAGACTCAAGTTTATC | e-e-e-d(10)-k-k-k | 39 | 1222 |
| 75273 | 75288 | 528914 | GCAGACTCAAGTTTAT | e-e-e-d(10)-k-k-k | 0 | 1223 |
| 75274 | 75289 | 528915 | GGCAGACTCAAGTTTA | e-e-e-d(10)-k-k-k | 1 | 1224 |
| 75275 | 75290 | 528916 | GGGCAGACTCAAGTTT | e-e-e-d(10)-k-k-k | 0 | 1225 |
| 75276 | 75291 | 528917 | AGGGCAGACTCAAGTT | e-e-e-d(10)-k-k-k | 9 | 1226 |
| 75278 | 75293 | 528918 | CGAGGGCAGACTCAAG | e-e-e-d(10)-k-k-k | 2 | 1227 |
| 75280 | 75295 | 528919 | TACGAGGGCAGACTCA | e-e-e-d(10)-k-k-k | 20 | 324 |
| 75281 | 75296 | 528920 | ATACGAGGGCAGACTC | e-e-e-d(10)-k-k-k | 14 | 1228 |
| 75282 | 75297 | 528921 | CATACGAGGGCAGACT | e-e-e-d(10)-k-k-k | 0 | 1229 |
| 75283 | 75298 | 528922 | TCATACGAGGGCAGAC | e-e-e-d(10)-k-k-k | 8 | 1230 |
| 75285 | 75300 | 528923 | CCTCATACGAGGGCAG | e-e-e-d(10)-k-k-k | 2 | 1231 |
| 75286 | 75301 | 528924 | CCCTCATACGAGGGCA | e-e-e-d(10)-k-k-k | 2 | 1232 |
| 75287 | 75302 | 528925 | ACCCTCATACGAGGGC | e-e-e-d(10)-k-k-k | 0 | 1233 |
| 75412 | 75427 | 528926 | TACGCACAGGAGAGGC | e-e-e-d(10)-k-k-k | 20 | 1233 |
| 75413 | 75428 | 528927 | ATACGCACAGGAGAGG | e-e-e-d(10)-k-k-k | 0 | 1234 |
| 75414 | 75429 | 528928 | CATACGCACAGGAGAG | e-e-e-d(10)-k-k-k | 6 | 1235 |
| 75415 | 75430 | 528929 | CCATACGCACAGGAGA | e-e-e-d(10)-k-k-k | 4 | 1236 |
| 75416 | 75431 | 528930 | CCCATACGCACAGGAG | e-e-e-d(10)-k-k-k | 36 | 1237 |
| 75417 | 75432 | 528931 | TCCCATACGCACAGGA | e-e-e-d(10)-k-k-k | 22 | 1238 |
| 75418 | 75433 | 528932 | TTCCCATACGCACAGG | e-e-e-d(10)-k-k-k | 32 | 1239 |
| 75419 | 75434 | 528933 | GTTCCCATACGCACAG | e-e-e-d(10)-k-k-k | 45 | 1240 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75420 | 75435 | 528934 | TGTTCCCATACGCACA | e-e-e-d(10)-k-k-k | 36 | 1241 |
| 75421 | 75436 | 528935 | GTGTTCCCATACGCAC | e-e-e-d(10)-k-k-k | 20 | 1242 |
| 75421 | 75436 | 530395 | GTGTTCCCATACGCAC | k-d(10)-k-e-k-e-e | 71 | 1242 |
| 75422 | 75437 | 528936 | GGTGTTCCCATACGCA | e-e-e-d(10)-k-k-k | 71 | 1243 |
| 75422 | 75438 | 530025 | AGGTGTTCCCATACGCA | e-e-k-d(10)-k-e-k-e | 90 | 1244 |
| 75422 | 75437 | 530345 | GGTGTTCCCATACGCA | e-k-d(10)-k-e-k-e | 93 | 1243 |
| 75422 | 75437 | 530396 | GGTGTTCCCATACGCA | k-d(10)-k-e-k-e-e | 71 | 1243 |
| 75423 | 75438 | 528937 | AGGTGTTCCCATACGC | e-e-e-d(10)-k-k-k | 73 | 1245 |
| 75423 | 75439 | 530026 | TAGGTGTTCCCATACGC | e-e-k-d(10)-k-e-k-e | 87 | 1246 |
| 75423 | 75438 | 530093 | AGGTGTTCCCATACGC | e-k-k-d(10)-k-k-e | 95 | 1245 |
| 75423 | 75438 | 530140 | AGGTGTTCCCATACGC | e-e-k-d(10)-k-k-e | 89 | 1245 |
| 75423 | 75438 | 530190 | AGGTGTTCCCATACGC | e-d-k-d(10)-k-k-e | 82 | 1245 |
| 75423 | 75438 | 530240 | AGGTGTTCCCATACGC | e-d-d-k-d(9)-k-k-e | 50 | 1245 |
| 75423 | 75438 | 530290 | AGGTGTTCCCATACGC | e-e-e-e-d(9)-k-k-e | 69 | 1245 |
| 75423 | 75438 | 530346 | AGGTGTTCCCATACGC | e-k-d(10)-k-e-k-e | 89 | 1245 |
| 75424 | 75439 | 528938 | TAGGTGTTCCCATACG | e-e-e-d(10)-k-k-k | 72 | 336 |
| 75424 | 75439 | 530094 | TAGGTGTTCCCATACG | e-k-k-d(10)-k-k-e | 88 | 336 |
| 75424 | 75439 | 530141 | TAGGTGTTCCCATACG | e-e-k-d(10)-k-k-e | 80 | 336 |
| 75424 | 75439 | 530191 | TAGGTGTTCCCATACG | e-d-k-d(10)-k-k-e | 74 | 336 |
| 75424 | 75439 | 530241 | TAGGTGTTCCCATACG | e-d-d-k-d(9)-k-k-e | 53 | 336 |
| 75424 | 75439 | 530291 | TAGGTGTTCCCATACG | e-e-e-e-d(9)-k-k-e | 68 | 336 |
| 75425 | 75440 | 528939 | CTAGGTGTTCCCATAC | e-e-e-d(10)-k-k-k | 39 | 1247 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75426 | 75441 | 528940 | GCTAGGTGTTCCCATA | e-e-e-d(10)-k-k-k | 62 | 1248 |
| 75427 | 75442 | 528941 | TGCTAGGTGTTCCCAT | e-e-e-d(10)-k-k-k | 49 | 1249 |
| 75429 | 75444 | 528942 | CGTGCTAGGTGTTCCC | e-e-e-d(10)-k-k-k | 77 | 1250 |
| 75491 | 75506 | 528943 | CAAGGTGGTTTTGAGT | e-e-e-d(10)-k-k-k | 25 | 1251 |
| 75492 | 75507 | 528944 | GCAAGGTGGTTTTGAG | e-e-e-d(10)-k-k-k | 28 | 344 |
| 75507 | 75522 | 528945 | CTCTGATCAGCTGAGG | e-e-e-d(10)-k-k-k | 74 | 1252 |
| 75508 | 75523 | 528946 | ACTCTGATCAGCTGAG | e-e-e-d(10)-k-k-k | 56 | 1253 |
| 75549 | 75564 | 528947 | GAGACCAGCTAATTTG | e-e-e-d(10)-k-k-k | 36 | 1254 |
| 75582 | 75597 | 528948 | CATCTTAGAGAAGGTC | e-e-e-d(10)-k-k-k | 59 | 1255 |
| 75622 | 75637 | 528949 | TCAACTGTCTCCAGGC | e-e-e-d(10)-k-k-k | 67 | 1256 |
| 75622 | 75637 | 530397 | TCAACTGTCTCCAGGC | k-d(10)-k-e-k-e-e | 60 | 1256 |
| 75623 | 75638 | 528950 | ATCAACTGTCTCCAGG | e-e-e-d(10)-k-k-k | 57 | 1257 |
| 75623 | 75639 | 530027 | CATCAACTGTCTCCAGG | e-e-k-d(10)-k-e-k-e | 56 | 1258 |
| 75623 | 75638 | 530347 | ATCAACTGTCTCCAGG | e-k-d(10)-k-e-k-e | 49 | 1257 |
| 75624 | 75639 | 530095 | CATCAACTGTCTCCAG | e-k-k-d(10)-k-k-e | 40 | 354 |
| 75624 | 75639 | 530142 | CATCAACTGTCTCCAG | e-e-k-d(10)-k-k-e | 43 | 354 |
| 75624 | 75639 | 530192 | CATCAACTGTCTCCAG | e-d-k-d(10)-k-k-e | 42 | 354 |
| 75624 | 75639 | 530242 | CATCAACTGTCTCCAG | e-d-d-k-d(9)-k-k-e | 0 | 354 |
| 75624 | 75639 | 530292 | CATCAACTGTCTCCAG | e-e-e-e-d(9)-k-k-e | 36 | 354 |
| 75624 | 75639 | 530398 | CATCAACTGTCTCCAG | k-d(10)-k-e-k-e-e | 28 | 354 |
| 75625 | 75641 | 530028 | CACATCAACTGTCTCCA | e-e-k-d(10)-k-e-k-e | 57 | 1259 |
| 75625 | 75640 | 530348 | ACATCAACTGTCTCCA | e-k-d(10)-k-e-k-e | 58 | 1260 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75626 | 75641 | 530096 | CACATCAACTGTCTCC | e-k-k-d(10)-k-k-e | 72 | 356 |
| 75626 | 75641 | 530143 | CACATCAACTGTCTCC | e-e-k-d(10)-k-k-e | 74 | 356 |
| 75626 | 75641 | 530193 | CACATCAACTGTCTCC | e-d-k-d(10)-k-k-e | 62 | 356 |
| 75626 | 75641 | 530243 | CACATCAACTGTCTCC | e-d-d-k-d(9)-k-k-e | 34 | 356 |
| 75626 | 75641 | 530293 | CACATCAACTGTCTCC | e-e-e-e-d(9)-k-k-e | 59 | 356 |
| 75628 | 75643 | 528951 | GACACATCAACTGTCT | e-e-e-d(10)-k-k-k | 16 | 1261 |
| 75662 | 75677 | 528952 | GAAGAGTGTTGCTGGA | e-e-e-d(10)-k-k-k | 57 | 1262 |
| 75664 | 75679 | 528953 | CTGAAGAGTGTTGCTG | e-e-e-d(10)-k-k-k | 46 | 1263 |
| 75666 | 75681 | 528954 | TACTGAAGAGTGTTGC | e-e-e-d(10)-k-k-k | 42 | 1264 |
| 75672 | 75687 | 530510 | ATTATGTACTGAAGAG | k-d(10)-k-e-k-e-e | 53 | 1265 |
| 75673 | 75688 | 530504 | TATTATGTACTGAAGA | e-k-d(10)-k-e-k-e | 25 | 1266 |
| 75673 | 75688 | 530511 | TATTATGTACTGAAGA | k-d(10)-k-e-k-e-e | 31 | 1266 |
| 75674 | 75689 | 530432 | TTATTATGTACTGAAG | k-d(10)-k-e-k-e-e | 15 | 1267 |
| 75674 | 75689 | 530463 | TTATTATGTACTGAAG | e-k-k-d(10)-k-k-e | 20 | 1267 |
| 75674 | 75689 | 530472 | TTATTATGTACTGAAG | e-e-k-d(10)-k-k-e | 17 | 1267 |
| 75674 | 75689 | 530480 | TTATTATGTACTGAAG | e-d-k-d(10)-k-k-e | 4 | 1267 |
| 75674 | 75689 | 530488 | TTATTATGTACTGAAG | e-d-d-k-d(9)-k-k-e | 13 | 1267 |
| 75674 | 75689 | 530496 | TTATTATGTACTGAAG | e-e-e-e-d(9)-k-k-e | 0 | 1267 |
| 75674 | 75689 | 530505 | TTATTATGTACTGAAG | e-k-d(10)-k-e-k-e | 37 | 1267 |
| 75675 | 75691 | 530063 | GCTTATTATGTACTGAA | e-e-k-d(10)-k-e-k-e | 74 | 1268 |
| 75675 | 75690 | 530382 | CTTATTATGTACTGAA | e-k-d(10)-k-e-k-e | 17 | 1269 |
| 75675 | 75690 | 530465 | CTTATTATGTACTGAA | e-k-k-d(10)-k-k-e | 63 | 1269 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75675 | 75690 | 530473 | CTTATTATGTACTGAA | e-e-k-d(10)-k-k-e | 45 | 1269 |
| 75675 | 75690 | 530481 | CTTATTATGTACTGAA | e-d-k-d(10)-k-k-e | 14 | 1269 |
| 75675 | 75690 | 530489 | CTTATTATGTACTGAA | e-d-d-k-d(9)-k-k-e | 13 | 1269 |
| 75675 | 75690 | 530497 | CTTATTATGTACTGAA | e-e-e-e-d(9)-k-k-e | 7 | 1269 |
| 75675 | 75690 | 530512 | CTTATTATGTACTGAA | k-d(10)-k-e-k-e-e | 21 | 1269 |
| 75676 | 75691 | 519638 | GCTTATTATGTACTGA | e-k-k-d(10)-k-k-e | 86 | 362 |
| 75676 | 75691 | 530177 | GCTTATTATGTACTGA | e-e-k-d(10)-k-k-e | 71 | 362 |
| 75676 | 75691 | 530227 | GCTTATTATGTACTGA | e-d-k-d(10)-k-k-e | 51 | 362 |
| 75676 | 75691 | 530277 | GCTTATTATGTACTGA | e-d-d-k-d(9)-k-k-e | 70 | 362 |
| 75676 | 75691 | 530327 | GCTTATTATGTACTGA | e-e-e-e-d(9)-k-k-e | 61 | 362 |
| 75677 | 75692 | 530466 | AGCTTATTATGTACTG | e-k-k-d(10)-k-k-e | 82 | 1270 |
| 75677 | 75692 | 530474 | AGCTTATTATGTACTG | e-e-k-d(10)-k-k-e | 62 | 1270 |
| 75677 | 75692 | 530482 | AGCTTATTATGTACTG | e-d-k-d(10)-k-k-e | 53 | 1270 |
| 75677 | 75692 | 530490 | AGCTTATTATGTACTG | e-d-d-k-d(9)-k-k-e | 42 | 1270 |
| 75677 | 75692 | 530498 | AGCTTATTATGTACTG | e-e-e-e-d(9)-k-k-e | 45 | 1270 |
| 75677 | 75692 | 530506 | AGCTTATTATGTACTG | e-k-d(10)-k-e-k-e | 70 | 1270 |
| 75678 | 75693 | 530467 | AAGCTTATTATGTACT | e-k-k-d(10)-k-k-e | 50 | 1271 |
| 75678 | 75693 | 530475 | AAGCTTATTATGTACT | e-e-k-d(10)-k-k-e | 26 | 1271 |
| 75678 | 75693 | 530483 | AAGCTTATTATGTACT | e-d-k-d(10)-k-k-e | 19 | 1271 |
| 75678 | 75693 | 530491 | AAGCTTATTATGTACT | e-d-d-k-d(9)-k-k-e | 13 | 1271 |
| 75678 | 75693 | 530499 | AAGCTTATTATGTACT | e-e-e-e-d(9)-k-k-e | 15 | 1271 |
| 75679 | 75694 | 528955 | TAAGCTTATTATGTAC | e-e-e-d(10)-k-k-k | 0 | 1272 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75686 | 75701 | 528956 | TATCAGTTAAGCTTAT | e-e-e-d(10)-k-k-k | 0 | 1273 |
| 75689 | 75704 | 528957 | GTTTATCAGTTAAGCT | e-e-e-d(10)-k-k-k | 31 | 1274 |
| 75726 | 75741 | 530433 | CAATGGTAAGCCCAAG | k-d(10)-k-e-k-e-e | 62 | 1275 |
| 75727 | 75742 | 528958 | CCAATGGTAAGCCCAA | e-e-e-d(10)-k-k-k | 66 | 1276 |
| 75727 | 75743 | 530056 | CCCAATGGTAAGCCCAA | e-e-k-d(10)-k-e-k-e | 73 | 1277 |
| 75727 | 75742 | 530383 | CCAATGGTAAGCCCAA | e-k-d(10)-k-e-k-e | 64 | 1276 |
| 75728 | 75743 | 518345 | CCCAATGGTAAGCCCA | e-e-e-d(10)-k-k-k | 80 | 366 |
| 75728 | 75743 | 519636 | CCCAATGGTAAGCCCA | e-k-k-d(10)-k-k-e | 90 | 366 |
| 75728 | 75743 | 530178 | CCCAATGGTAAGCCCA | e-e-k-d(10)-k-k-e | 86 | 366 |
| 75728 | 75743 | 530228 | CCCAATGGTAAGCCCA | e-d-k-d(10)-k-k-e | 77 | 366 |
| 75728 | 75743 | 530278 | CCCAATGGTAAGCCCA | e-d-d-k-d(9)-k-k-e | 86 | 366 |
| 75728 | 75743 | 530328 | CCCAATGGTAAGCCCA | e-e-e-e-d(9)-k-k-e | 80 | 366 |
| 75729 | 75744 | 528959 | ACCCAATGGTAAGCCC | e-e-e-d(10)-k-k-k | 73 | 1277 |
| 75731 | 75746 | 528960 | AAACCCAATGGTAAGC | e-e-e-d(10)-k-k-k | 43 | 1278 |
| 75732 | 75747 | 528961 | TAAACCCAATGGTAAG | e-e-e-d(10)-k-k-k | 18 | 1279 |
| 75733 | 75748 | 528962 | TTAAACCCAATGGTAA | e-e-e-d(10)-k-k-k | 13 | 1280 |
| 75734 | 75749 | 528963 | TTTAAACCCAATGGTA | e-e-e-d(10)-k-k-k | 2 | 1281 |
| 75741 | 75756 | 528964 | CCTATGATTTAAACCC | e-e-e-d(10)-k-k-k | 17 | 1282 |
| 75745 | 75760 | 528965 | GGTCCCTATGATTTAA | e-e-e-d(10)-k-k-k | 31 | 1283 |
| 75746 | 75761 | 528966 | AGGTCCCTATGATTTA | e-e-e-d(10)-k-k-k | 22 | 1284 |
| 75802 | 75817 | 528967 | CCTAAGGCCATGAACT | e-e-e-d(10)-k-k-k | 19 | 374 |
| 75803 | 75818 | 528968 | ACCTAAGGCCATGAAC | e-e-e-d(10)-k-k-k | 25 | 1285 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75804 | 75819 | 528969 | TACCTAAGGCCATGAA | e-e-e-d(10)-k-k-k | 41 | 1286 |
| 75805 | 75820 | 528970 | CTACCTAAGGCCATGA | e-e-e-d(10)-k-k-k | 55 | 1287 |
| 75806 | 75821 | 528971 | GCTACCTAAGGCCATG | e-e-e-d(10)-k-k-k | 66 | 1288 |
| 75807 | 75822 | 528972 | TGCTACCTAAGGCCAT | e-e-e-d(10)-k-k-k | 56 | 1289 |
| 75808 | 75823 | 528973 | ATGCTACCTAAGGCCA | e-e-e-d(10)-k-k-k | 71 | 1290 |
| 75809 | 75824 | 528974 | CATGCTACCTAAGGCC | e-e-e-d(10)-k-k-k | 58 | 1291 |
| 75810 | 75825 | 528975 | ACATGCTACCTAAGGC | e-e-e-d(10)-k-k-k | 34 | 1292 |
| 75823 | 75838 | 528976 | GTTAAGACCAGATACA | e-e-e-d(10)-k-k-k | 45 | 1293 |
| 75824 | 75839 | 528977 | AGTTAAGACCAGATAC | e-e-e-d(10)-k-k-k | 40 | 1294 |
| 75825 | 75840 | 528978 | GAGTTAAGACCAGATA | e-e-e-d(10)-k-k-k | 40 | 1295 |
| 75826 | 75841 | 528979 | AGAGTTAAGACCAGAT | e-e-e-d(10)-k-k-k | 62 | 1296 |
| 75831 | 75846 | 530399 | CAATCAGAGTTAAGAC | k-d(10)-k-e-k-e-e | 36 | 1297 |
| 75832 | 75848 | 530029 | TACAATCAGAGTTAAGA | e-e-k-d(10)-k-e-k-e | 29 | 1298 |
| 75832 | 75847 | 530349 | ACAATCAGAGTTAAGA | e-k-d(10)-k-e-k-e | 33 | 1299 |
| 75833 | 75848 | 528980 | TACAATCAGAGTTAAG | e-e-e-d(10)-k-k-k | 0 | 378 |
| 75833 | 75848 | 530097 | TACAATCAGAGTTAAG | e-k-k-d(10)-k-k-e | 41 | 378 |
| 75833 | 75848 | 530144 | TACAATCAGAGTTAAG | e-e-k-d(10)-k-k-e | 16 | 378 |
| 75833 | 75848 | 530194 | TACAATCAGAGTTAAG | e-d-k-d(10)-k-k-e | 28 | 378 |
| 75833 | 75848 | 530244 | TACAATCAGAGTTAAG | e-d-d-k-d(9)-k-k-e | 0 | 378 |
| 75833 | 75848 | 530294 | TACAATCAGAGTTAAG | e-e-e-e-d(9)-k-k-e | 7 | 378 |
| 75835 | 75850 | 528981 | GCTACAATCAGAGTTA | e-e-e-d(10)-k-k-k | 52 | 1300 |
| 75836 | 75851 | 528982 | TGCTACAATCAGAGTT | e-e-e-d(10)-k-k-k | 47 | 1301 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75837 | 75852 | 528983 | TTGCTACAATCAGAGT | e-e-e-d(10)-k-k-k | 44 | 1302 |
| 75849 | 75864 | 530400 | CTCTCAGAACTTTTGC | k-d(10)-k-e-k-e-e | 65 | 1303 |
| 75850 | 75866 | 530030 | TCCTCTCAGAACTTTTG | e-e-k-d(10)-k-e-k-e | 47 | 1304 |
| 75850 | 75865 | 530350 | CCTCTCAGAACTTTTG | e-k-d(10)-k-e-k-e | 54 | 1305 |
| 75851 | 75866 | 530098 | TCCTCTCAGAACTTTT | e-k-k-d(10)-k-k-e | 42 | 380 |
| 75851 | 75866 | 530145 | TCCTCTCAGAACTTTT | e-e-k-d(10)-k-k-e | 38 | 380 |
| 75851 | 75866 | 530195 | TCCTCTCAGAACTTTT | e-d-k-d(10)-k-k-e | 43 | 380 |
| 75851 | 75866 | 530245 | TCCTCTCAGAACTTTT | e-d-d-k-d(9)-k-k-e | 28 | 380 |
| 75851 | 75866 | 530295 | TCCTCTCAGAACTTTT | e-e-e-e-d(9)-k-k-e | 39 | 380 |
| 75957 | 75972 | 528984 | CCCACGGGATTCCCTC | e-e-e-d(10)-k-k-k | 39 | 1306 |
| 75958 | 75973 | 528985 | ACCCACGGGATTCCCT | e-e-e-d(10)-k-k-k | 36 | 1307 |
| 75959 | 75974 | 528986 | AACCCACGGGATTCCC | e-e-e-d(10)-k-k-k | 47 | 1308 |
| 75960 | 75975 | 528987 | CAACCCACGGGATTCC | e-e-e-d(10)-k-k-k | 39 | 1309 |
| 75961 | 75976 | 528988 | GCAACCCACGGGATTC | e-e-e-d(10)-k-k-k | 48 | 1310 |
| 75962 | 75977 | 528989 | AGCAACCCACGGGATT | e-e-e-d(10)-k-k-k | 40 | 1311 |
| 75964 | 75979 | 528990 | TAAGCAACCCACGGGA | e-e-e-d(10)-k-k-k | 27 | 1312 |
| 75965 | 75980 | 528991 | GTAAGCAACCCACGGG | e-e-e-d(10)-k-k-k | 47 | 1313 |
| 75966 | 75981 | 528992 | GGTAAGCAACCCACGG | e-e-e-d(10)-k-k-k | 42 | 1314 |
| 75967 | 75982 | 528993 | AGGTAAGCAACCCACG | e-e-e-d(10)-k-k-k | 54 | 1315 |
| 75967 | 75982 | 530434 | AGGTAAGCAACCCACG | k-d(10)-k-e-k-e-e | 51 | 1315 |
| 75968 | 75983 | 528994 | TAGGTAAGCAACCCAC | e-e-e-d(10)-k-k-k | 53 | 1316 |
| 75968 | 75984 | 530064 | GTAGGTAAGCAACCCAC | e-e-k-d(10)-k-e-k-e | 53 | 1317 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 75968 | 75983 | 530384 | TAGGTAAGCAACCCAC | e-k-d(10)-k-e-k-e | 48 | 1316 |
| 75969 | 75984 | 528995 | GTAGGTAAGCAACCCA | e-e-e-d(10)-k-k-k | 64 | 388 |
| 75969 | 75984 | 530129 | GTAGGTAAGCAACCCA | e-k-k-d(10)-k-k-e | 79 | 388 |
| 75969 | 75984 | 530179 | GTAGGTAAGCAACCCA | e-e-k-d(10)-k-k-e | 74 | 388 |
| 75969 | 75984 | 530229 | GTAGGTAAGCAACCCA | e-d-k-d(10)-k-k-e | 64 | 388 |
| 75969 | 75984 | 530279 | GTAGGTAAGCAACCCA | e-d-d-k-d(9)-k-k-e | 55 | 388 |
| 75969 | 75984 | 530329 | GTAGGTAAGCAACCCA | e-e-e-e-d(9)-k-k-e | 61 | 388 |
| 75971 | 75986 | 528996 | AGGTAGGTAAGCAACC | e-e-e-d(10)-k-k-k | 21 | 1318 |
| 75975 | 75990 | 528997 | TTATAGGTAGGTAAGC | e-e-e-d(10)-k-k-k | 10 | 1319 |
| 75979 | 75994 | 528998 | CACCTTATAGGTAGGT | e-e-e-d(10)-k-k-k | 22 | 1320 |
| 75981 | 75996 | 528999 | ACCACCTTATAGGTAG | e-e-e-d(10)-k-k-k | 15 | 1321 |
| 75984 | 75999 | 529000 | TAAACCACCTTATAGG | e-e-e-d(10)-k-k-k | 0 | 1322 |
| 75985 | 76000 | 529001 | ATAAACCACCTTATAG | e-e-e-d(10)-k-k-k | 7 | 1323 |
| 75997 | 76012 | 529002 | GGACAGCAGCTTATAA | e-e-e-d(10)-k-k-k | 12 | 1324 |
| 75998 | 76013 | 529003 | AGGACAGCAGCTTATA | e-e-e-d(10)-k-k-k | 40 | 1325 |
| 75998 | 76013 | 530401 | AGGACAGCAGCTTATA | k-d(10)-k-e-k-e-e | 41 | 1325 |
| 75999 | 76014 | 529004 | CAGGACAGCAGCTTAT | e-e-e-d(10)-k-k-k | 38 | 1326 |
| 75999 | 76015 | 530031 | CCAGGACAGCAGCTTAT | e-e-k-d(10)-k-e-k-e | 58 | 1327 |
| 75999 | 76014 | 530351 | CAGGACAGCAGCTTAT | e-k-d(10)-k-e-k-e | 58 | 1326 |
| 75999 | 76014 | 530402 | CAGGACAGCAGCTTAT | k-d(10)-k-e-k-e-e | 60 | 1326 |
| 76000 | 76016 | 530032 | GCCAGGACAGCAGCTTA | e-e-k-d(10)-k-e-k-e | 74 | 1328 |
| 76000 | 76015 | 530099 | CCAGGACAGCAGCTTA | e-k-k-d(10)-k-k-e | 73 | 1329 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 76000 | 76015 | 530146 | CCAGGACAGCAGCTTA | e-e-k-d(10)-k-k-e | 70 | 1329 |
| 76000 | 76015 | 530196 | CCAGGACAGCAGCTTA | e-d-k-d(10)-k-k-e | 67 | 1329 |
| 76000 | 76015 | 530246 | CCAGGACAGCAGCTTA | e-d-d-k-d(9)-k-k-e | 39 | 1329 |
| 76000 | 76015 | 530296 | CCAGGACAGCAGCTTA | e-e-e-e-d(9)-k-k-e | 67 | 1329 |
| 76000 | 76015 | 530352 | CCAGGACAGCAGCTTA | e-k-d(10)-k-e-k-e | 67 | 1329 |
| 76001 | 76016 | 530100 | GCCAGGACAGCAGCTT | e-k-k-d(10)-k-k-e | 77 | 1330 |
| 76001 | 76016 | 530147 | GCCAGGACAGCAGCTT | e-e-k-d(10)-k-k-e | 84 | 1330 |
| 76001 | 76016 | 530197 | GCCAGGACAGCAGCTT | e-d-k-d(10)-k-k-e | 71 | 1330 |
| 76001 | 76016 | 530247 | GCCAGGACAGCAGCTT | e-d-d-k-d(9)-k-k-e | 53 | 1330 |
| 76001 | 76016 | 530297 | GCCAGGACAGCAGCTT | e-e-e-e-d(9)-k-k-e | 75 | 1330 |
| 76001 | 76016 | 530403 | GCCAGGACAGCAGCTT | k-d(10)-k-e-k-e-e | 77 | 1330 |
| 76002 | 76018 | 530033 | TGGCCAGGACAGCAGCT | e-e-k-d(10)-k-e-k-e | 65 | 1331 |
| 76002 | 76017 | 530353 | GGCCAGGACAGCAGCT | e-k-d(10)-k-e-k-e | 83 | 1332 |
| 76003 | 76018 | 530101 | TGGCCAGGACAGCAGC | e-k-k-d(10)-k-k-e | 59 | 1333 |
| 76003 | 76018 | 530148 | TGGCCAGGACAGCAGC | e-e-k-d(10)-k-k-e | 79 | 1333 |
| 76003 | 76018 | 530198 | TGGCCAGGACAGCAGC | e-d-k-d(10)-k-k-e | 54 | 1333 |
| 76003 | 76018 | 530248 | TGGCCAGGACAGCAGC | e-d-d-k-d(9)-k-k-e | 32 | 1333 |
| 76003 | 76018 | 530298 | TGGCCAGGACAGCAGC | e-e-e-e-d(9)-k-k-e | 73 | 1333 |
| 76014 | 76029 | 530404 | TTTGAATGCAGTGGCC | k-d(10)-k-e-k-e-e | 67 | 1334 |
| 76015 | 76031 | 530034 | AATTTGAATGCAGTGGC | e-e-k-d(10)-k-e-k-e | 69 | 1335 |
| 76015 | 76030 | 530354 | ATTTGAATGCAGTGGC | e-k-d(10)-k-e-k-e | 85 | 1336 |
| 76015 | 76030 | 530405 | ATTTGAATGCAGTGGC | k-d(10)-k-e-k-e-e | 55 | 1336 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 76016 | 76032 | 530035 | GAATTTGAATGCAGTGG | e-e-k-d(10)-k-e-k-e | 69 | 1337 |
| 76016 | 76031 | 530102 | AATTTGAATGCAGTGG | e-k-k-d(10)-k-k-e | 71 | 1338 |
| 76016 | 76031 | 530149 | AATTTGAATGCAGTGG | e-e-k-d(10)-k-k-e | 70 | 1338 |
| 76016 | 76031 | 530199 | AATTTGAATGCAGTGG | e-d-k-d(10)-k-k-e | 58 | 1338 |
| 76016 | 76031 | 530249 | AATTTGAATGCAGTGG | e-d-d-k-d(9)-k-k-e | 47 | 1338 |
| 76016 | 76031 | 530299 | AATTTGAATGCAGTGG | e-e-e-e-d(9)-k-k-e | 47 | 1338 |
| 76016 | 76031 | 530355 | AATTTGAATGCAGTGG | e-k-d(10)-k-e-k-e | 72 | 1338 |
| 76017 | 76032 | 530103 | GAATTTGAATGCAGTG | e-k-k-d(10)-k-k-e | 77 | 390 |
| 76017 | 76032 | 530150 | GAATTTGAATGCAGTG | e-e-k-d(10)-k-k-e | 73 | 390 |
| 76017 | 76032 | 530200 | GAATTTGAATGCAGTG | e-d-k-d(10)-k-k-e | 63 | 390 |
| 76017 | 76032 | 530250 | GAATTTGAATGCAGTG | e-d-d-k-d(9)-k-k-e | 59 | 390 |
| 76017 | 76032 | 530300 | GAATTTGAATGCAGTG | e-e-e-e-d(9)-k-k-e | 65 | 390 |
| 76029 | 76044 | 530435 | AAGTACACATTGGAAT | k-d(10)-k-e-k-e-e | 62 | 1339 |
| 76030 | 76046 | 530057 | TGAAGTACACATTGGAA | e-e-k-d(10)-k-e-k-e | 69 | 1340 |
| 76030 | 76045 | 530385 | GAAGTACACATTGGAA | e-k-d(10)-k-e-k-e | 70 | 1341 |
| 76031 | 76046 | 529005 | TGAAGTACACATTGGA | e-e-e-d(10)-k-k-k | 64 | 392 |
| 76031 | 76046 | 530130 | TGAAGTACACATTGGA | e-k-k-d(10)-k-k-e | 85 | 392 |
| 76031 | 76046 | 530180 | TGAAGTACACATTGGA | e-e-k-d(10)-k-k-e | 82 | 392 |
| 76031 | 76046 | 530230 | TGAAGTACACATTGGA | e-d-k-d(10)-k-k-e | 65 | 392 |
| 76031 | 76046 | 530280 | TGAAGTACACATTGGA | e-d-d-k-d(9)-k-k-e | 75 | 392 |
| 76031 | 76046 | 530330 | TGAAGTACACATTGGA | e-e-e-e-d(9)-k-k-e | 52 | 392 |
| 76039 | 76054 | 529006 | TTACACTATGAAGTAC | e-e-e-d(10)-k-k-k | 16 | 1342 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 76116 | 76131 | 529007 | AGTTAAAGTAGATACA | e-e-e-d(10)-k-k-k | 0 | 1343 |
| 76121 | 76136 | 529008 | CTGGAAGTTAAAGTAG | e-e-e-d(10)-k-k-k | 30 | 397 |
| 76130 | 76145 | 529009 | CGTTTATTTCTGGAAG | e-e-e-d(10)-k-k-k | 52 | 1344 |
| 76144 | 76159 | 529010 | CGGTTCCTATATAACG | e-e-e-d(10)-k-k-k | 21 | 1345 |
| 76145 | 76160 | 529011 | ACGGTTCCTATATAAC | e-e-e-d(10)-k-k-k | 10 | 1346 |

**Example 14: Dose-dependent antisense inhibition of human STAT3 in HuVEC cells**

**[0285]** Gapmers from the study described in Example 13 exhibiting significant *in vitro* inhibition of STAT3 were tested at various doses in HuVEC cells. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 39.1 nM, 156.3 nM, 625.0 nM, and 2,500.0 nM concentrations of antisense oligonucleotide, as specified in Table 15. After a treatment period of approximately 16 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0286]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 15. As illustrated in Table 15, STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 15**

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 39.1 nM | 156.3nM | 625.0 nM | 2500.0 nM | $IC_{50}$ (μM) |
| 481464 | 6 | 51 | 84 | 94 | 0.2 |
| 518345 | 0 | 9 | 56 | 84 | 0.6 |
| 518349 | 16 | 3 | 47 | 83 | 0.6 |
| 519636 | 16 | 41 | 75 | 89 | 0.2 |
| 519637 | 24 | 43 | 84 | 94 | 0.2 |
| 519638 | 6 | 34 | 70 | 92 | 0.3 |
| 528403 | 0 | 4 | 39 | 77 | 0.9 |
| 528458 | 0 | 15 | 46 | 81 | 0.7 |
| 528475 | 1 | 10 | 51 | 76 | 0.7 |
| 528476 | 0 | 11 | 42 | 80 | 0.7 |
| 528869 | 25 | 19 | 67 | 86 | 0.3 |
| 528880 | 0 | 3 | 45 | 76 | 0.8 |
| 528937 | 0 | 1 | 49 | 82 | 0.8 |

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 39.1 nM | 156.3nM | 625.0 nM | 2500.0 nM | $IC_{50}$ (μM) |
| 528938 | 0 | 9 | 50 | 82 | 0.7 |
| 528942 | 0 | 20 | 59 | 88 | 0.5 |
| 528959 | 0 | 4 | 55 | 79 | 0.7 |
| 529022 | 0 | 0 | 52 | 81 | 0.8 |
| 529023 | 0 | 0 | 53 | 90 | 0.6 |
| 529024 | 0 | 0 | 47 | 80 | 0.8 |
| 529025 | 0 | 11 | 50 | 90 | 0.6 |
| 529026 | 0 | 31 | 73 | 96 | 0.4 |
| 529027 | 0 | 7 | 36 | 80 | 0.9 |
| 530021 | 6 | 30 | 69 | 92 | 0.3 |
| 530025 | 10 | 33 | 73 | 92 | 0.3 |
| 530026 | 3 | 18 | 52 | 80 | 0.6 |
| 530041 | 0 | 28 | 72 | 91 | 0.4 |
| 530048 | 0 | 22 | 53 | 83 | 0.5 |
| 530049 | 2 | 16 | 69 | 92 | 0.4 |
| 530053 | 0 | 16 | 66 | 90 | 0.5 |
| 530062 | 4 | 56 | 85 | 94 | 0.2 |
| 530066 | 0 | 12 | 46 | 84 | 0.7 |
| 530088 | 2 | 39 | 77 | 93 | 0.3 |
| 530091 | 3 | 12 | 59 | 84 | 0.5 |
| 530092 | 7 | 27 | 65 | 85 | 0.4 |
| 530093 | 7 | 46 | 79 | 96 | 0.2 |
| 530094 | 0 | 17 | 63 | 89 | 0.5 |
| 530109 | 9 | 30 | 72 | 94 | 0.3 |
| 530110 | 0 | 23 | 61 | 83 | 0.5 |
| 530112 | 0 | 13 | 42 | 90 | 0.6 |
| 530114 | 0 | 21 | 62 | 79 | 0.6 |
| 530116 | 22 | 40 | 71 | 92 | 0.2 |
| 530123 | 8 | 19 | 72 | 93 | 0.3 |
| 530130 | 0 | 33 | 64 | 89 | 0.4 |
| 530131 | 4 | 34 | 81 | 93 | 0.3 |
| 530135 | 22 | 38 | 79 | 94 | 0.2 |
| 530138 | 6 | 23 | 57 | 86 | 0.4 |
| 530140 | 4 | 22 | 62 | 91 | 0.4 |
| 530147 | 0 | 15 | 51 | 83 | 0.6 |
| 530156 | 7 | 41 | 81 | 96 | 0.2 |
| 530161 | 0 | 20 | 46 | 78 | 0.7 |
| 530170 | 0 | 29 | 67 | 90 | 0.4 |
| 530175 | 37 | 52 | 84 | 95 | 0.1 |

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 39.1 nM | 156.3nM | 625.0 nM | 2500.0 nM | $IC_{50}$ (μM) |
| 530178 | 8 | 24 | 70 | 86 | 0.4 |
| 530180 | 0 | 0 | 61 | 82 | 0.6 |
| 530181 | 0 | 27 | 52 | 86 | 0.5 |
| 530185 | 0 | 22 | 54 | 86 | 0.5 |
| 530190 | 17 | 17 | 60 | 87 | 0.4 |
| 530206 | 8 | 29 | 73 | 93 | 0.3 |
| 530225 | 0 | 27 | 67 | 91 | 0.4 |
| 530228 | 11 | 16 | 64 | 86 | 0.4 |
| 530261 | 5 | 25 | 57 | 91 | 0.4 |
| 530270 | 7 | 11 | 62 | 91 | 0.4 |
| 530275 | 14 | 34 | 73 | 91 | 0.3 |
| 530278 | 1 | 27 | 60 | 85 | 0.4 |
| 530285 | 5 | 20 | 61 | 82 | 0.5 |
| 530306 | 3 | 14 | 66 | 85 | 0.5 |
| 530311 | 6 | 27 | 59 | 86 | 0.4 |
| 530320 | 3 | 17 | 56 | 85 | 0.5 |
| 530325 | 5 | 35 | 70 | 92 | 0.3 |
| 530328 | 4 | 34 | 61 | 87 | 0.4 |
| 530340 | 8 | 34 | 74 | 90 | 0.3 |
| 530341 | 2 | 23 | 77 | 89 | 0.4 |
| 530344 | 16 | 20 | 64 | 89 | 0.4 |
| 530345 | 15 | 35 | 77 | 94 | 0.2 |
| 530346 | 5 | 24 | 66 | 92 | 0.4 |
| 530353 | 7 | 25 | 57 | 83 | 0.5 |
| 530354 | 2 | 24 | 60 | 81 | 0.5 |
| 530359 | 0 | 4 | 44 | 89 | 0.7 |
| 530361 | 13 | 30 | 59 | 92 | 0.3 |
| 530365 | 0 | 0 | 45 | 88 | 0.7 |
| 530367 | 0 | 15 | 49 | 88 | 0.5 |
| 530368 | 0 | 27 | 64 | 89 | 0.4 |
| 530369 | 10 | 28 | 78 | 95 | 0.3 |
| 530373 | 13 | 29 | 64 | 92 | 0.3 |
| 530375 | 0 | 14 | 53 | 90 | 0.5 |
| 530380 | 8 | 40 | 80 | 94 | 0.2 |
| 530390 | 11 | 21 | 66 | 90 | 0.4 |
| 530391 | 20 | 7 | 49 | 86 | 0.5 |
| 530411 | 5 | 19 | 81 | 95 | 0.3 |
| 530430 | 0 | 8 | 53 | 91 | 0.6 |
| 530466 | 0 | 4 | 53 | 87 | 0.6 |

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 39.1 nM | 156.3nM | 625.0 nM | 2500.0 nM | $IC_{50}$ (μM) |
| 530468 | 4 | 17 | 65 | 90 | 0.4 |
| 530469 | 8 | 38 | 86 | 94 | 0.2 |
| 530470 | 5 | 39 | 78 | 91 | 0.3 |
| 530471 | 0 | 21 | 69 | 91 | 0.4 |
| 530476 | 7 | 9 | 32 | 89 | 0.7 |
| 530477 | 0 | 12 | 64 | 87 | 0.5 |
| 530478 | 0 | 14 | 59 | 90 | 0.5 |
| 530485 | 0 | 10 | 61 | 85 | 0.5 |
| 530486 | 0 | 17 | 64 | 80 | 0.5 |
| 530492 | 0 | 25 | 71 | 89 | 0.4 |
| 530493 | 4 | 23 | 58 | 88 | 0.4 |
| 530507 | 5 | 17 | 65 | 82 | 0.5 |
| 530508 | 0 | 14 | 56 | 89 | 0.5 |
| 530509 | 0 | 17 | 54 | 86 | 0.5 |
| 530513 | 6 | 24 | 74 | 91 | 0.3 |
| 530514 | 1 | 7 | 52 | 78 | 0.7 |
| 530515 | 0 | 19 | 73 | 89 | 0.4 |

**Example 15: Antisense inhibition of human STAT3 in HuVEC cells**

**[0287]** Additional antisense oligonucleotides were designed targeting a STAT3 nucleic acid and were tested for their effects on STAT3 mRNA *in vitro*. Cultured HuVEC 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 STAT3 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0288]** The chimeric antisense oligonucleotides in Table 16 are 3-10-3 deoxy, MOE and cEt gapmers or 3-10-4 deoxy, MOE and cEt gapmers. The 3-10-3 gapmers are 16 nucleosides in length, wherein the central gap segment comprises ten 2'-deoxynucleosides and is flanked on both sides (in the 5' and 3' directions) by wings comprising 3 nucleosides each. The 3-10-4 gapmers are 17 nucleosides in length, wherein the central gap segment comprises ten 2'-deoxynucleosides and is flanked on the 5' directions by a wing comprising 3 nucleosides and on the 3' direction by a wing comprising 4 nucleosides. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. The chemistry column of Table 16 presents the sugar motif of each gapmer, where 'e' indicates a 2'-MOE nucleoside, 'k' indicates a constrained ethyl (cEt) nucleoside, and 'd' indicates a 2'-deoxynucleoside.

**[0289]** "Human Target start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Human Target stop site" indicates the 3'-most nucleoside to which the gapmer is targeted in the human gene sequence. Each gapmer listed in Table 16 is targeted to human STAT3 mRNA,

designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_139276.2). Each gapmer listed in Table 17 is targeted to human STAT3 genomic sequence, designated herein as SEQ ID NO: 2 (the complement of GENBANK Accession No. NT_010755.14 truncated from nucleotides 4185000 to 4264000).

**Table 16**

Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1

| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
|---|---|---|---|---|---|---|
| 730 | 745 | 530011 | GGAGATTCTCTACCAC | k-k-k-d(10)-e-e-e | 73 | 53 |
| 1901 | 1916 | 529974 | AAGCCCTTGCCAGCCA | e-e-e-d(10)-k-k-k | 83 | 144 |
| 1901 | 1916 | 530012 | AAGCCCTTGCCAGCCA | k-k-k-d(10)-e-e-e | 73 | 144 |
| 2206 | 2221 | 530015 | CCATGATCTTATAGCC | k-k-k-d(10)-e-e-e | 38 | 175 |
| 3016 | 3031 | 481464 | CTATTTGGATGTCAGC | k-k-k-d(10)-k-k-k | 94 | 245 |
| 3461 | 3476 | 529975 | AGCACCAAGGAGGCTG | e-e-e-d(10)-k-k-k | 54 | 257 |
| 3461 | 3476 | 530013 | AGCACCAAGGAGGCTG | k-k-k-d(10)-e-e-e | 58 | 257 |
| 3584 | 3600 | 530018 | TCCTTAAACCTTCCTAT | e-e-k-d(10)-k-e-k-e | 46 | 1510 |
| 3585 | 3600 | 529944 | TCCTTAAACCTTCCTA | e-e-e-d(10)-k-k-k | 44 | 273 |
| 3585 | 3600 | 529977 | TCCTTAAACCTTCCTA | k-k-k-d(10)-e-e-e | 66 | 273 |
| 3592 | 3608 | 530019 | TTAGATTCTCCTTAAAC | e-e-k-d(10)-k-e-k-e | 43 | 1511 |
| 3593 | 3608 | 529945 | TTAGATTCTCCTTAAA | e-e-e-d(10)-k-k-k | 22 | 1166 |
| 3593 | 3608 | 529978 | TTAGATTCTCCTTAAA | k-k-k-d(10)-e-e-e | 49 | 1166 |
| 3596 | 3612 | 530020 | ATGCTTAGATTCTCCTT | e-e-k-d(10)-k-e-k-e | 85 | 1512 |
| 3597 | 3612 | 529979 | ATGCTTAGATTCTCCT | k-k-k-d(10)-e-e-e | 86 | 1169 |
| 3599 | 3614 | 529946 | AAATGCTTAGATTCTC | e-e-e-d(10)-k-k-k | 46 | 1172 |
| 3599 | 3614 | 529980 | AAATGCTTAGATTCTC | k-k-k-d(10)-e-e-e | 25 | 1172 |
| 3716 | 3731 | 529947 | CAGATCAAGTCCAGGG | e-e-e-d(10)-k-k-k | 68 | 1187 |
| 3716 | 3731 | 529981 | CAGATCAAGTCCAGGG | k-k-k-d(10)-e-e-e | 83 | 1187 |
| 3718 | 3733 | 529948 | AGCAGATCAAGTCCAG | e-e-e-d(10)-k-k-k | 75 | 1190 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 1 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 3718 | 3733 | 529982 | AGCAGATCAAGTCCAG | k-k-k-d(10)-e-e-e | 84 | 1190 |
| 4236 | 4251 | 529983 | AGGTGTTCCCATACGC | k-k-k-d(10)-e-e-e | 96 | 1245 |
| 4237 | 4252 | 529984 | TAGGTGTTCCCATACG | k-k-k-d(10)-e-e-e | 91 | 336 |
| 4437 | 4452 | 529949 | CATCAACTGTCTCCAG | e-e-e-d(10)-k-k-k | 48 | 354 |
| 4437 | 4452 | 529985 | CATCAACTGTCTCCAG | k-k-k-d(10)-e-e-e | 37 | 354 |
| 4439 | 4454 | 529950 | CACATCAACTGTCTCC | e-e-e-d(10)-k-k-k | 58 | 356 |
| 4439 | 4454 | 529986 | CACATCAACTGTCTCC | k-k-k-d(10)-e-e-e | 72 | 356 |
| 4646 | 4661 | 529987 | TACAATCAGAGTTAAG | k-k-k-d(10)-e-e-e | 0 | 378 |
| 4664 | 4679 | 529951 | TCCTCTCAGAACTTTT | e-e-e-d(10)-k-k-k | 38 | 380 |
| 4664 | 4679 | 529988 | TCCTCTCAGAACTTTT | k-k-k-d(10)-e-e-e | 40 | 380 |
| 4782 | 4797 | 530016 | GTAGGTAAGCAACCCA | k-k-k-d(10)-e-e-e | 60 | 388 |
| 4813 | 4828 | 529952 | CCAGGACAGCAGCTTA | e-e-e-d(10)-k-k-k | 65 | 1329 |
| 4813 | 4828 | 529989 | CCAGGACAGCAGCTTA | k-k-k-d(10)-e-e-e | 63 | 1329 |
| 4814 | 4829 | 529953 | GCCAGGACAGCAGCTT | e-e-e-d(10)-k-k-k | 65 | 1330 |
| 4814 | 4829 | 529990 | GCCAGGACAGCAGCTT | k-k-k-d(10)-e-e-e | 75 | 1330 |
| 4816 | 4831 | 529954 | TGGCCAGGACAGCAGC | e-e-e-d(10)-k-k-k | 79 | 1333 |
| 4816 | 4831 | 529991 | TGGCCAGGACAGCAGC | k-k-k-d(10)-e-e-e | 52 | 1333 |
| 4829 | 4844 | 529955 | AATTTGAATGCAGTGG | e-e-e-d(10)-k-k-k | 52 | 1338 |
| 4829 | 4844 | 529992 | AATTTGAATGCAGTGG | k-k-k-d(10)-e-e-e | 23 | 1338 |
| 4830 | 4845 | 529956 | GAATTTGAATGCAGTG | e-e-e-d(10)-k-k-k | 60 | 390 |
| 4830 | 4845 | 529993 | GAATTTGAATGCAGTG | k-k-k-d(10)-e-e-e | 51 | 390 |
| 4844 | 4859 | 530014 | TGAAGTACACATTGGA | k-k-k-d(10)-e-e-e | 67 | 392 |

**Table 17**

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74203 | 74218 | CTATTTGGATGTCAGC | 481464 | k-k-k-d(10)-k-k-k | 94 | 245 |
| 74772 | 74787 | TCCTTAAACCTTCCTA | 529944 | e-e-e-d(10)-k-k-k | 44 | 273 |
| 74780 | 74795 | TTAGATTCTCCTTAAA | 529945 | e-e-e-d(10)-k-k-k | 22 | 1166 |
| 74786 | 74801 | AAATGCTTAGATTCTC | 529946 | e-e-e-d(10)-k-k-k | 46 | 1172 |
| 74903 | 74918 | CAGATCAAGTCCAGGG | 529947 | e-e-e-d(10)-k-k-k | 68 | 1187 |
| 74905 | 74920 | AGCAGATCAAGTCCAG | 529948 | e-e-e-d(10)-k-k-k | 75 | 1190 |
| 75624 | 75639 | CATCAACTGTCTCCAG | 529949 | e-e-e-d(10)-k-k-k | 48 | 354 |
| 75626 | 75641 | CACATCAACTGTCTCC | 529950 | e-e-e-d(10)-k-k-k | 58 | 356 |
| 75851 | 75866 | TCCTCTCAGAACTTTT | 529951 | e-e-e-d(10)-k-k-k | 38 | 380 |
| 76000 | 76015 | CCAGGACAGCAGCTTA | 529952 | e-e-e-d(10)-k-k-k | 65 | 1329 |
| 76001 | 76016 | GCCAGGACAGCAGCTT | 529953 | e-e-e-d(10)-k-k-k | 65 | 1330 |
| 76003 | 76018 | TGGCCAGGACAGCAGC | 529954 | e-e-e-d(10)-k-k-k | 79 | 1333 |
| 76016 | 76031 | AATTTGAATGCAGTGG | 529955 | e-e-e-d(10)-k-k-k | 52 | 1338 |
| 76017 | 76032 | GAATTTGAATGCAGTG | 529956 | e-e-e-d(10)-k-k-k | 60 | 390 |
| 2340 | 2355 | ACATACAGTAAGACCA | 529957 | e-e-e-d(10)-k-k-k | 21 | 1376 |
| 2385 | 2400 | CAAAAATTTACAACCC | 529958 | e-e-e-d(10)-k-k-k | 10 | 1380 |
| 2410 | 2425 | CCAATGCTTTATCAGC | 529959 | e-e-e-d(10)-k-k-k | 51 | 1384 |
| 2671 | 2686 | AGACTAAAATCAAGGC | 529960 | e-e-e-d(10)-k-k-k | 30 | 1388 |
| 5002 | 5017 | AACTGAAATTCCTTGG | 529961 | e-e-e-d(10)-k-k-k | 52 | 1395 |
| 5701 | 5716 | GTACTCTTTCAGTGGT | 529962 | e-e-e-d(10)-k-k-k | 91 | 1399 |
| 8080 | 8095 | GCAGATTTACCTTCCT | 529963 | e-e-e-d(10)-k-k-k | 55 | 1409 |
| 9125 | 9140 | CTGCCCCTATGTATAA | 529964 | e-e-e-d(10)-k-k-k | 18 | 1413 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 11263 | 11278 | CTGCCCCTATGTATAA | 529964 | e-e-e-d(10)-k-k-k | 18 | 1413 |
| 9864 | 9879 | GCTTCTTCCTGAGACA | 529965 | e-e-e-d(10)-k-k-k | 52 | 1417 |
| 12347 | 12362 | GCTTCTTCCTGAGACA | 529965 | e-e-e-d(10)-k-k-k | 52 | 1417 |
| 9866 | 9881 | TGGCTTCTTCCTGAGA | 529966 | e-e-e-d(10)-k-k-k | 51 | 1420 |
| 12349 | 12364 | TGGCTTCTTCCTGAGA | 529966 | e-e-e-d(10)-k-k-k | 51 | 1420 |
| 9875 | 9890 | TCCTCCTGTTGGCTTC | 529967 | e-e-e-d(10)-k-k-k | 80 | 1425 |
| 12358 | 12373 | TCCTCCTGTTGGCTTC | 529967 | e-e-e-d(10)-k-k-k | 80 | 1425 |
| 9876 | 9891 | TTCCTCCTGTTGGCTT | 529968 | e-e-e-d(10)-k-k-k | 56 | 1426 |
| 12359 | 12374 | TTCCTCCTGTTGGCTT | 529968 | e-e-e-d(10)-k-k-k | 56 | 1426 |
| 9878 | 9893 | GGTTCCTCCTGTTGGC | 529969 | e-e-e-d(10)-k-k-k | 69 | 1429 |
| 12361 | 12376 | GGTTCCTCCTGTTGGC | 529969 | e-e-e-d(10)-k-k-k | 69 | 1429 |
| 16865 | 16880 | TATAATTGTGTACTGG | 529970 | e-e-e-d(10)-k-k-k | 41 | 1441 |
| 26063 | 26078 | CAACTTTAGCCCCTTC | 529971 | e-e-e-d(10)-k-k-k | 32 | 1452 |
| 48404 | 48419 | CACACTTTCCATTCTA | 529972 | e-e-e-d(10)-k-k-k | 30 | 1476 |
| 71616 | 71631 | CAGTACAATTGCTTCA | 529973 | e-e-e-d(10)-k-k-k | 49 | 1505 |
| 66138 | 66153 | AAGCCCTTGCCAGCCA | 529974 | e-e-e-d(10)-k-k-k | 83 | 144 |
| 74648 | 74663 | AGCACCAAGGAGGCTG | 529975 | e-e-e-d(10)-k-k-k | 54 | 257 |
| 2705 | 2720 | CTAATGGTTCTTTGTG | 529976 | e-e-e-d(10)-k-k-k | 25 | 411 |
| 74772 | 74787 | TCCTTAAACCTTCCTA | 529977 | k-k-k-d(10)-e-e-e | 66 | 273 |
| 74780 | 74795 | TTAGATTCTCCTTAAA | 529978 | k-k-k-d(10)-e-e-e | 49 | 1166 |
| 74784 | 74799 | ATGCTTAGATTCTCCT | 529979 | k-k-k-d(10)-e-e-e | 86 | 1169 |
| 74786 | 74801 | AAATGCTTAGATTCTC | 529980 | k-k-k-d(10)-e-e-e | 25 | 1172 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74903 | 74918 | CAGATCAAGTCCAGGG | 529981 | k-k-k-d(10)-e-e-e | 83 | 1187 |
| 74905 | 74920 | AGCAGATCAAGTCCAG | 529982 | k-k-k-d(10)-e-e-e | 84 | 1190 |
| 75423 | 75438 | AGGTGTTCCCATACGC | 529983 | k-k-k-d(10)-e-e-e | 96 | 1245 |
| 75424 | 75439 | TAGGTGTTCCCATACG | 529984 | k-k-k-d(10)-e-e-e | 91 | 336 |
| 75624 | 75639 | CATCAACTGTCTCCAG | 529985 | k-k-k-d(10)-e-e-e | 37 | 354 |
| 75626 | 75641 | CACATCAACTGTCTCC | 529986 | k-k-k-d(10)-e-e-e | 72 | 356 |
| 75833 | 75848 | TACAATCAGAGTTAAG | 529987 | k-k-k-d(10)-e-e-e | 0 | 378 |
| 75851 | 75866 | TCCTCTCAGAACTTTT | 529988 | k-k-k-d(10)-e-e-e | 40 | 380 |
| 76000 | 76015 | CCAGGACAGCAGCTTA | 529989 | k-k-k-d(10)-e-e-e | 63 | 1329 |
| 76001 | 76016 | GCCAGGACAGCAGCTT | 529990 | k-k-k-d(10)-e-e-e | 75 | 1330 |
| 76003 | 76018 | TGGCCAGGACAGCAGC | 529991 | k-k-k-d(10)-e-e-e | 52 | 1333 |
| 76016 | 76031 | AATTTGAATGCAGTGG | 529992 | k-k-k-d(10)-e-e-e | 23 | 1338 |
| 76017 | 76032 | GAATTTGAATGCAGTG | 529993 | k-k-k-d(10)-e-e-e | 51 | 390 |
| 2340 | 2355 | ACATACAGTAAGACCA | 529994 | k-k-k-d(10)-e-e-e | 44 | 1376 |
| 2385 | 2400 | CAAAAATTTACAACCC | 529995 | k-k-k-d(10)-e-e-e | 0 | 1380 |
| 2410 | 2425 | CCAATGCTTTATCAGC | 529996 | k-k-k-d(10)-e-e-e | 65 | 1384 |
| 2671 | 2686 | AGACTAAAATCAAGGC | 529997 | k-k-k-d(10)-e-e-e | 44 | 1388 |
| 5002 | 5017 | AACTGAAATTCCTTGG | 529998 | k-k-k-d(10)-e-e-e | 35 | 1395 |
| 5701 | 5716 | GTACTCTTTCAGTGGT | 529999 | k-k-k-d(10)-e-e-e | 91 | 1399 |
| 8080 | 8095 | GCAGATTTACCTTCCT | 530000 | k-k-k-d(10)-e-e-e | 80 | 1409 |
| 9125 | 9140 | CTGCCCCTATGTATAA | 530001 | k-k-k-d(10)-e-e-e | 21 | 1413 |
| 11263 | 11278 | CTGCCCCTATGTATAA | 530001 | k-k-k-d(10)-e-e-e | 21 | 1413 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 9864 | 9879 | GCTTCTTCCTGAGACA | 530002 | k-k-k-d(10)-e-e-e | 74 | 1417 |
| 12347 | 12362 | GCTTCTTCCTGAGACA | 530002 | k-k-k-d(10)-e-e-e | 74 | 1417 |
| 9866 | 9881 | TGGCTTCTTCCTGAGA | 530003 | k-k-k-d(10)-e-e-e | 67 | 1420 |
| 12349 | 12364 | TGGCTTCTTCCTGAGA | 530003 | k-k-k-d(10)-e-e-e | 67 | 1420 |
| 9875 | 9890 | TCCTCCTGTTGGCTTC | 530004 | k-k-k-d(10)-e-e-e | 83 | 1425 |
| 12358 | 12373 | TCCTCCTGTTGGCTTC | 530004 | k-k-k-d(10)-e-e-e | 83 | 1425 |
| 9876 | 9891 | TTCCTCCTGTTGGCTT | 530005 | k-k-k-d(10)-e-e-e | 77 | 1426 |
| 12359 | 12374 | TTCCTCCTGTTGGCTT | 530005 | k-k-k-d(10)-e-e-e | 77 | 1426 |
| 9878 | 9893 | GGTTCCTCCTGTTGGC | 530006 | k-k-k-d(10)-e-e-e | 89 | 1427 |
| 12361 | 12376 | GGTTCCTCCTGTTGGC | 530006 | k-k-k-d(10)-e-e-e | 89 | 1427 |
| 16865 | 16880 | TATAATTGTGTACTGG | 530007 | k-k-k-d(10)-e-e-e | 21 | 1441 |
| 26063 | 26078 | CAACTTTAGCCCCTTC | 530008 | k-k-k-d(10)-e-e-e | 58 | 1452 |
| 48404 | 48419 | CACACTTTCCATTCTA | 530009 | k-k-k-d(10)-e-e-e | 59 | 1476 |
| 71616 | 71631 | CAGTACAATTGCTTCA | 530010 | k-k-k-d(10)-e-e-e | 75 | 1505 |
| 50694 | 50709 | GGAGATTCTCTACCAC | 530011 | k-k-k-d(10)-e-e-e | 73 | 53 |
| 66138 | 66153 | AAGCCCTTGCCAGCCA | 530012 | k-k-k-d(10)-e-e-e | 73 | 144 |
| 74648 | 74663 | AGCACCAAGGAGGCTG | 530013 | k-k-k-d(10)-e-e-e | 58 | 257 |
| 76031 | 76046 | TGAAGTACACATTGGA | 530014 | k-k-k-d(10)-e-e-e | 67 | 392 |
| 67068 | 67083 | CCATGATCTTATAGCC | 530015 | k-k-k-d(10)-e-e-e | 38 | 175 |
| 75969 | 75984 | GTAGGTAAGCAACCCA | 530016 | k-k-k-d(10)-e-e-e | 60 | 388 |
| 2705 | 2720 | CTAATGGTTCTTTGTG | 530017 | k-k-k-d(10)-e-e-e | 46 | 411 |
| 74771 | 74787 | TCCTTAAACCTTCCTAT | 530018 | e-e-k-d(10)-k-e-k-e | 46 | 1510 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | | |
|---|---|---|---|---|---|---|
| Human Start Site | Human Stop Site | ISIS No | Sequence | Chemistry | % inhibition | SEQ ID NO |
| 74779 | 74795 | TTAGATTCTCCTTAAAC | 530019 | e-e-k-d(10)-k-e-k-e | 43 | 1511 |
| 74783 | 74799 | ATGCTTAGATTCTCCTT | 530020 | e-e-k-d(10)-k-e-k-e | 85 | 1512 |

**Example 16: Dose-dependent antisense inhibition of human STAT3 in HuVEC cells**

**[0290]** Gapmers from the study described in Example 15 exhibiting significant *in vitro* inhibition of STAT3 were tested at various doses in HuVEC cells. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 39.1 nM, 156.3 nM, 625.0 nM, and 2,500.0 nM concentrations of antisense oligonucleotide, as specified in Table 18. After a treatment period of approximately 16 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0291]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 18. As illustrated in Table 18, STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 18**

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 39.1 nM | 156.3 nM | 625.0 nM | 2500.0 nM | $IC_{50}$ (μM) |
| 481464 | 41 | 78 | 92 | 91 | 0.04 |
| 529962 | 30 | 51 | 86 | 95 | 0.12 |
| 529979 | 0 | 43 | 81 | 95 | 0.27 |
| 529982 | 0 | 0 | 70 | 90 | 0.56 |
| 529983 | 31 | 67 | 87 | 94 | 0.08 |
| 529984 | 17 | 44 | 83 | 97 | 0.19 |
| 529999 | 29 | 51 | 83 | 96 | 0.13 |
| 530006 | 18 | 38 | 77 | 94 | 0.22 |
| 530020 | 2 | 39 | 75 | 92 | 0.28 |

**Example 17: Effect of ISIS antisense oligonucleotides targeting STAT3 in the treatment of an MDA-MB-231 human breast cancer xenograft model**

**[0292]** BALB/c nude mice inoculated with human breast cancer cells MDA-MB-231 were treated with ISIS 481464 and ISIS 481549. ISIS 481549 is cross-reactive with the mouse sequence (i.e, hybridizes to the mouse sequence). Tumor growth and tolerability of oligonucleotides in the mice was evaluated.

***Treatment***

**[0293]** The study was conducted at Pharmaron Inc (Beijing, P.R. China). The BALB/c nude mice were obtained from Beijing HFK Bio-Technology Co., Ltd. MDA-MB-231 human breast cancer cells were maintained *in vitro* as a monolayer culture in Leibovitz's L-15 medium supplemented with 10% heat-inactivated fetal calf serum, 100 U/mL penicillin, 100 µg/mL streptomycin, and 2 mM L-glutamine. The cells were maintained at 37°C in an atmosphere of 5% $CO_2$ in air. The tumor cells were routinely sub-cultured twice weekly with trypsin-EDTA treatment. Cells growing at exponential growth phase were harvested and counted for tumor inoculation.

**[0294]** Three groups of eight randomly assigned 6-8 week-old female BALB/c nude mice each were inoculated in the right flank with the MDA-MB-231 tumor fragments (3 mm x 2 mm x 2 mm, which were generated from tumor inoculation passage) for tumor development. Antisense oligonucleotide treatment started at day 11 after tumor inoculation when the mean tumor size reached approximately 100 $mm^3$. Two of the groups were injected intraperitoneally twice a week for 3 weeks with 25 mg/kg of ISIS 481464 or ISIS 481549. A control group of mice was injected intraperitoneally twice a week for 3 weeks with PBS.

**[0295]** All procedures related to animal handling, care, and treatment, were performed according to the guidelines approved by the Institutional Animal Care and Use Committee (IACUC). Animals were routinely checked for any effects of tumor growth on normal behavior, such as mobility, food consumption, body weight changes, and any other abnormal effect.

***RNA analysis***

**[0296]** RNA was extracted from tumor tissue for real-time PCR analysis of human STAT3 mRNA levels using primer probe set RTS199, described hereinabove. Murine STAT3 mRNA levels were also measured using primer probe set mSTAT3_LTS00664 (forward sequence CGACAGCTTCCCCATGGA, designated herein as SEQ ID NO: 1513; reverse sequence ATGCCCAGTCTTGACTCTCAATC, designated herein as SEQ ID NO: 1514; probe sequence CTGCGGCAGTTCCTGGCACCTT, designated herein as SEQ ID NO: 1515). Results are presented as percent inhibition of STAT3, relative to PBS control, normalized to cyclophilin. As shown in Table 19, treatment with ISIS antisense oligonucleotides resulted in reduction of both human and murine STAT3 mRNA in comparison to the PBS control.

**Table 19**

| Percent inhibition of STAT3 mRNA in the treatment groups relative to the PBS control in the MDA-MB-231 xenograft model | | |
|---|---|---|
| ISIS No | human STAT3 | murine STAT3 |
| 481464 | 25 | 16 |
| 481549 | 22 | 44 |

***Effect on tumor growth***

**[0297]** Tumor size was measured twice weekly in two dimensions using a caliper. Tumor volumes were calculated using the formula: $V = 0.536 \times a \times b^2$, where *a* and *b* are the long and short diameters of the tumor, respectively. The tumor size was utilized for calculations of the T-C and $T_V/C_V$ values. T-C was calculated with T as the median time (in days) required for the tumors in the treatment groups to reach a pre-determined size (900 $mm^3$), and C as the median time (in days) for the tumors in the control group to reach the same size. The

$T_V/C_V$ value (expressed as percentage) is an indication of the anti-tumor effectiveness of the ISIS oligonucleotides, where $T_V$ and $C_V$ were the mean volume of the treated and control groups, respectively, on a given day (day 32).

**[0298]** The results are presented in Tables 20 and 21. The data indicates that treatment with ISIS 481464 and ISIS 481549 significantly impeded tumor growth.

**Table 20**

| Effect of antisense inhibition of STAT3 on tumor growth in the MDA-MB-231 xenograft model | | | |
|---|---|---|---|
| Day | PBS | ISIS 481464 | ISIS 481549 |
| 11 | 103 | 104 | 104 |
| 15 | 185 | 142 | 158 |
| 18 | 292 | 200 | 205 |
| 22 | 519 | 305 | 326 |
| 25 | 745 | 430 | 436 |
| 29 | 1,332 | 643 | 688 |
| 32 | 1,741 | 921 | 984 |

**Table 21**

| Effect of antisense inhibition of STAT3 on tumor growth inhibition in the MDA-MB-231 xenograft model | | | |
|---|---|---|---|
| Treatment | Tumor Size ($mm^3$) at day 32 | $T_V/C_V$ (%) | T-C at 900 $mm^3$ |
| PBS | 1,741 | - | - |
| ISIS 481464 | 921 | 53 | 6 |
| ISIS 481549 | 984 | 57 | 5 |

***Body weight measurements***

**[0299]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were measured on a regular basis during the treatment period. The data is presented in Table 22 and indicate that treatment with either ISIS 481464 or ISIS 481549 does not cause significant weight gain or loss.

**Table 22**

| Body weight measurements of mice in the MDA-MB-231 xenograft model | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Day 11 | Day 15 | Day 18 | Day 22 | Day 25 | Day 29 | Day 32 |
| PBS | 21.8 | 22.2 | 22.5 | 22.5 | 22.9 | 23.4 | 24.0 |
| ISIS 481464 | 22.3 | 22.8 | 23.0 | 23.2 | 23.8 | 23.9 | 24.9 |
| ISIS 481549 | 22.2 | 22.5 | 23.0 | 23.3 | 23.7 | 23.7 | 24.6 |

**Example 18: Effect of ISIS antisense oligonucleotides targeting STAT3 in the treatment of an A431 human epidermoid carcinoma xenograft model**

**[0300]** BALB/c nude mice inoculated with human epidermoid cancer cells A431 were treated with ISIS 481464 and ISIS 481549. ISIS 481549 is cross-reactive with the mouse sequence (i.e, hybridizes to the mouse

sequence). The effect of the treatment on tumor growth and tolerability in the mice was evaluated.

***Treatment***

**[0301]** The study was conducted at Pharmaron Inc (Beijing, P.R. China). The BALB/c nude mice were obtained from Beijing HFK Bio-Technology Co., Ltd. A431 human epidermoid carcinoma cells were maintained *in vitro* as a monolayer culture in DMEM medium supplemented with 10% heat-inactivated fetal calf serum, 100 U/mL penicillin, 100 µg/mL streptomycin, and 2 mM L-glutamine. The cells were maintained at 37°C in an atmosphere of 5% $CO_2$ in air. The tumor cells were routinely sub-cultured twice weekly with trypsin-EDTA treatment. Cells growing in an exponential growth phase were harvested and counted for tumor inoculation.

**[0302]** Three groups of eight randomly assigned 6-8 week-old female BALB/c nude mice each were inoculated subcutaneously with 5 x $10^6$ A431 tumor cells for tumor development. Antisense oligonucleotide treatment started at day 8 after tumor inoculation when the mean tumor size reached approximately 95 $mm^3$. Two of the groups were injected intraperitoneally twice a week for 4 weeks with 25 mg/kg of ISIS 481464 or ISIS 481549. A control group of mice was injected intraperitoneally twice a week for 4 weeks with PBS.

**[0303]** All procedures related to animal handling, care, and treatment, were performed according to the guidelines approved by the Institutional Animal Care and Use Committee (IACUC). At the time of routine monitoring, the animals were checked for any effects of tumor growth on normal behavior, such as mobility, food consumption, body weight changes and any other abnormal effect.

***RNA analysis***

**[0304]** RNA was extracted from tumor tissue for real-time PCR analysis of human STAT3 mRNA levels using primer probe set RTS199, described hereinabove. Murine STAT3 mRNA levels were also measured using primer probe set mSTAT3_LTS00664, described hereinabove. Results are presented as percent inhibition of STAT3, relative to PBS control, normalized to cyclophilin. As shown in Table 23, treatment with ISIS antisense oligonucleotides resulted in reduction of both human and murine STAT3 mRNA in comparison to the PBS control.

**Table 23**

| Inhibition of STAT3 mRNA in the treatment groups relative to the PBS control in the A431 xenograft model | | |
|---|---|---|
| ISIS No | human STAT3 | murine STAT3 |
| 481464 | 63 | 26 |
| 481549 | 29 | 38 |

***Protein analysis***

**[0305]** Protein was extracted from tumor lysates for western analysis of human STAT3 protein levels with STAT3 monoclonal antibody (Cell Signaling Technology, Cat #9135). Results are presented as percent inhibition of STAT3, relative to PBS control, normalized to the house-keeping protein, COX-II. As shown in Table 24, treatment with ISIS antisense oligonucleotides resulted in reduction of STAT3 protein levels in comparison to the PBS control.

**Table 24**

| Inhibition of STAT3 protein levels in the treatment groups relative to the PBS control in the A431 xenograft model | |
|---|---|
| ISIS No | % reduction |
| 481464 | 99 |
| 481549 | 22 |

***Effect on tumor growth***

**[0306]** Tumor size was measured twice weekly in two dimensions using a caliper, and tumor volumes were calculated using the formula: $V = 0.5 \times a \times b^2$, where *a* and *b* are the long and short diameters of the tumor, respectively. The tumor size was utilized for calculations of the T-C and $T_V/C_V$ values. T-C was calculated with T as the median time (in days) required for the tumors in the treatment groups to reach a pre-determined size (800 $mm^3$), and C as the median time (in days) for the tumors in the control group to reach the same size. The Tv/Cv value (expressed as percentage) is an indication of the anti-tumor effectiveness of the ISIS oligonucleotides, where $T_V$ and $C_V$ were the mean volume of the treated and control groups, respectively, on a given day (day 33).

**[0307]** The results are presented in Tables 25 and 26. The data indicates that treatment with either ISIS 481464 or ISIS 481549 significantly impeded tumor growth.

**Table 25**

| Effect of antisense inhibition of STAT3 on tumor growth in the A431 xenograft model | | | |
|---|---|---|---|
| Days | PBS | ISIS 481464 | ISIS 481549 |
| 8 | 94 | 95 | 95 |
| 14 | 178 | 157 | 132 |
| 17 | 308 | 261 | 202 |
| 21 | 528 | 412 | 304 |
| 24 | 682 | 552 | 426 |
| 28 | 875 | 698 | 555 |
| 31 | 1,071 | 898 | 716 |
| 33 | 1,210 | 1,030 | 858 |

**Table 26**

| Effect of antisense inhibition of STAT3 on tumor growth inhibition in the A431 xenograft model | | | |
|---|---|---|---|
| Treatment | Tumor Size ($mm^3$) at day 33 | $T_V/C_V$ (%) | T-C at 800 $mm^3$ |
| PBS | 1,210 | - | |
| ISIS 481464 | 1,030 | 85 | 3 |
| ISIS 481549 | 858 | 71 | 6 |

***Body weight measurements***

**[0308]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were measured on a regular basis during the treatment period. The data is presented in Table 27 and indicate that

treatment with either ISIS 481464 or ISIS 481549 does not affect the overall health of the mice.

**Table 27**

| Body weight measurements of mice in the A431 xenograft model | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day 8 | Day 14 | Day 17 | Day 21 | Day 24 | Day 28 | Day 31 | Day 33 |
| PBS | 20 | 20 | 20 | 21 | 21 | 21 | 22 | 22 |
| ISIS 481464 | 20 | 21 | 21 | 21 | 21 | 22 | 22 | 23 |
| ISIS 481549 | 20 | 20 | 21 | 21 | 21 | 22 | 22 | 22 |

**Example 19: Effect of ISIS antisense oligonucleotides targeting STAT3 in the treatment of an NCI-H460 human non-small cell lung cancer (NSCLC) xenograft model**

**[0309]** BALB/c nude mice inoculated with human NCI-H460 human NSCLC were treated with ISIS 491464, which targets human STAT3, and ISIS 481549, which targets both human and murine STAT3. The effect of the treatment on tumor growth and tolerability in the mice was evaluated.

***Treatment***

**[0310]** The study was conducted at Pharmaron Inc (Beijing, P.R. China). The BALB/c nude mice were obtained from Beijing HFK Bio-Technology Co., Ltd. NCI-H460 human NSCLC cells were maintained *in vitro* as a monolayer culture in RPMI-1640 medium supplemented with 10% heat-inactivated fetal calf serum, 100 U/mL penicillin, 100 µg/mL streptomycin, and 2 mM L-glutamine. The cells were maintained at 37°C in an atmosphere of 5% $CO_2$ in air. The tumor cells were routinely sub-cultured twice weekly with trypsin-EDTA treatment. Cells growing in an exponential growth phase were harvested and counted for tumor inoculation.

**[0311]** Three groups of eight randomly assigned 6-8 week-old female BALB/c nude mice each were inoculated subcutaneously with 2 x $10^6$ NCI-H460 tumor cells for tumor development. Antisense oligonucleotide treatment started at day 6 after tumor inoculation when the mean tumor size reached approximately 100 $mm^3$. Two of the groups were injected intraperitoneally twice a week for 3 weeks with 25 mg/kg of ISIS 481464 or ISIS 481549. The third group of mice was injected intraperitoneally twice a week for 3 weeks with PBS, and served as the control group.

**[0312]** All procedures related to animal handling, care, and treatment, were performed according to the guidelines approved by the Institutional Animal Care and Use Committee (IACUC). At the time of routine monitoring, the animals were checked for any effects of tumor growth on normal behavior, such as mobility, food consumption, body weight changes and any other abnormal effect.

***RNA analysis***

**[0313]** RNA was extracted from tumor tissue for real-time PCR analysis of human STAT3 mRNA levels using primer probe set RTS199, described hereinabove. Murine STAT3 mRNA levels were also measured using primer probe set mSTAT3_LTS00664, described hereinabove. Results are presented as percent inhibition of STAT3, relative to PBS control, normalized to cyclophilin. As shown in Table 28, treatment with ISIS antisense oligonucleotides resulted in reduction of both human and murine STAT3 mRNA in comparison to the PBS control.

**Table 28**

| Inhibition of STAT3 mRNA in the treatment groups relative to the PBS control in the NCI-H460 xenograft model | | |
|---|---|---|
| ISIS No | human STAT3 | murine STAT3 |
| 481464 | 34 | 0 |
| 481549 | 20 | 35 |

***Effect on tumor growth***

**[0314]** Tumor size was measured twice weekly in two dimensions using a caliper, and tumor volumes were calculated using the formula: $V = 0.5 \times a \times b^2$, where *a* and *b* are the long and short diameters of the tumor, respectively. The tumor size was utilized for calculations of the T-C and $T_V/C_V$ values. T-C was calculated with T as the median time (in days) required for the tumors in the treatment groups to reach a pre-determined size (1,500 $mm^3$), and C as the median time (in days) for the tumors in the control group to reach the same size. The $T_V/C_V$ value (expressed as percentage) is an indication of the anti-tumor effectiveness of the ISIS oligonucleotides, where $T_V$ and $C_V$ were the mean volume of the treated and control groups, respectively, on a given day (day 20).

**[0315]** The results are presented in Tables 29 and 30. The data indicates that treatment with either ISIS 481464 or ISIS 481549 significantly impeded tumor growth.

**Table 29**

| Effect of antisense inhibition of STAT3 on tumor growth in the NCI-H460 xenograft model | | | |
|---|---|---|---|
| Days | PBS | ISIS 481464 | ISIS 481549 |
| 6 | 104 | 104 | 103 |
| 8 | 303 | 197 | 197 |
| 11 | 746 | 498 | 443 |
| 13 | 1,175 | 676 | 654 |
| 15 | 1,642 | 982 | 954 |
| 18 | 2,277 | 1,571 | 1,577 |
| 20 | 2,859 | 1,996 | 2,093 |
| 22 | - | 2,609 | 2,679 |

**Table 30**

| Effect of antisense inhibition of STAT3 on tumor growth inhibition in the NCI-H460 xenograft model | | | |
|---|---|---|---|
| Treatment | Tumor Size ($mm^3$) at day 20 | $T_V/C_V$ (%) | T-C at 1,500 $mm^3$ |
| PBS | 1,210 | - | - |
| ISIS 481464 | 1,030 | 85 | 3 |
| ISIS 481549 | 858 | 71 | 6 |

***Body weight measurements***

**[0316]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were

measured on a regular basis during the treatment period. The data is presented in Table 31 and indicate that treatment with either ISIS 481464 or ISIS 481549 does not affect the overall health of the mice.

**Table 31**

| Body weight measurements of mice in the NCI-H460 xenograft model | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day 6 | Day 8 | Day 11 | Day 13 | Day 15 | Day 18 | Day 20 | Day 22 |
| PBS | 20 | 20 | 20 | 20 | 20 | 20 | 21 | - |
| ISIS 481464 | 20 | 20 | 20 | 20 | 19 | 19 | 20 | 20 |
| ISIS 481549 | 20 | 20 | 20 | 20 | 20 | 19 | 20 | 20 |

**Example 20: Effect of antisense inhibition of human STAT3 in a human glioblastoma orthotopic mouse model**

**[0317]** NU/J mice orthotopically implanted with human glioblastoma cells were treated with ISIS 455291, a 5-10-5 MOE gapmer having a sequence of CAGCAGATCAAGTCCAGGGA (SEQ ID NO: 1590). The effect of the treatment on tumor growth and tolerability in the mice was evaluated.

***Treatment***

**[0318]** Thirty NU/J mice were stereotactically implanted in the right frontal lobe with 5 x $10^5$ U-87 MG-luc2 cells. On day 15 after tumor cell implantation, 15 of these mice were dosed intracranially with a bolus injection at the site of tumor implantation with 100 µg of ISIS 455291, which was dissolved in 2 µL of PBS. The remaining 15 mice were dosed intracranially with a bolus injection at the site of tumor implantation with 2 µL of PBS. The second group of mice served as the control group.

***Analysis***

**[0319]** On day 18 after tumor transplantation, five mice from each group were euthanized by $CO_2$ inhalation and brain samples were collected for RNA analysis. RNA was extracted from tumor tissue for real-time PCR analysis of human STAT3 mRNA levels using primer probe set RTS199, described hereinabove. Treatment with ISIS 455291 resulted in 27% reduction of human STAT3 mRNA in the tumor tissue in comparison to the PBS control.

**[0320]** The remaining mice in each group were monitored regularly up to 2 weeks for survival analysis. The median survival for the PBS control group was 30.5 days. The medial survival for the ISIS oligonucleotide-treated mice was 35 days. The P value was 0.2088.

**Example 21: Effect of treatment with ISIS 481549 in APC/Min$^+$ mice**

**[0321]** The effect of treatment with ISIS 481549 on STAT3 mRNA levels and intestinal adenoma numbers in the APC/Min$^+$ mouse model was evaluated. The APC/Min$^+$ mice strain is predisposed to spontaneous intestinal adenoma formation throughout the entire intestinal tract at an early age (Moser A.R. et al., Science 1990. 247: 322-324).

***Treatment***

**[0322]** Two groups of 4 male nine-week-old APC/Min$^+$ mice were injected subcutaneously with 5 mg/kg or 25 mg/kg of ISIS 481549 administered five times a week (total weekly doses of 25 mg/kg and 125 mg/kg, respectively) for 4 weeks. A group of 4 male nine-week-old APC/Min$^+$ mice were injected subcutaneously with 50 mg/kg of control oligonucleotide, ISIS 141923, administered five times a week (total weekly dose of 250 mg/kg) for 4 weeks. A control group of 4 male nine-week-old APC/Min$^+$ mice were injected subcutaneously with PBS administered five times a week for 4 weeks. Mice were euthanized with isoflurance followed by cervical dislocation 48 hrs after the final injection.

**[0323]** Colons and intestines were removed, separated from each other and cleaned. Approximately 5 cm of the upper intestinal tract was excised and homogenized in 2.5 mL RLT buffer (Qiagen) with 1% of 2-mercaptoethanol (RLT-BMe) and placed in dry ice. The colon was cut in half and the proximal half of the tissue was homogenized in 2.5 mL RLT-BMe and placed in dry ice. A small piece of the liver (0.2 g) was excised and homogenized in RLT-BMe and placed in dry ice.

***RNA analysis***

**[0324]** RNA was isolated from the tissues using PureLink™ Total RNA Purification kit (Invitrogen; #12173-011A), according to the manufacturer's protocol. RT-PCR was performed using the StepOnePlus system (Applied Biosystems), according to the manufacturer's protocol. Murine primer probe set mSTAT3_LTS000664 (forward primer CGACAGCTTCCCCATGGA, designated herein as SEQ ID NO: 1513; reverse primer ATGCCCAGTCTTGACTCTCAATC, designated herein as SEQ ID NO: 1514; probe CTGCGGCAGTTCCTGGCACCTT, designated herein as SEQ ID NO: 1515) was used for measuring STAT3 mRNA levels. The mRNA level of the housekeeping gene, Cyclophilin, was measured with the primer probe set mcyclo_24 (forward primer TCGCCGCTTGCTGCA, designated herein as SEQ ID NO: 1516; reverse primer ATCGGCCGTGATGTCGA, designated herein as SEQ ID NO: 1517; probe CCATGGTCAACCCCACCGTGTTC, designated herein as SEQ ID NO: 1518) and was used to normalize STAT3 mRNA levels.

**[0325]** Treatment with ISIS 481549 resulted in statistically significant reduction in STAT3 mRNA expression in liver at 25 mg/kg/wk and 125 mg/kg/wk dosing in liver, small intestine and colon (Table 32) compared to the PBS control. Significant differences between the treatment and the control groups were determined using the Student's two-tailed t test ($p<0.05$).

**Table 32**

| Percent inhibition of STAT3 mRNA expression levels in APC/Min$^+$ mice | | | |
|---|---|---|---|
| **Treatment (mg/kg/week)** | **Liver** | **Small intestine** | **Colon** |
| ISIS 141923 (250) | 0 | 0 | 0 |
| ISIS 481549 (125) | 98 | 73 | 82 |
| ISIS 481549 (25) | 79 | 41 | 32 |

***Adenoma number analysis***

**[0326]** Histological analysis of the small intestine was performed to microscopically evaluate adenoma numbers. Treatment with ISIS 481549 at 125 mg/kg/week resulted in a statistically significant decrease in

tumor number compared to the PBS control (Table 33). Significant differences between the treatment and the control groups were determined using the Student's two-tailed t test ($p<0.05$).

**Table 33**

| Adenoma counts in APC/Min$^+$ mice | |
|---|---|
| **Treatment (mg/kg/week)** | **Colon count** |
| ISIS 141923 (250) | 5 |
| ISIS 481549 (125) | 1 |
| ISIS 481549 (25) | 5 |
| PBS | 6 |

**Example 22: Effect of antisense oligonucleotides targeting STAT3 in the treatment of a PC-9 NSCLC xenograft model**

**[0327]** BALB/c nude mice (Charles River) inoculated with the human non-small cell lung cancer cell line, PC-9, were treated with ISIS 481549 and ISIS 481464. Tumor growth and STAT3 target reduction in the mice were evaluated.

***Treatment***

**[0328]** Six- to eight-week old female BALB/c nude mice were inoculated subcutaneously with 7 x $10^6$ PC-9 human NSCLC cells. Mice that displayed a mean tumor volume of 150-200 $mm^3$ were selected and randomized into different treatment groups. Two groups of 7 mice were injected subcutaneously with 25 mg/kg of ISIS 481549 or ISIS 481464 administered five times a week (total weekly doses of 125 mg/kg) for 6 weeks. A group of 7 mice were injected subcutaneously with 25 mg/kg of ISIS 347526 (TCTTATGTTTCCGAACCGTT, no known murine or human target, designated herein as SEQ ID NO: 1519) administered five times a week (total weekly doses of 125 mg/kg) for 6 weeks. A final dose of antisense oligonucleotide was given 24 hrs before the mice were euthanized.

***RNA analysis***

**[0329]** Tumors were harvested and RNA was isolated using Qiagen RNAeasy Mini Kit (#74106), according to the manufacturer's protocol. STAT3 mRNA levels were measured using an ABI StepOnePlus RT-PCR instrument with human STAT3 primer probe set RTS2033 (forward primer GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse primer TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522). The mRNA levels of the housekeeping gene, GAPDH, was measured with the human primer probe set (forward primer GAAGGTGAAGGTCGGAGTC, designated herein as SEQ ID NO: 1523; reverse primer GAAGATGGTGATGGGATTTC, designated herein as SEQ ID NO: 1524; probe CAAGCTTCCCGTTCTCAGCC, designated herein as SEQ ID NO: 1525) and was used to normalize RNA levels. The results are presented in Table 34 and indicate that the antisense oligonucleotides reduced STAT3 mRNA levels.

**Table 34**

| Percent inhibition of STAT3 mRNA expression levels in the NSCLC xenograft model compared to the ASO control | |
|---|---|
| **Treatment (mg/kg)** | **% inhibition** |
| ISIS 481464 (25) | 40 |
| ISIS 481549 (25) | 22 |

***Tumor growth analysis***

**[0330]** Tumors were measured regularly throughout the study period. Tumor growth inhibition (TGI) was calculated using the formula

TGI = [1-(X of STAT3 ASO group (final))-**X** of STAT3 ASO group (day1))/(**X** of control ASO group (final)-X of control ASO group (day1))] x 100%, where **X** = mean tumor volume.

where **X** = mean tumor volume.

**[0331]** The difference of the treatment group from the control group was evaluated using the ANOVA statistical test. The results are presented in Table 35. The data indicates that tumor growth was significantly inhibited by ISIS 481464 with TGI of 97% by day 52. Treatment by ISIS 481549 inhibited PC-9 tumor growth by 78%.

**Table 35**

| Tumor growth measurements in the NSCLC xenograft model | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Day** | **10** | **13** | **18** | **20** | **25** | **28** | **31** | **34** | **38** | **42** | **45** | **48** | **52** |
| ISIS 481464 | 233 | 241 | 267 | 240 | 229 | 201 | 201 | 254 | 218 | 222 | 221 | 236 | 255 |
| ISIS 481549 | 233 | 217 | 239 | 188 | 237 | 299 | 326 | 318 | 328 | 410 | 341 | 389 | 398 |
| ISIS 347526 | 240 | 279 | 295 | 344 | 295 | 354 | 383 | 407 | 540 | 573 | 655 | 890 | 940 |

***Body weight analysis***

**[0332]** Body weights were measured regularly throughout the study period. The results are presented in Table 36 and indicate that there were no significant changes in body weight of the treatment groups compared to the control groups.

**Table 36**

| Body weight measurements in the NSCLC xenograft model | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Day** | **10** | **13** | **18** | **20** | **25** | **28** | **31** | **34** | **38** | **42** | **45** | **48** | **52** |
| ISIS 481464 | 18.65 | 19.44 | 18.98 | 19.66 | 19.40 | 19.45 | 19.89 | 20.26 | 19.86 | 20.31 | 20.13 | 20.03 | 20.11 |
| ISIS 481549 | 18.13 | 19.06 | 18.65 | 19.30 | 19.31 | 19.36 | 19.23 | 19.18 | 18.28 | 17.21 | 16.49 | 15.48 | 15.01 |
| ISIS 347526 | 18.34 | 19.29 | 19.05 | 19.65 | 19.63 | 19.98 | 20.08 | 20.69 | 19.90 | 20.19 | 20.25 | 20.09 | 20.19 |

**Example 23: Effect of ISIS 481464 in the treatment of an LG-476 NSCLC xenograft model**

**[0333]** NOD.Cg-*Prkdc*$^{scid}$ *Il2rg*$^{tm1Wjl}$/SzJ mice (NSG; JAX #5557), which are immunodeficient, were inoculated with the human non-small cell lung cancer cell line, LG-476 (Jackson Laboratory) and treated with ISIS 481464. Tumor growth and STAT3 target reduction in the mice was evaluated.

***Treatment***

**[0334]** Four- to six-week old female NSG mice were inoculated subcutaneously with LG-476 human NSCLC cells and monitored three times weekly for clinical observations, body weights and tumor volume. Once tumors reached 1,000 $mm^3$, the tumors were harvested and fragmented. Tumor fragments measuring 3-5 $mm^3$ were implanted subcutaneously into the right hind flank of 30 NSG mice. The mice were monitored three times a week. When individual tumors reached a volume of 200-250 $mm^3$, the mice were randomly assigned to 2 groups and were injected with 25 mg/kg of ISIS 481464 or PBS administered 5 times a week (weekly doses of 125 mg/kg) for 3 weeks. Tumors were harvested 24 hrs after the last dose.

***RNA analysis***

**[0335]** Lysates from tumors were prepared using an ABI StepOnePlus RT-PCR instrument with a human-specific primer probe set RTS2033. The mRNA levels of the housekeeping gene, Cyclophilin, was measured with a human-specific primer probe set (forward primer GACGGCGAGCCCTTGG, designated herein as SEQ ID NO: 1526; reverse primer TGCTGTCTTTGGGACCTTGTC, designated herein as SEQ ID NO: 1527; probe CCGCGTCTCCTTTGAGCTGTTTGC, designated herein as SEQ ID NO: 1528). Significant differences between the treatment and the control groups were determined using the Student's two-tailed *t* test ($p<0.05$).

**[0336]** Treatment with ISIS 481464 resulted in 43% reduction of STAT3 mRNA levels in the tumor mass compared to the PBS control (Figure 8), which is statistically significant.

***Protein analysis***

**[0337]** Total cell lysates were prepared by homogenizing tumor in ice-cold radio-immunoprecipitation assay (RIPA) buffer containing protease inhibitor cocktail. The lysates were analyzed by western blotting using STAT3 antibody (Abcam Antibodies, #ab32500). The house-keeping proteins, cytochrome oxidase II (COXII; #ab79393) and survivin (#ab76424) were also probed. STAT3 levels were normalized to either COXII protein or survivin protein and quantified using ImageJ software.

**[0338]** Treatment with ISIS 481464 resulted in 50% reduction in STAT3 protein levels in the tumor mass compared to the PBS control, which is statistically significant.

***Tumor growth analysis***

**[0339]** Tumors were measured regularly throughout the study period. Treatment with ISIS 481464 resulted in decrease in tumor volume of approximately 39% compared to the PBS control.

**Example 24: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in PC9 cells**

**[0340]** ISIS 481464, from the studies described above, was further tested at different doses in PC9 cells, a non small cell lung carcinoma cell line. Cells were plated at a density of 3,000 cells per well. Cells were incubated with 0.02μM, 0.1 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 37. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0341]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 37. As illustrated in Table 37, ISIS 481464 was able to penetrate the cell membrane.

**Table 37**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by PC9 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 20 | 51 | 84 | 94 | 96 | 0.19 |

**Example 25: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in C42B cells**

**[0342]** ISIS 481464, from the studies described above, was further tested at different doses in C42B cells, a prostate cancer cell line. Cells were plated at a density of 3,000 cells per well. Cells were incubated with 0.02μM, 0.1 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 38. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0343]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 38. As illustrated in Table 38, ISIS 481464 was able to penetrate the cell membrane.

**Table 38**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by C42B cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 21 | 38 | 75 | 87 | 96 | 0.45 |

**Example 26: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in Colo201 cells**

**[0344]** ISIS 481464, from the studies described above, was further tested at different doses in Colo201 cells, a colorectal cancer cell line. Cells were plated at a density of 3,000 cells per well. Cells were incubated with 0.02μM, 0.1 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 39. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0345]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 39. As illustrated in Table 39, ISIS 481464 was able to penetrate the cell membrane.

**Table 39**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by Colo201 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 36 | 53 | 81 | 93 | 96 | 0.09 |

**Example 27: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in BT474M1 cells**

**[0346]** ISIS 481464, from the studies described above, was further tested at different doses in BT474M1 cells, a breast cancer cell line. Cells were plated at a density of 3,000 cells per well. Cells were incubated with 0.02μM, 0.1 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 40. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531).

Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0347]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 40. As illustrated in Table 40, ISIS 481464 was able to penetrate the cell membrane.

**Table 40**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by BT474M1 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 13 | 25 | 74 | 94 | 95 | 0.24 |

**Example 28: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in H929 cells**

**[0348]** ISIS 481464, from the studies described above, was further tested at different doses in H929 cells, a multiple myeloma cell line. Cells were plated at a density of 10,000-12,000 cells per well. Cells were incubated with 0.01 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 41. After approximately 72 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0349]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 41. As illustrated in Table 41, ISIS 481464 was able to penetrate the cell membrane.

**Table 41**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by H929 cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 91 | 95 | 95 | 95 | 0.04 |

**Example 29: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in MM1R cells**

**[0350]** ISIS 481464, from the studies described above, was further tested at different doses in MM1R cells, a multiple myeloma cell line. Cells were plated at a density of 10,000-12,000 cells per well. Cells were incubated with 0.01 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 42. After approximately 72 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence

CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0351]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 42. As illustrated in Table 42, ISIS 481464 was able to penetrate the cell membrane.

**Table 42**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by MM1R cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 481464 | 91 | 96 | 95 | 95 | 0.04 |

**Example 30: Effect of antisense oligonucleotides targeting STAT3 in the treatment of an SK-OV3 ovarian cancer xenograft model**

**[0352]** BALB/c nude mice were inoculated with the human ovarian cancer cell line, SK-OV3 and treated with ISIS 481464 or ISIS 481549. ISIS 481549 is cross-reactive with the mouse sequence (i.e., hybridizes to the mouse sequence).

***Study 1***

**[0353]** Human ovarian cancer SK-OV3 cells (approximately $100mm^3$) were intraperitoneally injected into nude mice. Ten days later, the mice were inoculated subcutaneously with 25 mg/kg of ISIS 481464 or ISIS 481549, administered twice a week for 11 weeks. The mice were euthanized 24 hrs after the final dose.

***RNA analysis***

**[0354]** Lysates were prepared by using the RNA extraction kit (Invitrogen) in for RT-PCR analysis of STAT3 mRNA levels, using human primer probe set (RTS2033) and mouse primer probe set (mSTAT3-LTS0664). The results are presented in Table 43. The results are presented as percent inhibition of STAT3, relative to the PBS control. The data indicates that treatment with ISIS antisense oligonucleotides resulted in reduction of both human and murine STAT3 mRNA in comparison to the PBS control.

**Table 43**

| Percent inhibition of STAT3 mRNA in the treatment groups relative to the PBS control in the SK-OV3 xenograft model | | |
|---|---|---|
| ISIS No | human STAT3 | murine STAT3 |
| 481464 | 63 | 0 |
| 481549 | 21 | 61 |

***Protein analysis***

**[0355]** Lysates were prepared with RIPA buffer for western blot analysis of STAT3 protein levels, using an antibody against phosphorylated STAT3 (Cell Signaling). The results are presented in Figure 1. The data indicates that treatment with ISIS 481549 resulted in reduction of phosphorylated STAT3 protein in comparison to the PBS control.

***IL-6 level analysis***

**[0356]** Lysates were prepared by using the RNA extraction kit (Invitrogen) for RT-PCR analysis of IL-6 mRNA levels, using mouse primer probe set mIL6-LTS00629. The results are presented in Table 44. The results are presented as percent inhibition of IL-6, relative to the PBS control. The data indicates that treatment with ISIS 481549 resulted in significant reduction of both IL-6 mRNA in comparison to the PBS control.

**Table 44**

| Percent inhibition of IL-6 mRNA in the treatment groups relative to the PBS control in the SK-OV3 xenograft model | |
|---|---|
| ISIS No | Murine IL-6 (%) |
| 481464 | 8 |
| 481549 | 54 |

***Tumor weight analysis***

**[0357]** Tumors were harvested. Tumor weights were measured and the results are presented in Table 45. The results are presented as percent of the PBS control tumor weight. The data indicates that treatment with ISIS 481549 resulted in significant reduction of tumor weight in comparison to the PBS control.

**Table 45**

| Percent decrease of tumor weight in the treatment groups relative to the PBS control in the SK-OV3 xenograft model | |
|---|---|
| ISIS No | Weight (%) |
| 481464 | 58 |
| 481549 | 89 |

***Study 2***

**[0358]** Human ovarian cancer SK-OV3 cells (approximately $100mm^3$) were subcutaneously inoculated into nude mice. Ten days later, the mice were inoculated intraperitoneally with 50 mg/kg of either ISIS 481464 or 50 mg/kg of ISIS 481464 and ISIS 481549 in combination, administered five times a week for 6 weeks. The mice were euthanized 24 hrs after the final dose.

***Tumor volume analysis***

**[0359]** Tumors were measured regularly using Vernier calipers and tumor volumes were calculated using the

formula, tumor volume = ½ (length x width$^2$). The results are presented in Figure 2. The data indicates that treatment of the mice with a combination of ISIS 481464 and ISIS 481549 resulted in significant inhibition of tumor growth.

**Example 31: Tolerability study of ISIS 481464 in cynomolgus monkeys**

**[0360]** The efficacy and tolerability of ISIS 481464 in cynomolgus monkeys was evaluated.

***Treatment***

**[0361]** Male and female naive cynomolgus monkeys were assigned to five treatment groups. Three groups of 5 monkeys each received loading doses of 3 mg/kg, 10 mg/kg or 30 mg/kg every two days during the first week of the study (on Days 1, 3, 5 and 7) followed by once weekly administration thereafter (commencing on Day 14). A control group of 5 monkeys received PBS every two days during the first week of the study (on Days 1, 3, 5 and 7) as the loading dose, followed by once weekly administration thereafter (commencing on Day 14). These doses were administered via a one-hour intravenous (i.v.) infusion. A fifth group of 5 monkeys received loading doses of 30 mg/kg administered subcutaneously every two days during the first week of the study (on Days 1, 3, 5 and 7) followed by once weekly subcutaneous (s.c.) administration thereafter (commencing on Day 14).

**[0362]** For the i.v. infusions, the animals were restrained, without sedation, to a chair restraint. A catheter was placed in one of the cephalic veins and ISIS 481464 solution at the appropriate dose was infused at a constant rate over approximately 1 hour using a calibrated syringe pump (Stoelting Co, USA). The dosing site was rotated between right and left arms and the dosing time was recorded. The infusion rate was selected to deliver the calculated dose volume and the accuracy of the pumps was monitored and recorded for each dose. At the end of infusion period, the dosing solution was switched to PBS. In case of s.c. administration, the injections were performed in clock-wise rotation at 4 sites on the back. Injection sites were maintained by periodic shaving and permanently numbered by tattooing.

**[0363]** Three monkeys from each group were sacrificed on day 44, which was approximately 48 hrs following the last dose on day 42. The other 2 monkeys from each group are being observed for toxicological effects. Scheduled euthanasia of the animals was conducted by exsanguination after ketamine/xylazine-induced anesthesia and administration of sodium pentobarbital. The protocols described in the Example were approved by the Institutional Animal Care and Use Committee (IACUC).

***RNA analysis***

**[0364]** Liver tissue was homogenized in 3 mL of RLT lysis buffer (Qiagen) supplemented with 1% of 2-mercaptoethanol (Sigma). RNA was purified from the resulting homogenate using Qiagen RNeasy 96-well plate for RNA purification, according to the manufacturer's protocol. After purification, the RNA samples were subjected to RT-PCR analysis using Perkin-Elmer ABI Prism 7700 Sequence Detection System and STAT3 primer probe set RTS3235 (forward primer AAGTTTATCTGTGTGACACCAACGA, designated herein as SEQ ID NO: 1532; reverse primer CTTCACCATTATTTCCAAACTGCAT, designated herein as SEQ ID NO: 1533; probe TGCCGATGTCCCCCCGCA, designated herein as SEQ ID NO: 1534). STAT3 mRNA levels were normalized to monkey CyclophilinA, which was quantitated using primer probe set mk_cycloA_2$^{nd}$ (forward primer TGCTGGACCCAACACAAATG, designated herein as SEQ ID NO: 1535; reverse primer TGCCATCCAACCACTCAGTC, designated herein as SEQ ID NO: 1536; probe

TTCCCAGTTTTTCATCTGCACTGCCAX, designated herein as SEQ ID NO: 1537).

**[0365]** Treatment with ISIS 481464 at 30 mg/kg dose concentrations either via i.v. infusion or s.c. injection resulted in statistically significant reduction in STAT3 mRNA expression in liver (Table 46) compared to the PBS control. Significant differences between the treatment and the control groups were determined using the Student's t test ($p<0.05$).

**Table 46**

| Percent inhibition of STAT3 mRNA levels in cynomolgus monkeys | |
|---|---|
| Treatment | % inhibition |
| 3 mg i.v. | 0 |
| 10 mg i.v. | 7 |
| 30 mg i.v. | 52 |
| 30 mg s.c. | 51 |

***Protein analysis***

**[0366]** Liver tissue was homogenized in 1 mL of ice-cold RIPA buffer (Sigma) containing inhibitor cocktails of both proteases and phosphatases (Roche). Total lysates were separated by Bis-Tris PAGE (Invitrogen), transferred to a PVDF membrane, and immunoblotted using primary antibodies for STAT3 (Cell Signaling, #9132) and GAPDH (Advanced Immunochemicals, #06-1-G4-C5). Immunospecific bands were detected with the Enhanced Chemiluminescence Plus detection kit (Amersham Biosciences) after exposure to X-ray film. The intensity of the bands was then scanned and quantified using ImageJ software. Significant differences between the treatment and the control groups were determined using the Student's t test ($p<0.05$).

**[0367]** There was a dose-dependent decrease in STAT3 protein levels, as shown in Table 47, with 33% and 82% reduction at 3 mg/kg/week and 10 mg/kg/week respectively. STAT3 protein was undetectable at 30 mg/kg/week irrespective of the dosing route.

**Table 47**

| Percent inhibition of STAT3 protein levels in cynomolgus monkeys | |
|---|---|
| Treatment | % inhibition |
| 3 mg i.v. | 33 |
| 10 mg i.v. | 82 |
| 30 mg i.v. | 100 |
| 30 mg s.c. | 100 |

***Liver function***

**[0368]** 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 44, 48 hrs post-dosing. Blood samples (1mL) were collected in tubes without anticoagulant for serum separation. The tubes were kept at room temperature for approximately 60 min and then centrifuged at 3,000 rpm for 10 min to obtain serum. Levels of various liver function markers were measured using a Toshiba 200FR NEO chemistry analyzer (Toshiba Co., Japan). Plasma levels of ALT and AST were measured and the results are presented in Table 48, expressed in IU/L. Male and female monkey data is presented separately. The results indicate that

treatment with ISIS 481464 had no effect on liver function outside the expected range for antisense oligonucleotides.

**Table 48**

| Effect of antisense oligonucleotide treatment on liver function markers in cynomolgus monkey plasma | | | | |
|---|---|---|---|---|
| | Male ALT (IU/L) | Female ALT (IU/L) | Male AST (IU/L) | Female AST (IU/L) |
| PBS | 59 | 69 | 83 | 69 |
| 3 mg/kg i.v. | 47 | 56 | 50 | 47 |
| 10 mg/kg i.v. | 56 | 89 | 70 | 60 |
| 30 mg/kg i.v. | 74 | 75 | 60 | 73 |
| 30 mg/kg s.c. | 62 | 78 | 61 | 92 |

***Kidney function***

**[0369]** 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 44, 48 hrs post-dosing. Blood samples (1mL) were collected in tubes without anticoagulant for serum separation. The tubes were kept at room temperature for approximately 60 min and then centrifuged at 3,000 rpm for 10 min to obtain serum. Levels of various kidney function markers were measured using a Toshiba 200FR NEO chemistry analyzer (Toshiba Co., Japan). Results are presented in Table 49, expressed in mg/dL. The plasma chemistry data indicate that treatment with ISIS 481464 did not have any effect on the kidney function outside the expected range for antisense oligonucleotides.

**Table 49**

| Effect of antisense oligonucleotide treatment on plasma BUN and creatinine levels (mg/dL) in cynomolgus monkeys | | | | |
|---|---|---|---|---|
| | Male BUN | Female BUN | Male Creatinine | Female Creatinine |
| PBS | 19 | 30 | 0.68 | 0.88 |
| 3 mg/kg i.v. | 23 | 28 | 0.85 | 0.86 |
| 10 mg/kg i.v. | 26 | 27 | 0.89 | 0.94 |
| 30 mg/kg i.v. | 25 | 26 | 0.91 | 0.86 |
| 30 mg/kg s.c. | 27 | 28 | 0.97 | 0.85 |

***Body weight measurements***

**[0370]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were measured and are presented in Tables 50 and 51. The results indicate that effect of treatment with ISIS 481464 on body weights was within the expected range for antisense oligonucleotides.

**Table 50**

| Effect of antisense oligonucleotide treatment on body weights (g) in male cynomolgus monkeys | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Day 1 | Day 7 | Day 14 | Day 21 | Day 28 | Day 35 | Day 42 |
| PBS | 2523 | 2463 | 2484 | 2471 | 2509 | 2523 | 2551 |
| 3 mg/kg i.v. | 2604 | 2564 | 2594 | 2572 | 2589 | 2654 | 2687 |

| Effect of antisense oligonucleotide treatment on body weights (g) in male cynomolgus monkeys | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Day 1 | Day 7 | Day 14 | Day 21 | Day 28 | Day 35 | Day 42 |
| 10 mg/kg i.v. | 2603 | 2453 | 2581 | 2561 | 2591 | 2633 | 2655 |
| 30 mg/kg i.v. | 2608 | 2583 | 2613 | 2644 | 2668 | 2713 | 2776 |
| 30 mg/kg s.c. | 2533 | 2441 | 2470 | 2521 | 2554 | 2609 | 2619 |

**Table 51**

| Effect of antisense oligonucleotide treatment on body weights (g) in female cynomolgus monkeys | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Day 1 | Day 7 | Day 14 | Day 21 | Day 28 | Day 35 | Day 42 |
| PBS | 2266 | 2252 | 2276 | 2237 | 2362 | 2365 | 2373 |
| 3 mg/kg i.v. | 2253 | 2242 | 2283 | 2250 | 2346 | 2350 | 2377 |
| 10 mg/kg i.v. | 2293 | 2277 | 2318 | 2254 | 2358 | 2387 | 2361 |
| 30 mg/kg i.v. | 2259 | 2261 | 2289 | 2268 | 2368 | 2412 | 2406 |
| 30 mg/kg s.c. | 2293 | 2275 | 2322 | 2281 | 2385 | 2389 | 2394 |

**Example 32: Antisense inhibition of human STAT3 in HuVEC cells**

**[0371]** Antisense oligonucleotides were designed targeting a STAT3 nucleic acid and were tested for their effects on STAT3 mRNA in vitro. Cultured HuVEC cells at a density of 5,000 cells per well were transfected using LipofectAMINE 2000® reagent with 30 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 5; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 6; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 7) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0372]** The chimeric antisense oligonucleotides in Tables 52 and 53 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 on both sides (in the 5' and 3' directions) by wings comprising five nucleosides each. Each nucleoside in the 5' wing segment and each nucleotide 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. "Human Target start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Human Target stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in Table 52 is targeted to human STAT3 mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM-139276.2). Each gapmer listed in Table 53 is targeted to human STAT3 genomic sequence, designated herein as SEQ ID NO: 2 (the complement of GENBANK Accession No. NT_010755.14 truncated from nucleotides 4185000 to 4264000).

**[0373]** The potency of the gapmers was compared to ISIS 337332, ISIS 337333, and ISIS 345785, which are also 5-10-5 MOE gapmers targeting human STAT3, and which are further described in USPN 7,307,069.

**Table 52**

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 1 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 337332 | 1898 | 1917 | GAAGCCCTTGCCAGCCATGT | 91 | 1541 |
| 337333 | 1903 | 1922 | AAGGAGAAGCCCTTGCCAGC | 87 | 1542 |
| 345785 | 2267 | 2286 | TGCCTCCTCCTTGGGAATGT | 82 | 1543 |
| 455860 | 2831 | 2850 | ACACAAGACATTTCCTTTTT | 64 | 1544 |
| 455246 | 3452 | 3471 | CAAGGAGGCTGTTAACTGAA | 84 | 1545 |
| 455247 | 3454 | 3473 | ACCAAGGAGGCTGTTAACTG | 78 | 1546 |
| 455248 | 3456 | 3475 | GCACCAAGGAGGCTGTTAAC | 69 | 1547 |
| 455249 | 3458 | 3477 | AAGCACCAAGGAGGCTGTTA | 83 | 1548 |
| 455250 | 3460 | 3479 | TAAAGCACCAAGGAGGCTGT | 77 | 1549 |
| 455251 | 3462 | 3481 | CTTAAAGCACCAAGGAGGCT | 78 | 1550 |
| 455252 | 3464 | 3483 | TGCTTAAAGCACCAAGGAGG | 80 | 1551 |
| 455253 | 3466 | 3485 | AATGCTTAAAGCACCAAGGA | 75 | 1552 |
| 455254 | 3468 | 3487 | TGAATGCTTAAAGCACCAAG | 80 | 1553 |
| 455255 | 3470 | 3489 | GCTGAATGCTTAAAGCACCA | 82 | 1554 |
| 455256 | 3472 | 3491 | AAGCTGAATGCTTAAAGCAC | 67 | 1555 |
| 455257 | 3474 | 3493 | GGAAGCTGAATGCTTAAAGC | 79 | 1556 |
| 455258 | 3476 | 3495 | AAGGAAGCTGAATGCTTAAA | 79 | 1557 |
| 455259 | 3478 | 3497 | TGAAGGAAGCTGAATGCTTA | 72 | 1558 |
| 455260 | 3480 | 3499 | CCTGAAGGAAGCTGAATGCT | 75 | 1559 |
| 455261 | 3527 | 3546 | TAAGGGTTTGACCTGAAGCC | 72 | 1560 |
| 455262 | 3577 | 3596 | TAAACCTTCCTATTTCAACA | 77 | 1561 |
| 455263 | 3579 | 3598 | CTTAAACCTTCCTATTTCAA | 64 | 1562 |
| 455264 | 3581 | 3600 | TCCTTAAACCTTCCTATTTC | 73 | 1563 |
| 455265 | 3583 | 3602 | TCTCCTTAAACCTTCCTATT | 87 | 1564 |
| 455266 | 3585 | 3604 | ATTCTCCTTAAACCTTCCTA | 80 | 1565 |
| 455267 | 3587 | 3606 | AGATTCTCCTTAAACCTTCC | 87 | 1566 |
| 455268 | 3589 | 3608 | TTAGATTCTCCTTAAACCTT | 84 | 1567 |
| 455269 | 3591 | 3610 | GCTTAGATTCTCCTTAAACC | 87 | 1568 |
| 455270 | 3593 | 3612 | ATGCTTAGATTCTCCTTAAA | 87 | 1569 |
| 455271 | 3595 | 3614 | AAATGCTTAGATTCTCCTTA | 89 | 1570 |
| 455272 | 3597 | 3616 | TAAAATGCTTAGATTCTCCT | 88 | 1571 |
| 455273 | 3639 | 3658 | ATACATTACAAAGGAAAATA | 12 | 1572 |
| 455274 | 3641 | 3660 | CAATACATTACAAAGGAAAA | 28 | 1573 |
| 455275 | 3673 | 3692 | CACCCTCTGCCCAGCCTTAC | 63 | 1574 |
| 455276 | 3675 | 3694 | AGCACCCTCTGCCCAGCCTT | 79 | 1575 |
| 455277 | 3677 | 3696 | TAAGCACCCTCTGCCCAGCC | 65 | 1576 |
| 455278 | 3679 | 3698 | TGTAAGCACCCTCTGCCCAG | 62 | 1577 |
| 455279 | 3681 | 3700 | GTTGTAAGCACCCTCTGCCC | 62 | 1578 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 1 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455280 | 3683 | 3702 | AGGTTGTAAGCACCCTCTGC | 75 | 1579 |
| 455281 | 3685 | 3704 | CAAGGTTGTAAGCACCCTCT | 83 | 1580 |
| 455282 | 3687 | 3706 | GTCAAGGTTGTAAGCACCCT | 86 | 1581 |
| 455283 | 3689 | 3708 | GAGTCAAGGTTGTAAGCACC | 69 | 1582 |
| 455284 | 3691 | 3710 | GGGAGTCAAGGTTGTAAGCA | 37 | 1583 |
| 455285 | 3693 | 3712 | AAGGGAGTCAAGGTTGTAAG | 56 | 1584 |
| 455286 | 3695 | 3714 | GAAAGGGAGTCAAGGTTGTA | 61 | 1585 |
| 455287 | 3697 | 3716 | GAGAAAGGGAGTCAAGGTTG | 56 | 1586 |
| 455288 | 3709 | 3728 | ATCAAGTCCAGGGAGAAAGG | 55 | 1587 |
| 455289 | 3711 | 3730 | AGATCAAGTCCAGGGAGAAA | 69 | 1588 |
| 455290 | 3713 | 3732 | GCAGATCAAGTCCAGGGAGA | 80 | 1589 |
| 455291 | 3715 | 3734 | CAGCAGATCAAGTCCAGGGA | 90 | 1590 |
| 455292 | 3717 | 3736 | AACAGCAGATCAAGTCCAGG | 77 | 1591 |
| 455293 | 3719 | 3738 | GAAACAGCAGATCAAGTCCA | 81 | 1592 |
| 455294 | 3721 | 3740 | CTGAAACAGCAGATCAAGTC | 75 | 1593 |
| 455295 | 3723 | 3742 | CTCTGAAACAGCAGATCAAG | 76 | 1594 |
| 455296 | 3725 | 3744 | GCCTCTGAAACAGCAGATCA | 74 | 1595 |
| 455297 | 3727 | 3746 | TAGCCTCTGAAACAGCAGAT | 75 | 1596 |
| 455298 | 3729 | 3748 | CCTAGCCTCTGAAACAGCAG | 76 | 1597 |
| 455299 | 3731 | 3750 | AACCTAGCCTCTGAAACAGC | 83 | 1598 |
| 455300 | 3733 | 3752 | ACAACCTAGCCTCTGAAACA | 57 | 1599 |
| 455301 | 3735 | 3754 | AAACAACCTAGCCTCTGAAA | 72 | 1600 |
| 455302 | 3737 | 3756 | AGAAACAACCTAGCCTCTGA | 78 | 1601 |
| 455303 | 3739 | 3758 | ACAGAAACAACCTAGCCTCT | 69 | 1602 |
| 455304 | 3741 | 3760 | CCACAGAAACAACCTAGCCT | 70 | 1603 |
| 455305 | 3743 | 3762 | ACCCACAGAAACAACCTAGC | 80 | 1604 |
| 455306 | 3745 | 3764 | GCACCCACAGAAACAACCTA | 70 | 1605 |
| 455307 | 3747 | 3766 | AGGCACCCACAGAAACAACC | 75 | 1606 |
| 455308 | 3749 | 3768 | TAAGGCACCCACAGAAACAA | 70 | 1607 |
| 455309 | 3751 | 3770 | GATAAGGCACCCACAGAAAC | 65 | 1608 |
| 455310 | 3753 | 3772 | CTGATAAGGCACCCACAGAA | 66 | 1609 |
| 455311 | 3755 | 3774 | CCCTGATAAGGCACCCACAG | 81 | 1610 |
| 455312 | 3757 | 3776 | AGCCCTGATAAGGCACCCAC | 79 | 1611 |
| 455313 | 3759 | 3778 | CCAGCCCTGATAAGGCACCC | 74 | 1612 |
| 455314 | 3761 | 3780 | TCCCAGCCCTGATAAGGCAC | 74 | 1613 |
| 455315 | 3763 | 3782 | TATCCCAGCCCTGATAAGGC | 66 | 1614 |
| 455316 | 3765 | 3784 | AGTATCCCAGCCCTGATAAG | 48 | 1615 |
| 455317 | 3767 | 3786 | GAAGTATCCCAGCCCTGATA | 63 | 1616 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 1 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455318 | 3769 | 3788 | CAGAAGTATCCCAGCCCTGA | 82 | 1617 |
| 455319 | 3771 | 3790 | ATCAGAAGTATCCCAGCCCT | 80 | 1618 |
| 455320 | 3879 | 3898 | GATTCCTAAAACAAACAGGA | 37 | 1619 |
| 455321 | 3881 | 3900 | AGGATTCCTAAAACAAACAG | 42 | 1620 |
| 455322 | 3883 | 3902 | CCAGGATTCCTAAAACAAAC | 72 | 1621 |
| 455323 | 3885 | 3904 | GACCAGGATTCCTAAAACAA | 71 | 1622 |
| 455324 | 3887 | 3906 | GAGACCAGGATTCCTAAAAC | 43 | 1623 |
| 455325 | 3889 | 3908 | CTGAGACCAGGATTCCTAAA | 77 | 1624 |
| 455326 | 3891 | 3910 | TCCTGAGACCAGGATTCCTA | 76 | 1625 |
| 455327 | 3893 | 3912 | GGTCCTGAGACCAGGATTCC | 69 | 1626 |
| 455328 | 3895 | 3914 | GAGGTCCTGAGACCAGGATT | 76 | 1627 |
| 455329 | 3897 | 3916 | ATGAGGTCCTGAGACCAGGA | 81 | 1628 |
| 455330 | 3899 | 3918 | CCATGAGGTCCTGAGACCAG | 84 | 1629 |
| 455331 | 3901 | 3920 | TTCCATGAGGTCCTGAGACC | 75 | 1630 |
| 455332 | 3903 | 3922 | TCTTCCATGAGGTCCTGAGA | 75 | 1631 |
| 455333 | 3905 | 3924 | CTTCTTCCATGAGGTCCTGA | 79 | 1632 |
| 455334 | 3907 | 3926 | CTCTTCTTCCATGAGGTCCT | 83 | 1633 |
| 455335 | 3909 | 3928 | CCCTCTTCTTCCATGAGGTC | 74 | 1634 |
| 455336 | 3911 | 3930 | CCCCCTCTTCTTCCATGAGG | 72 | 1635 |
| 455337 | 3913 | 3932 | CTCCCCCTCTTCTTCCATGA | 72 | 1636 |
| 455338 | 3977 | 3996 | CCTGAGCTCAACCAGACACG | 79 | 1637 |
| 455339 | 3979 | 3998 | TCCCTGAGCTCAACCAGACA | 73 | 1638 |
| 455340 | 3981 | 4000 | ATTCCCTGAGCTCAACCAGA | 75 | 1639 |
| 455341 | 3983 | 4002 | ATATTCCCTGAGCTCAACCA | 65 | 1640 |
| 455342 | 3985 | 4004 | CCATATTCCCTGAGCTCAAC | 78 | 1641 |
| 455343 | 3987 | 4006 | AACCATATTCCCTGAGCTCA | 81 | 1642 |
| 455344 | 3989 | 4008 | AGAACCATATTCCCTGAGCT | 77 | 1643 |
| 455345 | 3991 | 4010 | TAAGAACCATATTCCCTGAG | 73 | 1644 |
| 455346 | 3993 | 4012 | GCTAAGAACCATATTCCCTG | 81 | 1645 |
| 455347 | 4067 | 4086 | TCAGTAAGCCTTTGCCCTGC | 79 | 1646 |
| 455348 | 4069 | 4088 | TATCAGTAAGCCTTTGCCCT | 72 | 1647 |
| 455349 | 4071 | 4090 | TTTATCAGTAAGCCTTTGCC | 76 | 1648 |
| 455350 | 4073 | 4092 | AGTTTATCAGTAAGCCTTTG | 84 | 1649 |
| 455351 | 4075 | 4094 | CAAGTTTATCAGTAAGCCTT | 82 | 1650 |
| 455352 | 4077 | 4096 | CTCAAGTTTATCAGTAAGCC | 82 | 1651 |
| 455353 | 4079 | 4098 | GACTCAAGTTTATCAGTAAG | 70 | 1652 |
| 455354 | 4081 | 4100 | CAGACTCAAGTTTATCAGTA | 78 | 1653 |
| 455355 | 4083 | 4102 | GGCAGACTCAAGTTTATCAG | 67 | 1654 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 1 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455356 | 4085 | 4104 | AGGGCAGACTCAAGTTTATC | 51 | 1655 |
| 455357 | 4087 | 4106 | CGAGGGCAGACTCAAGTTTA | 54 | 1656 |
| 455358 | 4089 | 4108 | TACGAGGGCAGACTCAAGTT | 56 | 1657 |
| 455359 | 4091 | 4110 | CATACGAGGGCAGACTCAAG | 59 | 1658 |
| 455360 | 4093 | 4112 | CTCATACGAGGGCAGACTCA | 74 | 1659 |
| 455361 | 4095 | 4114 | CCCTCATACGAGGGCAGACT | 67 | 1660 |
| 455362 | 4122 | 4141 | CAGCCTCAGAGGGAGGCCAG | 40 | 1661 |
| 455363 | 4124 | 4143 | ACCAGCCTCAGAGGGAGGCC | 34 | 1662 |
| 455364 | 4126 | 4145 | TCACCAGCCTCAGAGGGAGG | 49 | 1663 |
| 455365 | 4128 | 4147 | AGTCACCAGCCTCAGAGGGA | 50 | 1664 |
| 455366 | 4225 | 4244 | CCCATACGCACAGGAGAGGC | 81 | 1665 |
| 455367 | 4227 | 4246 | TTCCCATACGCACAGGAGAG | 72 | 1666 |
| 455368 | 4229 | 4248 | TGTTCCCATACGCACAGGAG | 80 | 1667 |
| 455369 | 4231 | 4250 | GGTGTTCCCATACGCACAGG | 76 | 1668 |
| 455370 | 4233 | 4252 | TAGGTGTTCCCATACGCACA | 87 | 1669 |
| 455371 | 4235 | 4254 | GCTAGGTGTTCCCATACGCA | 92 | 1670 |
| 455372 | 4237 | 4256 | GTGCTAGGTGTTCCCATACG | 81 | 1671 |
| 455373 | 4304 | 4323 | GAGGCAAGGTGGTTTTGAGT | 55 | 1672 |
| 455374 | 4306 | 4325 | CTGAGGCAAGGTGGTTTTGA | 74 | 1673 |
| 455375 | 4308 | 4327 | AGCTGAGGCAAGGTGGTTTT | 79 | 1674 |
| 455376 | 4310 | 4329 | TCAGCTGAGGCAAGGTGGTT | 80 | 1675 |
| 455377 | 4312 | 4331 | GATCAGCTGAGGCAAGGTGG | 77 | 1676 |
| 455378 | 4314 | 4333 | CTGATCAGCTGAGGCAAGGT | 60 | 1677 |
| 455379 | 4316 | 4335 | CTCTGATCAGCTGAGGCAAG | 74 | 1678 |
| 455380 | 4318 | 4337 | AACTCTGATCAGCTGAGGCA | 77 | 1679 |
| 455381 | 4320 | 4339 | GAAACTCTGATCAGCTGAGG | 78 | 1680 |
| 455382 | 4322 | 4341 | CAGAAACTCTGATCAGCTGA | 78 | 1681 |
| 455383 | 4360 | 4379 | CAGAGACCAGCTAATTTGAT | 69 | 1682 |
| 455384 | 4362 | 4381 | TTCAGAGACCAGCTAATTTG | 78 | 1683 |
| 455385 | 4364 | 4383 | AATTCAGAGACCAGCTAATT | 77 | 1684 |
| 455386 | 4366 | 4385 | TTAATTCAGAGACCAGCTAA | 83 | 1685 |
| 455387 | 4423 | 4442 | CTCCAGGCAGGAGGACTGGG | 79 | 1686 |
| 455388 | 4425 | 4444 | GTCTCCAGGCAGGAGGACTG | 65 | 1687 |
| 455389 | 4427 | 4446 | CTGTCTCCAGGCAGGAGGAC | 57 | 1688 |
| 455390 | 4429 | 4448 | AACTGTCTCCAGGCAGGAGG | 75 | 1689 |
| 455391 | 4431 | 4450 | TCAACTGTCTCCAGGCAGGA | 86 | 1690 |
| 455392 | 4433 | 4452 | CATCAACTGTCTCCAGGCAG | 80 | 1691 |
| 455393 | 4435 | 4454 | CACATCAACTGTCTCCAGGC | 86 | 1692 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 1 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455394 | 4437 | 4456 | GACACATCAACTGTCTCCAG | 85 | 1693 |
| 455395 | 4471 | 4490 | GAAGAGTGTTGCTGGAGAAG | 73 | 1694 |
| 455396 | 4473 | 4492 | CTGAAGAGTGTTGCTGGAGA | 78 | 1695 |
| 455397 | 4475 | 4494 | TACTGAAGAGTGTTGCTGGA | 83 | 1696 |
| 455398 | 4477 | 4496 | TGTACTGAAGAGTGTTGCTG | 86 | 1697 |
| 455399 | 4479 | 4498 | TATGTACTGAAGAGTGTTGC | 74 | 1698 |
| 455400 | 4481 | 4500 | ATTATGTACTGAAGAGTGTT | 74 | 1699 |
| 455401 | 4483 | 4502 | TTATTATGTACTGAAGAGTG | 84 | 1700 |
| 455402 | 4485 | 4504 | GCTTATTATGTACTGAAGAG | 84 | 1701 |
| 455403 | 4487 | 4506 | AAGCTTATTATGTACTGAAG | 77 | 1702 |
| 455404 | 4489 | 4508 | TTAAGCTTATTATGTACTGA | 75 | 1703 |
| 455405 | 4491 | 4510 | AGTTAAGCTTATTATGTACT | 81 | 1704 |
| 455406 | 4493 | 4512 | TCAGTTAAGCTTATTATGTA | 58 | 1705 |
| 455407 | 4495 | 4514 | TATCAGTTAAGCTTATTATG | 65 | 1706 |
| 455408 | 4497 | 4516 | TTTATCAGTTAAGCTTATTA | 46 | 1707 |
| 455409 | 4499 | 4518 | TGTTTATCAGTTAAGCTTAT | 68 | 1708 |
| 455410 | 4501 | 4520 | TCTGTTTATCAGTTAAGCTT | 83 | 1709 |
| 455411 | 4539 | 4558 | AACCCAATGGTAAGCCCAAG | 87 | 1710 |
| 455412 | 4541 | 4560 | TAAACCCAATGGTAAGCCCA | 87 | 1711 |
| 455413 | 4543 | 4562 | TTTAAACCCAATGGTAAGCC | 78 | 1712 |
| 455414 | 4545 | 4564 | GATTTAAACCCAATGGTAAG | 31 | 1713 |
| 455415 | 4547 | 4566 | ATGATTTAAACCCAATGGTA | 71 | 1714 |
| 455416 | 4549 | 4568 | CTATGATTTAAACCCAATGG | 67 | 1715 |
| 455417 | 4551 | 4570 | CCCTATGATTTAAACCCAAT | 70 | 1716 |
| 455418 | 4553 | 4572 | GTCCCTATGATTTAAACCCA | 83 | 1717 |
| 455419 | 4555 | 4574 | AGGTCCCTATGATTTAAACC | 64 | 1718 |
| 455420 | 4589 | 4608 | TATCTGCTCCAGAGAAGCCC | 76 | 1719 |
| 455421 | 4591 | 4610 | AATATCTGCTCCAGAGAAGC | 78 | 1720 |
| 455422 | 4614 | 4633 | CTACCTAAGGCCATGAACTT | 74 | 1721 |
| 455423 | 4616 | 4635 | TGCTACCTAAGGCCATGAAC | 82 | 1722 |
| 455424 | 4618 | 4637 | CATGCTACCTAAGGCCATGA | 84 | 1723 |
| 455425 | 4636 | 4655 | CAGAGTTAAGACCAGATACA | 84 | 1724 |
| 455426 | 4638 | 4657 | ATCAGAGTTAAGACCAGATA | 83 | 1725 |
| 455427 | 4640 | 4659 | CAATCAGAGTTAAGACCAGA | 77 | 1726 |
| 455428 | 4642 | 4661 | TACAATCAGAGTTAAGACCA | 81 | 1727 |
| 455429 | 4644 | 4663 | GCTACAATCAGAGTTAAGAC | 86 | 1728 |
| 455430 | 4646 | 4665 | TTGCTACAATCAGAGTTAAG | 85 | 1729 |
| 455431 | 4648 | 4667 | TTTTGCTACAATCAGAGTTA | 85 | 1730 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 1 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455432 | 4650 | 4669 | ACTTTTGCTACAATCAGAGT | 73 | 1731 |
| 455433 | 4652 | 4671 | GAACTTTTGCTACAATCAGA | 80 | 1732 |
| 455434 | 4654 | 4673 | CAGAACTTTTGCTACAATCA | 82 | 1733 |
| 455435 | 4656 | 4675 | CTCAGAACTTTTGCTACAAT | 79 | 1734 |
| 455436 | 4658 | 4677 | CTCTCAGAACTTTTGCTACA | 76 | 1735 |
| 455437 | 4660 | 4679 | TCCTCTCAGAACTTTTGCTA | 75 | 1736 |
| 455438 | 4662 | 4681 | GCTCCTCTCAGAACTTTTGC | 85 | 1737 |
| 455439 | 4664 | 4683 | CAGCTCCTCTCAGAACTTTT | 85 | 1738 |
| 455440 | 4666 | 4685 | CTCAGCTCCTCTCAGAACTT | 80 | 1739 |
| 455441 | 4668 | 4687 | GGCTCAGCTCCTCTCAGAAC | 75 | 1740 |
| 455442 | 4770 | 4789 | GCAACCCACGGGATTCCCTC | 82 | 1741 |
| 455443 | 4772 | 4791 | AAGCAACCCACGGGATTCCC | 77 | 1742 |
| 455444 | 4774 | 4793 | GTAAGCAACCCACGGGATTC | 74 | 1743 |
| 455445 | 4776 | 4795 | AGGTAAGCAACCCACGGGAT | 76 | 1744 |
| 455446 | 4778 | 4797 | GTAGGTAAGCAACCCACGGG | 82 | 1745 |
| 455447 | 4780 | 4799 | AGGTAGGTAAGCAACCCACG | 88 | 1746 |
| 455448 | 4782 | 4801 | ATAGGTAGGTAAGCAACCCA | 83 | 1747 |
| 455449 | 4784 | 4803 | TTATAGGTAGGTAAGCAACC | 59 | 1748 |
| 455450 | 4786 | 4805 | CCTTATAGGTAGGTAAGCAA | 65 | 1749 |
| 455451 | 4788 | 4807 | CACCTTATAGGTAGGTAAGC | 62 | 1750 |
| 455452 | 4790 | 4809 | ACCACCTTATAGGTAGGTAA | 57 | 1751 |
| 455453 | 4792 | 4811 | AAACCACCTTATAGGTAGGT | 75 | 1752 |
| 455454 | 4794 | 4813 | ATAAACCACCTTATAGGTAG | 35 | 1753 |
| 455455 | 4796 | 4815 | TTATAAACCACCTTATAGGT | 39 | 1754 |
| 455456 | 4798 | 4817 | GCTTATAAACCACCTTATAG | 58 | 1755 |
| 455457 | 4800 | 4819 | CAGCTTATAAACCACCTTAT | 86 | 1756 |
| 455458 | 4802 | 4821 | AGCAGCTTATAAACCACCTT | 86 | 1757 |
| 455459 | 4804 | 4823 | ACAGCAGCTTATAAACCACC | 80 | 1758 |
| 455460 | 4806 | 4825 | GGACAGCAGCTTATAAACCA | 69 | 1759 |
| 455461 | 4808 | 4827 | CAGGACAGCAGCTTATAAAC | 72 | 1760 |
| 455462 | 4810 | 4829 | GCCAGGACAGCAGCTTATAA | 76 | 1761 |
| 455463 | 4812 | 4831 | TGGCCAGGACAGCAGCTTAT | 89 | 1762 |
| 455464 | 4814 | 4833 | AGTGGCCAGGACAGCAGCTT | 80 | 1763 |
| 455465 | 4816 | 4835 | GCAGTGGCCAGGACAGCAGC | 78 | 1764 |
| 455466 | 4818 | 4837 | ATGCAGTGGCCAGGACAGCA | 85 | 1765 |
| 455467 | 4820 | 4839 | GAATGCAGTGGCCAGGACAG | 80 | 1766 |
| 455468 | 4822 | 4841 | TTGAATGCAGTGGCCAGGAC | 83 | 1767 |
| 455469 | 4824 | 4843 | ATTTGAATGCAGTGGCCAGG | 84 | 1768 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 1 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455470 | 4826 | 4845 | GAATTTGAATGCAGTGGCCA | 81 | 1769 |
| 455471 | 4828 | 4847 | TGGAATTTGAATGCAGTGGC | 85 | 1770 |
| 455472 | 4830 | 4849 | ATTGGAATTTGAATGCAGTG | 64 | 1771 |
| 455473 | 4832 | 4851 | ACATTGGAATTTGAATGCAG | 80 | 1772 |
| 455474 | 4834 | 4853 | ACACATTGGAATTTGAATGC | 73 | 1773 |
| 455475 | 4836 | 4855 | GTACACATTGGAATTTGAAT | 80 | 1774 |
| 455476 | 4838 | 4857 | AAGTACACATTGGAATTTGA | 77 | 1775 |
| 455477 | 4840 | 4859 | TGAAGTACACATTGGAATTT | 68 | 1776 |
| 455478 | 4842 | 4861 | TATGAAGTACACATTGGAAT | 66 | 1777 |
| 455479 | 4844 | 4863 | ACTATGAAGTACACATTGGA | 83 | 1778 |
| 455480 | 4846 | 4865 | ACACTATGAAGTACACATTG | 76 | 1779 |
| 455481 | 4848 | 4867 | TTACACTATGAAGTACACAT | 78 | 1780 |
| 455482 | 4850 | 4869 | TTTTACACTATGAAGTACAC | 76 | 1781 |
| 455483 | 4852 | 4871 | ATTTTTACACTATGAAGTAC | 60 | 1782 |
| 455484 | 4854 | 4873 | AAATTTTTACACTATGAAGT | 35 | 1783 |
| 455485 | 4856 | 4875 | ATAAATTTTTACACTATGAA | 9 | 1784 |
| 455486 | 4858 | 4877 | ATATAAATTTTTACACTATG | 0 | 1785 |
| 455487 | 4860 | 4879 | TAATATAAATTTTTACACTA | 21 | 1786 |
| 455488 | 4862 | 4881 | AATAATATAAATTTTTACAC | 10 | 1787 |
| 455489 | 4864 | 4883 | ACAATAATATAAATTTTTAC | 7 | 1788 |
| 455490 | 4925 | 4944 | AGTTAAAGTAGATACAGCAA | 71 | 1789 |
| 455491 | 4927 | 4946 | GAAGTTAAAGTAGATACAGC | 63 | 1790 |
| 455492 | 4929 | 4948 | TGGAAGTTAAAGTAGATACA | 69 | 1791 |
| 455493 | 4931 | 4950 | TCTGGAAGTTAAAGTAGATA | 65 | 1792 |
| 455494 | 4933 | 4952 | TTTCTGGAAGTTAAAGTAGA | 55 | 1793 |
| 455495 | 4935 | 4954 | TATTTCTGGAAGTTAAAGTA | 57 | 1794 |
| 455496 | 4937 | 4956 | TTTATTTCTGGAAGTTAAAG | 36 | 1795 |
| 455497 | 4939 | 4958 | CGTTTATTTCTGGAAGTTAA | 77 | 1796 |

**Table 53**

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455498 | 917 | 936 | CACGCCGTCATGCATAATTC | 0 | 1797 |
| 455499 | 919 | 938 | GGCACGCCGTCATGCATAAT | 0 | 1798 |
| 455500 | 940 | 959 | GCCCAGCCCCAGCCTGGCCG | 35 | 1799 |
| 455501 | 962 | 981 | ACAGCCCCTTCAGCCAATCC | 15 | 1800 |
| 455502 | 964 | 983 | TTACAGCCCCTTCAGCCAAT | 14 | 1801 |
| 455503 | 966 | 985 | AATTACAGCCCCTTCAGCCA | 28 | 1802 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455504 | 968 | 987 | TGAATTACAGCCCCTTCAGC | 6 | 1803 |
| 455505 | 970 | 989 | GCTGAATTACAGCCCCTTCA | 15 | 1804 |
| 455506 | 972 | 991 | CCGCTGAATTACAGCCCCTT | 4 | 1805 |
| 455507 | 974 | 993 | AACCGCTGAATTACAGCCCC | 8 | 1806 |
| 455508 | 976 | 995 | GAAACCGCTGAATTACAGCC | 16 | 1807 |
| 455509 | 978 | 997 | CGGAAACCGCTGAATTACAG | 24 | 1808 |
| 455510 | 980 | 999 | TCCGGAAACCGCTGAATTAC | 12 | 1809 |
| 455511 | 982 | 1001 | GCTCCGGAAACCGCTGAATT | 15 | 1810 |
| 455512 | 984 | 1003 | CAGCTCCGGAAACCGCTGAA | 23 | 1811 |
| 455513 | 986 | 1005 | CGCAGCTCCGGAAACCGCTG | 4 | 1812 |
| 455514 | 988 | 1007 | GCCGCAGCTCCGGAAACCGC | 13 | 1813 |
| 455515 | 1378 | 1397 | AGTCCCTTCCGAGGCCCGCT | 81 | 1814 |
| 455516 | 1408 | 1427 | CGAAGAACGAAACTTCCCTC | 68 | 1815 |
| 455517 | 1697 | 1716 | CAGACACACCTATTCCTGCC | 82 | 1816 |
| 455518 | 1748 | 1767 | TTATGCAATAAAGCCTACCC | 70 | 1817 |
| 455519 | 1795 | 1814 | TTAGAAAGAGTACCGGTCTG | 75 | 1818 |
| 455520 | 1987 | 2006 | AATGGCTCAATTATTTATCT | 59 | 1819 |
| 455521 | 2083 | 2102 | TTTACCCAAGATCTTGGCTC | 76 | 1820 |
| 455522 | 2175 | 2194 | ACTTCAGTGCAACCACACCC | 70 | 1821 |
| 455523 | 2205 | 2224 | CCAACTTGGGCGACGGTTTG | 67 | 1822 |
| 455524 | 2281 | 2300 | CTAACCACTGATTTTGTCAC | 56 | 1823 |
| 455525 | 2316 | 2335 | GTACACACTATACACATTTT | 85 | 1824 |
| 455526 | 2346 | 2365 | CTTTAGTTGCACATACAGTA | 80 | 1825 |
| 455527 | 2383 | 2402 | GCCAAAAATTTACAACCCAT | 86 | 1826 |
| 455528 | 2413 | 2432 | TTCAAGCCCAATGCTTTATC | 76 | 1827 |
| 455529 | 2561 | 2580 | CTGGAACATGTAATAAGGAA | 71 | 1828 |
| 455530 | 2669 | 2688 | AGAGACTAAAATCAAGGCTC | 87 | 1829 |
| 455531 | 2900 | 2919 | TAGACTCTAGACCCAATTCC | 77 | 1830 |
| 455532 | 3780 | 3799 | GAAATGACCACTGATCAAGC | 74 | 1831 |
| 455533 | 3867 | 3886 | AAGTTGGTCACCACCTCTAC | 81 | 1832 |
| 455534 | 4291 | 4310 | AACTTATTCTTCATAGCAAC | 58 | 1833 |
| 455535 | 4587 | 4606 | TATTTGGGACCCAGTTGAAA | 60 | 1834 |
| 455536 | 5000 | 5019 | AGAACTGAAATTCCTTGGTC | 88 | 1835 |
| 455537 | 5030 | 5049 | AAGTTTTAAAAGCTTCCCCT | 76 | 1836 |
| 455538 | 5554 | 5573 | TCACCCAAAGTACCAAATCA | 71 | 1837 |
| 455539 | 5667 | 5686 | CAAAAGTTATGGTGAAATTT | 44 | 1838 |
| 455540 | 5699 | 5718 | AAGTACTCTTTCAGTGGTTT | 88 | 1839 |
| 455541 | 6844 | 6863 | AATTAAAGAGTTGCGGTAAT | 68 | 1840 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455542 | 6926 | 6945 | GTTTCATGAAAACGGACAAT | 78 | 1841 |
| 455543 | 7050 | 7069 | AGGATTCAGTCCCAGATCTG | 18 | 1842 |
| 455544 | 7282 | 7301 | TCAATAATGATGACTTTCTC | 72 | 1843 |
| 455545 | 7528 | 7547 | TTAAACCCAATTATTAACAG | 45 | 1844 |
| 455546 | 7624 | 7643 | GTAAAACACACATTTTATAT | 62 | 1845 |
| 455547 | 7682 | 7701 | GTAAACAGAAAGGGCTGCAA | 86 | 1846 |
| 455548 | 8078 | 8097 | GGGCAGATTTACCTTCCTTA | 89 | 1847 |
| 455549 | 8126 | 8145 | GGGTAGCAGGAAGGAAAGCC | 80 | 1848 |
| 455550 | 8214 | 8233 | AATATAAGTTCTTTGGCTGA | 60 | 1849 |
| 455551 | 8244 | 8263 | TACAATAGCAATCACCTTAG | 89 | 1850 |
| 455552 | 8284 | 8303 | CCATGAAACCCTCAAACATA | 75 | 1851 |
| 337332 | 66135 | 66154 | GAAGCCCTTGCCAGCCATGT | 91 | 1541 |
| 337333 | 66140 | 66159 | AAGGAGAAGCCCTTGCCAGC | 87 | 1542 |
| 345785 | 67129 | 67148 | TGCCTCCTCCTTGGGAATGT | 82 | 1543 |
| 455246 | 74639 | 74658 | CAAGGAGGCTGTTAACTGAA | 84 | 1545 |
| 455247 | 74641 | 74660 | ACCAAGGAGGCTGTTAACTG | 78 | 1546 |
| 455248 | 74643 | 74662 | GCACCAAGGAGGCTGTTAAC | 69 | 1547 |
| 455249 | 74645 | 74664 | AAGCACCAAGGAGGCTGTTA | 83 | 1548 |
| 455250 | 74647 | 74666 | TAAAGCACCAAGGAGGCTGT | 77 | 1549 |
| 455251 | 74649 | 74668 | CTTAAAGCACCAAGGAGGCT | 78 | 1550 |
| 455252 | 74651 | 74670 | TGCTTAAAGCACCAAGGAGG | 80 | 1551 |
| 455253 | 74653 | 74672 | AATGCTTAAAGCACCAAGGA | 75 | 1552 |
| 455254 | 74655 | 74674 | TGAATGCTTAAAGCACCAAG | 80 | 1553 |
| 455255 | 74657 | 74676 | GCTGAATGCTTAAAGCACCA | 82 | 1554 |
| 455256 | 74659 | 74678 | AAGCTGAATGCTTAAAGCAC | 67 | 1555 |
| 455257 | 74661 | 74680 | GGAAGCTGAATGCTTAAAGC | 79 | 1556 |
| 455258 | 74663 | 74682 | AAGGAAGCTGAATGCTTAAA | 79 | 1557 |
| 455259 | 74665 | 74684 | TGAAGGAAGCTGAATGCTTA | 72 | 1558 |
| 455260 | 74667 | 74686 | CCTGAAGGAAGCTGAATGCT | 75 | 1559 |
| 455261 | 74714 | 74733 | TAAGGGTTTGACCTGAAGCC | 72 | 1560 |
| 455262 | 74764 | 74783 | TAAACCTTCCTATTTCAACA | 77 | 1561 |
| 455263 | 74766 | 74785 | CTTAAACCTTCCTATTTCAA | 64 | 1562 |
| 455264 | 74768 | 74787 | TCCTTAAACCTTCCTATTTC | 73 | 1563 |
| 455265 | 74770 | 74789 | TCTCCTTAAACCTTCCTATT | 87 | 1564 |
| 455266 | 74772 | 74791 | ATTCTCCTTAAACCTTCCTA | 80 | 1565 |
| 455267 | 74774 | 74793 | AGATTCTCCTTAAACCTTCC | 87 | 1566 |
| 455268 | 74776 | 74795 | TTAGATTCTCCTTAAACCTT | 84 | 1567 |
| 455269 | 74778 | 74797 | GCTTAGATTCTCCTTAAACC | 87 | 1568 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455270 | 74780 | 74799 | ATGCTTAGATTCTCCTTAAA | 87 | 1569 |
| 455271 | 74782 | 74801 | AAATGCTTAGATTCTCCTTA | 89 | 1570 |
| 455272 | 74784 | 74803 | TAAAATGCTTAGATTCTCCT | 88 | 1571 |
| 455273 | 74826 | 74845 | ATACATTACAAAGGAAAATA | 12 | 1572 |
| 455274 | 74828 | 74847 | CAATACATTACAAAGGAAAA | 28 | 1573 |
| 455275 | 74860 | 74879 | CACCCTCTGCCCAGCCTTAC | 63 | 1574 |
| 455276 | 74862 | 74881 | AGCACCCTCTGCCCAGCCTT | 79 | 1575 |
| 455277 | 74864 | 74883 | TAAGCACCCTCTGCCCAGCC | 65 | 1576 |
| 455278 | 74866 | 74885 | TGTAAGCACCCTCTGCCCAG | 62 | 1577 |
| 455279 | 74868 | 74887 | GTTGTAAGCACCCTCTGCCC | 62 | 1578 |
| 455280 | 74870 | 74889 | AGGTTGTAAGCACCCTCTGC | 75 | 1579 |
| 455281 | 74872 | 74891 | CAAGGTTGTAAGCACCCTCT | 83 | 1580 |
| 455282 | 74874 | 74893 | GTCAAGGTTGTAAGCACCCT | 86 | 1581 |
| 455283 | 74876 | 74895 | GAGTCAAGGTTGTAAGCACC | 69 | 1582 |
| 455284 | 74878 | 74897 | GGGAGTCAAGGTTGTAAGCA | 37 | 1583 |
| 455285 | 74880 | 74899 | AAGGGAGTCAAGGTTGTAAG | 56 | 1584 |
| 455286 | 74882 | 74901 | GAAAGGGAGTCAAGGTTGTA | 61 | 1585 |
| 455287 | 74884 | 74903 | GAGAAAGGGAGTCAAGGTTG | 56 | 1586 |
| 455288 | 74896 | 74915 | ATCAAGTCCAGGGAGAAAGG | 55 | 1587 |
| 455289 | 74898 | 74917 | AGATCAAGTCCAGGGAGAAA | 69 | 1588 |
| 455290 | 74900 | 74919 | GCAGATCAAGTCCAGGGAGA | 80 | 1589 |
| 455291 | 74902 | 74921 | CAGCAGATCAAGTCCAGGGA | 90 | 1590 |
| 455292 | 74904 | 74923 | AACAGCAGATCAAGTCCAGG | 77 | 1591 |
| 455293 | 74906 | 74925 | GAAACAGCAGATCAAGTCCA | 81 | 1592 |
| 455294 | 74908 | 74927 | CTGAAACAGCAGATCAAGTC | 75 | 1593 |
| 455295 | 74910 | 74929 | CTCTGAAACAGCAGATCAAG | 76 | 1594 |
| 455296 | 74912 | 74931 | GCCTCTGAAACAGCAGATCA | 74 | 1595 |
| 455297 | 74914 | 74933 | TAGCCTCTGAAACAGCAGAT | 75 | 1596 |
| 455298 | 74916 | 74935 | CCTAGCCTCTGAAACAGCAG | 76 | 1597 |
| 455299 | 74918 | 74937 | AACCTAGCCTCTGAAACAGC | 83 | 1598 |
| 455300 | 74920 | 74939 | ACAACCTAGCCTCTGAAACA | 57 | 1599 |
| 455301 | 74922 | 74941 | AAACAACCTAGCCTCTGAAA | 72 | 1600 |
| 455302 | 74924 | 74943 | AGAAACAACCTAGCCTCTGA | 78 | 1601 |
| 455303 | 74926 | 74945 | ACAGAAACAACCTAGCCTCT | 69 | 1602 |
| 455304 | 74928 | 74947 | CCACAGAAACAACCTAGCCT | 70 | 1603 |
| 455305 | 74930 | 74949 | ACCCACAGAAACAACCTAGC | 80 | 1604 |
| 455306 | 74932 | 74951 | GCACCCACAGAAACAACCTA | 70 | 1605 |
| 455307 | 74934 | 74953 | AGGCACCCACAGAAACAACC | 75 | 1606 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455308 | 74936 | 74955 | TAAGGCACCCACAGAAACAA | 70 | 1607 |
| 455309 | 74938 | 74957 | GATAAGGCACCCACAGAAAC | 65 | 1608 |
| 455310 | 74940 | 74959 | CTGATAAGGCACCCACAGAA | 66 | 1609 |
| 455311 | 74942 | 74961 | CCCTGATAAGGCACCCACAG | 81 | 1610 |
| 455312 | 74944 | 74963 | AGCCCTGATAAGGCACCCAC | 79 | 1611 |
| 455313 | 74946 | 74965 | CCAGCCCTGATAAGGCACCC | 74 | 1612 |
| 455314 | 74948 | 74967 | TCCCAGCCCTGATAAGGCAC | 74 | 1613 |
| 455315 | 74950 | 74969 | TATCCCAGCCCTGATAAGGC | 66 | 1614 |
| 455316 | 74952 | 74971 | AGTATCCCAGCCCTGATAAG | 48 | 1615 |
| 455317 | 74954 | 74973 | GAAGTATCCCAGCCCTGATA | 63 | 1616 |
| 455318 | 74956 | 74975 | CAGAAGTATCCCAGCCCTGA | 82 | 1617 |
| 455319 | 74958 | 74977 | ATCAGAAGTATCCCAGCCCT | 80 | 1618 |
| 455320 | 75066 | 75085 | GATTCCTAAAACAAACAGGA | 37 | 1619 |
| 455321 | 75068 | 75087 | AGGATTCCTAAAACAAACAG | 42 | 1620 |
| 455322 | 75070 | 75089 | CCAGGATTCCTAAAACAAAC | 72 | 1621 |
| 455323 | 75072 | 75091 | GACCAGGATTCCTAAAACAA | 71 | 1622 |
| 455324 | 75074 | 75093 | GAGACCAGGATTCCTAAAAC | 43 | 1623 |
| 455325 | 75076 | 75095 | CTGAGACCAGGATTCCTAAA | 77 | 1624 |
| 455326 | 75078 | 75097 | TCCTGAGACCAGGATTCCTA | 76 | 1625 |
| 455327 | 75080 | 75099 | GGTCCTGAGACCAGGATTCC | 69 | 1626 |
| 455328 | 75082 | 75101 | GAGGTCCTGAGACCAGGATT | 76 | 1627 |
| 455329 | 75084 | 75103 | ATGAGGTCCTGAGACCAGGA | 81 | 1628 |
| 455330 | 75086 | 75105 | CCATGAGGTCCTGAGACCAG | 84 | 1629 |
| 455331 | 75088 | 75107 | TTCCATGAGGTCCTGAGACC | 75 | 1630 |
| 455332 | 75090 | 75109 | TCTTCCATGAGGTCCTGAGA | 75 | 1631 |
| 455333 | 75092 | 75111 | CTTCTTCCATGAGGTCCTGA | 79 | 1632 |
| 455334 | 75094 | 75113 | CTCTTCTTCCATGAGGTCCT | 83 | 1633 |
| 455335 | 75096 | 75115 | CCCTCTTCTTCCATGAGGTC | 74 | 1634 |
| 455336 | 75098 | 75117 | CCCCCTCTTCTTCCATGAGG | 72 | 1635 |
| 455337 | 75100 | 75119 | CTCCCCCTCTTCTTCCATGA | 72 | 1636 |
| 455338 | 75164 | 75183 | CCTGAGCTCAACCAGACACG | 79 | 1637 |
| 455339 | 75166 | 75185 | TCCCTGAGCTCAACCAGACA | 73 | 1638 |
| 455340 | 75168 | 75187 | ATTCCCTGAGCTCAACCAGA | 75 | 1639 |
| 455341 | 75170 | 75189 | ATATTCCCTGAGCTCAACCA | 65 | 1640 |
| 455342 | 75172 | 75191 | CCATATTCCCTGAGCTCAAC | 78 | 1641 |
| 455343 | 75174 | 75193 | AACCATATTCCCTGAGCTCA | 81 | 1642 |
| 455344 | 75176 | 75195 | AGAACCATATTCCCTGAGCT | 77 | 1643 |
| 455345 | 75178 | 75197 | TAAGAACCATATTCCCTGAG | 73 | 1644 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455346 | 75180 | 75199 | GCTAAGAACCATATTCCCTG | 81 | 1645 |
| 455347 | 75254 | 75273 | TCAGTAAGCCTTTGCCCTGC | 79 | 1646 |
| 455348 | 75256 | 75275 | TATCAGTAAGCCTTTGCCCT | 72 | 1647 |
| 455349 | 75258 | 75277 | TTTATCAGTAAGCCTTTGCC | 76 | 1648 |
| 455350 | 75260 | 75279 | AGTTTATCAGTAAGCCTTTG | 84 | 1649 |
| 455351 | 75262 | 75281 | CAAGTTTATCAGTAAGCCTT | 82 | 1650 |
| 455352 | 75264 | 75283 | CTCAAGTTTATCAGTAAGCC | 82 | 1651 |
| 455353 | 75266 | 75285 | GACTCAAGTTTATCAGTAAG | 70 | 1652 |
| 455354 | 75268 | 75287 | CAGACTCAAGTTTATCAGTA | 78 | 1653 |
| 455355 | 75270 | 75289 | GGCAGACTCAAGTTTATCAG | 67 | 1654 |
| 455356 | 75272 | 75291 | AGGGCAGACTCAAGTTTATC | 51 | 1655 |
| 455357 | 75274 | 75293 | CGAGGGCAGACTCAAGTTTA | 54 | 1656 |
| 455358 | 75276 | 75295 | TACGAGGGCAGACTCAAGTT | 56 | 1657 |
| 455359 | 75278 | 75297 | CATACGAGGGCAGACTCAAG | 59 | 1658 |
| 455360 | 75280 | 75299 | CTCATACGAGGGCAGACTCA | 74 | 1659 |
| 455361 | 75282 | 75301 | CCCTCATACGAGGGCAGACT | 67 | 1660 |
| 455362 | 75309 | 75328 | CAGCCTCAGAGGGAGGCCAG | 40 | 1661 |
| 455363 | 75311 | 75330 | ACCAGCCTCAGAGGGAGGCC | 34 | 1662 |
| 455364 | 75313 | 75332 | TCACCAGCCTCAGAGGGAGG | 49 | 1663 |
| 455365 | 75315 | 75334 | AGTCACCAGCCTCAGAGGGA | 50 | 1664 |
| 455366 | 75412 | 75431 | CCCATACGCACAGGAGAGGC | 81 | 1665 |
| 455367 | 75414 | 75433 | TTCCCATACGCACAGGAGAG | 72 | 1666 |
| 455368 | 75416 | 75435 | TGTTCCCATACGCACAGGAG | 80 | 1667 |
| 455369 | 75418 | 75437 | GGTGTTCCCATACGCACAGG | 76 | 1668 |
| 455370 | 75420 | 75439 | TAGGTGTTCCCATACGCACA | 87 | 1669 |
| 455371 | 75422 | 75441 | GCTAGGTGTTCCCATACGCA | 92 | 1670 |
| 455372 | 75424 | 75443 | GTGCTAGGTGTTCCCATACG | 81 | 1671 |
| 455373 | 75491 | 75510 | GAGGCAAGGTGGTTTTGAGT | 55 | 1672 |
| 455374 | 75493 | 75512 | CTGAGGCAAGGTGGTTTTGA | 74 | 1673 |
| 455375 | 75495 | 75514 | AGCTGAGGCAAGGTGGTTTT | 79 | 1674 |
| 455376 | 75497 | 75516 | TCAGCTGAGGCAAGGTGGTT | 80 | 1675 |
| 455377 | 75499 | 75518 | GATCAGCTGAGGCAAGGTGG | 77 | 1676 |
| 455378 | 75501 | 75520 | CTGATCAGCTGAGGCAAGGT | 60 | 1677 |
| 455379 | 75503 | 75522 | CTCTGATCAGCTGAGGCAAG | 74 | 1678 |
| 455380 | 75505 | 75524 | AACTCTGATCAGCTGAGGCA | 77 | 1679 |
| 455381 | 75507 | 75526 | GAAACTCTGATCAGCTGAGG | 78 | 1680 |
| 455382 | 75509 | 75528 | CAGAAACTCTGATCAGCTGA | 78 | 1681 |
| 455383 | 75547 | 75566 | CAGAGACCAGCTAATTTGAT | 69 | 1682 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455384 | 75549 | 75568 | TTCAGAGACCAGCTAATTTG | 78 | 1683 |
| 455385 | 75551 | 75570 | AATTCAGAGACCAGCTAATT | 77 | 1684 |
| 455386 | 75553 | 75572 | TTAATTCAGAGACCAGCTAA | 83 | 1685 |
| 455387 | 75610 | 75629 | CTCCAGGCAGGAGGACTGGG | 79 | 1686 |
| 455388 | 75612 | 75631 | GTCTCCAGGCAGGAGGACTG | 65 | 1687 |
| 455389 | 75614 | 75633 | CTGTCTCCAGGCAGGAGGAC | 57 | 1688 |
| 455390 | 75616 | 75635 | AACTGTCTCCAGGCAGGAGG | 75 | 1689 |
| 455391 | 75618 | 75637 | TCAACTGTCTCCAGGCAGGA | 86 | 1690 |
| 455392 | 75620 | 75639 | CATCAACTGTCTCCAGGCAG | 80 | 1691 |
| 455393 | 75622 | 75641 | CACATCAACTGTCTCCAGGC | 86 | 1692 |
| 455394 | 75624 | 75643 | GACACATCAACTGTCTCCAG | 85 | 1693 |
| 455395 | 75658 | 75677 | GAAGAGTGTTGCTGGAGAAG | 73 | 1694 |
| 455396 | 75660 | 75679 | CTGAAGAGTGTTGCTGGAGA | 78 | 1695 |
| 455397 | 75662 | 75681 | TACTGAAGAGTGTTGCTGGA | 83 | 1696 |
| 455398 | 75664 | 75683 | TGTACTGAAGAGTGTTGCTG | 86 | 1697 |
| 455399 | 75666 | 75685 | TATGTACTGAAGAGTGTTGC | 74 | 1698 |
| 455400 | 75668 | 75687 | ATTATGTACTGAAGAGTGTT | 74 | 1699 |
| 455401 | 75670 | 75689 | TTATTATGTACTGAAGAGTG | 84 | 1700 |
| 455402 | 75672 | 75691 | GCTTATTATGTACTGAAGAG | 84 | 1701 |
| 455403 | 75674 | 75693 | AAGCTTATTATGTACTGAAG | 77 | 1702 |
| 455404 | 75676 | 75695 | TTAAGCTTATTATGTACTGA | 75 | 1703 |
| 455405 | 75678 | 75697 | AGTTAAGCTTATTATGTACT | 81 | 1704 |
| 455406 | 75680 | 75699 | TCAGTTAAGCTTATTATGTA | 58 | 1705 |
| 455407 | 75682 | 75701 | TATCAGTTAAGCTTATTATG | 65 | 1706 |
| 455408 | 75684 | 75703 | TTTATCAGTTAAGCTTATTA | 46 | 1707 |
| 455409 | 75686 | 75705 | TGTTTATCAGTTAAGCTTAT | 68 | 1708 |
| 455410 | 75688 | 75707 | TCTGTTTATCAGTTAAGCTT | 83 | 1709 |
| 455411 | 75726 | 75745 | AACCCAATGGTAAGCCCAAG | 87 | 1710 |
| 455412 | 75728 | 75747 | TAAACCCAATGGTAAGCCCA | 87 | 1711 |
| 455413 | 75730 | 75749 | TTTAAACCCAATGGTAAGCC | 78 | 1712 |
| 455414 | 75732 | 75751 | GATTTAAACCCAATGGTAAG | 31 | 1713 |
| 455415 | 75734 | 75753 | ATGATTTAAACCCAATGGTA | 71 | 1714 |
| 455416 | 75736 | 75755 | CTATGATTTAAACCCAATGG | 67 | 1715 |
| 455417 | 75738 | 75757 | CCCTATGATTTAAACCCAAT | 70 | 1716 |
| 455418 | 75740 | 75759 | GTCCCTATGATTTAAACCCA | 83 | 1717 |
| 455419 | 75742 | 75761 | AGGTCCCTATGATTTAAACC | 64 | 1718 |
| 455420 | 75776 | 75795 | TATCTGCTCCAGAGAAGCCC | 76 | 1719 |
| 455421 | 75778 | 75797 | AATATCTGCTCCAGAGAAGC | 78 | 1720 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455422 | 75801 | 75820 | CTACCTAAGGCCATGAACTT | 74 | 1721 |
| 455423 | 75803 | 75822 | TGCTACCTAAGGCCATGAAC | 82 | 1722 |
| 455424 | 75805 | 75824 | CATGCTACCTAAGGCCATGA | 84 | 1723 |
| 455425 | 75823 | 75842 | CAGAGTTAAGACCAGATACA | 84 | 1724 |
| 455426 | 75825 | 75844 | ATCAGAGTTAAGACCAGATA | 83 | 1725 |
| 455427 | 75827 | 75846 | CAATCAGAGTTAAGACCAGA | 77 | 1726 |
| 455428 | 75829 | 75848 | TACAATCAGAGTTAAGACCA | 81 | 1727 |
| 455429 | 75831 | 75850 | GCTACAATCAGAGTTAAGAC | 86 | 1728 |
| 455430 | 75833 | 75852 | TTGCTACAATCAGAGTTAAG | 85 | 1729 |
| 455431 | 75835 | 75854 | TTTTGCTACAATCAGAGTTA | 85 | 1730 |
| 455432 | 75837 | 75856 | ACTTTTGCTACAATCAGAGT | 73 | 1731 |
| 455433 | 75839 | 75858 | GAACTTTTGCTACAATCAGA | 80 | 1732 |
| 455434 | 75841 | 75860 | CAGAACTTTTGCTACAATCA | 82 | 1733 |
| 455435 | 75843 | 75862 | CTCAGAACTTTTGCTACAAT | 79 | 1734 |
| 455436 | 75845 | 75864 | CTCTCAGAACTTTTGCTACA | 76 | 1735 |
| 455437 | 75847 | 75866 | TCCTCTCAGAACTTTTGCTA | 75 | 1736 |
| 455438 | 75849 | 75868 | GCTCCTCTCAGAACTTTTGC | 85 | 1737 |
| 455439 | 75851 | 75870 | CAGCTCCTCTCAGAACTTTT | 85 | 1738 |
| 455440 | 75853 | 75872 | CTCAGCTCCTCTCAGAACTT | 80 | 1739 |
| 455441 | 75855 | 75874 | GGCTCAGCTCCTCTCAGAAC | 75 | 1740 |
| 455442 | 75957 | 75976 | GCAACCCACGGGATTCCCTC | 82 | 1741 |
| 455443 | 75959 | 75978 | AAGCAACCCACGGGATTCCC | 77 | 1742 |
| 455444 | 75961 | 75980 | GTAAGCAACCCACGGGATTC | 74 | 1743 |
| 455445 | 75963 | 75982 | AGGTAAGCAACCCACGGGAT | 76 | 1744 |
| 455446 | 75965 | 75984 | GTAGGTAAGCAACCCACGGG | 82 | 1745 |
| 455447 | 75967 | 75986 | AGGTAGGTAAGCAACCCACG | 88 | 1746 |
| 455448 | 75969 | 75988 | ATAGGTAGGTAAGCAACCCA | 83 | 1747 |
| 455449 | 75971 | 75990 | TTATAGGTAGGTAAGCAACC | 59 | 1748 |
| 455450 | 75973 | 75992 | CCTTATAGGTAGGTAAGCAA | 65 | 1749 |
| 455451 | 75975 | 75994 | CACCTTATAGGTAGGTAAGC | 62 | 1750 |
| 455452 | 75977 | 75996 | ACCACCTTATAGGTAGGTAA | 57 | 1751 |
| 455453 | 75979 | 75998 | AAACCACCTTATAGGTAGGT | 75 | 1752 |
| 455454 | 75981 | 76000 | ATAAACCACCTTATAGGTAG | 35 | 1753 |
| 455455 | 75983 | 76002 | TTATAAACCACCTTATAGGT | 39 | 1754 |
| 455456 | 75985 | 76004 | GCTTATAAACCACCTTATAG | 58 | 1755 |
| 455457 | 75987 | 76006 | CAGCTTATAAACCACCTTAT | 86 | 1756 |
| 455458 | 75989 | 76008 | AGCAGCTTATAAACCACCTT | 86 | 1757 |
| 455459 | 75991 | 76010 | ACAGCAGCTTATAAACCACC | 80 | 1758 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455460 | 75993 | 76012 | GGACAGCAGCTTATAAACCA | 69 | 1759 |
| 455461 | 75995 | 76014 | CAGGACAGCAGCTTATAAAC | 72 | 1760 |
| 455462 | 75997 | 76016 | GCCAGGACAGCAGCTTATAA | 76 | 1761 |
| 455463 | 75999 | 76018 | TGGCCAGGACAGCAGCTTAT | 89 | 1762 |
| 455464 | 76001 | 76020 | AGTGGCCAGGACAGCAGCTT | 80 | 1763 |
| 455465 | 76003 | 76022 | GCAGTGGCCAGGACAGCAGC | 78 | 1764 |
| 455466 | 76005 | 76024 | ATGCAGTGGCCAGGACAGCA | 85 | 1765 |
| 455467 | 76007 | 76026 | GAATGCAGTGGCCAGGACAG | 80 | 1766 |
| 455468 | 76009 | 76028 | TTGAATGCAGTGGCCAGGAC | 83 | 1767 |
| 455469 | 76011 | 76030 | ATTTGAATGCAGTGGCCAGG | 84 | 1768 |
| 455470 | 76013 | 76032 | GAATTTGAATGCAGTGGCCA | 81 | 1769 |
| 455471 | 76015 | 76034 | TGGAATTTGAATGCAGTGGC | 85 | 1770 |
| 455472 | 76017 | 76036 | ATTGGAATTTGAATGCAGTG | 64 | 1771 |
| 455473 | 76019 | 76038 | ACATTGGAATTTGAATGCAG | 80 | 1772 |
| 455474 | 76021 | 76040 | ACACATTGGAATTTGAATGC | 73 | 1773 |
| 455475 | 76023 | 76042 | GTACACATTGGAATTTGAAT | 80 | 1774 |
| 455476 | 76025 | 76044 | AAGTACACATTGGAATTTGA | 77 | 1775 |
| 455477 | 76027 | 76046 | TGAAGTACACATTGGAATTT | 68 | 1776 |
| 455478 | 76029 | 76048 | TATGAAGTACACATTGGAAT | 66 | 1777 |
| 455479 | 76031 | 76050 | ACTATGAAGTACACATTGGA | 83 | 1778 |
| 455480 | 76033 | 76052 | ACACTATGAAGTACACATTG | 76 | 1779 |
| 455481 | 76035 | 76054 | TTACACTATGAAGTACACAT | 78 | 1780 |
| 455482 | 76037 | 76056 | TTTTACACTATGAAGTACAC | 76 | 1781 |
| 455483 | 76039 | 76058 | ATTTTTACACTATGAAGTAC | 60 | 1782 |
| 455484 | 76041 | 76060 | AAATTTTTACACTATGAAGT | 35 | 1783 |
| 455485 | 76043 | 76062 | ATAAATTTTTACACTATGAA | 9 | 1784 |
| 455486 | 76045 | 76064 | ATATAAATTTTTACACTATG | 0 | 1785 |
| 455487 | 76047 | 76066 | TAATATAAATTTTTACACTA | 21 | 1786 |
| 455488 | 76049 | 76068 | AATAATATAAATTTTTACAC | 10 | 1787 |
| 455489 | 76051 | 76070 | ACAATAATATAAATTTTTAC | 7 | 1788 |
| 455490 | 76112 | 76131 | AGTTAAAGTAGATACAGCAA | 71 | 1789 |
| 455491 | 76114 | 76133 | GAAGTTAAAGTAGATACAGC | 63 | 1790 |
| 455492 | 76116 | 76135 | TGGAAGTTAAAGTAGATACA | 69 | 1791 |
| 455493 | 76118 | 76137 | TCTGGAAGTTAAAGTAGATA | 65 | 1792 |
| 455494 | 76120 | 76139 | TTTCTGGAAGTTAAAGTAGA | 55 | 1793 |
| 455495 | 76122 | 76141 | TATTTCTGGAAGTTAAAGTA | 57 | 1794 |
| 455496 | 76124 | 76143 | TTTATTTCTGGAAGTTAAAG | 36 | 1795 |
| 455497 | 76126 | 76145 | CGTTTATTTCTGGAAGTTAA | 77 | 1796 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455553 | 9123 | 9142 | ACCTGCCCCTATGTATAAGC | 89 | 1852 |
| | 11261 | 11280 | | | |
| 455554 | 9484 | 9503 | TTTGTAATATCTAACAGATA | 20 | 1853 |
| 455555 | 9630 | 9649 | TATATGACAGCCTCAATTTC | 68 | 1854 |
| 455556 | 9677 | 9696 | GGCATTTGTGTAAACAGGAA | 81 | 1855 |
| 455557 | 9746 | 9765 | TGTTAAATATTACTTAAAAT | 4 | 1856 |
| 455558 | 9776 | 9795 | AATTCCTTGGGTGGTAATCC | 81 | 1857 |
| 455559 | 10071 | 10090 | GGAAAGTTACAGGACAGGAA | 77 | 1858 |
| 455560 | 10352 | 10371 | GAAATGGCTTCTACAAAAAC | 47 | 1859 |
| 455561 | 10472 | 10491 | GGTCAGAATACCACAAACTA | 80 | 1860 |
| 455562 | 10634 | 10653 | AGTCTAATGCTTTTAGATTC | 59 | 1861 |
| 455563 | 11567 | 11586 | CATTGGAAAACTTAGGGTAA | 37 | 1862 |
| 455564 | 11597 | 11616 | ATTCTCACTGGGTATAGAGG | 72 | 1863 |
| 455565 | 11700 | 11719 | TAGCATTAATCTTTCCTAGG | 92 | 1864 |
| 455566 | 9886 | 9905 | GACTCAAAATAAGGTTCCTC | 86 | 1865 |
| | 12369 | 12388 | | | |
| 455567 | 12430 | 12449 | ACAGATTTATTCATATAAGC | 62 | 1866 |
| 455568 | 14060 | 14079 | AGATCCATAGATTCTTTCTT | 80 | 1867 |
| 455569 | 14129 | 14148 | ATCTGAATCAGAATATCTGC | 88 | 1868 |
| 455570 | 14190 | 14209 | GAAGACTTTATATTCTATGG | 59 | 1869 |
| 455571 | 14355 | 14374 | TATCCTTAATATTCAGGTAC | 82 | 1870 |
| 455572 | 14501 | 14520 | TTATTAAGACATCTGAAATA | 31 | 1871 |
| 455573 | 14701 | 14720 | TTAAGTGACTACACATGGAT | 76 | 1872 |
| 455574 | 14761 | 14780 | GATAATGTAACAACCCTATC | 42 | 1873 |
| 455575 | 14828 | 14847 | CTGAAGCATGAATTCACATT | 83 | 1874 |
| 455576 | 15316 | 15335 | AAATTCCACTACTCATGAAA | 62 | 1875 |
| 455577 | 15370 | 15389 | CTTCAGAGAATATCTCATTT | 83 | 1876 |
| 455578 | 15400 | 15419 | CACATCATAGTTTTGCATGA | 70 | 1877 |
| 455579 | 15525 | 15544 | TCTGACCCATAAAGTTTAAA | 70 | 1878 |
| 455580 | 16568 | 16587 | TTGGTTAATAATAATGTATC | 44 | 1879 |
| 455581 | 16832 | 16851 | TCACACATTTGTCAAAATCC | 89 | 1880 |
| 455582 | 16863 | 16882 | TATATAATTGTGTACTGGCA | 93 | 1881 |
| 455583 | 16930 | 16949 | TGCCAGTGGTTCAGCAGAGG | 77 | 1882 |
| 455584 | 17215 | 17234 | AATGTTTATAGCAGCTTTAT | 56 | 1883 |
| 455585 | 17330 | 17349 | GTCACTTTGAATATAGTTTG | 79 | 1884 |
| 455586 | 17426 | 17445 | GGCTAAAATCCAAAACACTG | 65 | 1885 |
| 455587 | 18449 | 18468 | AACAGTATTTGAGAAAACTT | 21 | 1886 |
| 455588 | 19883 | 19902 | GGGCTACAACTCAATAACAA | 63 | 1887 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455589 | 20512 | 20531 | AAGTCCTTATCATTTAGCTC | 69 | 1888 |
| 455590 | 21035 | 21054 | GATATTCCCAAAGTGACAGG | 75 | 1889 |
| 455591 | 21188 | 21207 | ATAATGAGACTTTAGCACTC | 86 | 1890 |
| 455592 | 21422 | 21441 | AATCTAAACTTCCAGCCAGG | 78 | 1891 |
| 455593 | 21493 | 21512 | ACAATAATGCATGCAAATGT | 67 | 1892 |
| 455594 | 21675 | 21694 | CACTGCTATTTCCCCAGCAA | 89 | 1893 |
| 455595 | 21710 | 21729 | CTTAAGCCCCATAAGAACAA | 65 | 1894 |
| 455596 | 21823 | 21842 | ATCTAAAACAGCAACATCTC | 57 | 1895 |
| 455597 | 23917 | 23936 | TAGTGATTGAATGTAGACTT | 81 | 1896 |
| 455598 | 23980 | 23999 | TTAGGCCACTAAGTCTGAGC | 83 | 1897 |
| 455599 | 24178 | 24197 | CAGCTGAAATCAGCCTTTGA | 69 | 1898 |
| 455600 | 24345 | 24364 | AATCTAGCTAAGTCCATAAC | 43 | 1899 |
| 455601 | 24504 | 24523 | TGCTTGGATATATAGAAGTC | 80 | 1900 |
| 455602 | 24578 | 24597 | AGGTCACTTTCCCTATACGA | 81 | 1901 |
| 455603 | 24608 | 24627 | AGAAGGAAGATTCTTTTCTC | 73 | 1902 |
| 455604 | 24924 | 24943 | CTAAGAGAGGCAACTGAAAT | 60 | 1903 |
| 455605 | 25063 | 25082 | GGCTCGAGGGCCACTGAAGG | 59 | 1904 |
| 455606 | 25093 | 25112 | AGCAAGCACATTGTCATGTC | 83 | 1905 |
| 455607 | 25132 | 25151 | GGCTGCCAAACTTTTCAAAA | 76 | 1906 |
| 455608 | 25626 | 25645 | TTTGTTCTTGCCTAAAATGC | 45 | 1907 |
| 455609 | 25688 | 25707 | TTCCTTCAAGTCAACTTATC | 69 | 1908 |
| 455610 | 26031 | 26050 | CCAGCCTACAGATGACTTTC | 78 | 1909 |
| 455611 | 26061 | 26080 | GCCAACTTTAGCCCCTTCCA | 85 | 1910 |
| 455612 | 26104 | 26123 | AATGCAAAATCTTTACCCTT | 58 | 1911 |
| 455613 | 26139 | 26158 | CCAGCTCAAAAACACACACT | 80 | 1912 |
| 455614 | 26227 | 26246 | GTTTGAAAAATTCAAGAATG | 26 | 1913 |
| 455615 | 26388 | 26407 | ATAGTGTCTGGCTCATAATA | 48 | 1914 |
| 455616 | 26597 | 26616 | TCAGGTCCTCAAAAACACCA | 84 | 1915 |
| 455617 | 26648 | 26667 | TGGCTGGTACCAGCTGGTGG | 76 | 1916 |
| 455618 | 26766 | 26785 | ACAAATTCATCGAGCTAATG | 52 | 1917 |
| 455619 | 26908 | 26927 | AGAATAGCATGGATTTGAAT | 49 | 1918 |
| 455620 | 26999 | 27018 | CACAAACTTGATCTTGCCAC | 77 | 1919 |
| 455626 | 36534 | 36553 | GAATGTAAAGTATCTTGTTC | 47 | 1920 |
| 455627 | 36578 | 36597 | TATAAAATACACACTGGATT | 57 | 1921 |
| 455628 | 36614 | 36633 | GAAATGTGGCTGCTTCAAAC | 36 | 1922 |
| 455629 | 36649 | 36668 | TGGAGTCACTAGCCACATGT | 71 | 1923 |
| 455630 | 36691 | 36710 | GCATACAAATTTACTGAAAC | 58 | 1924 |
| 455631 | 36904 | 36923 | CAAGTTAAAATCTGCCTCAC | 62 | 1925 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455632 | 36975 | 36994 | GGCATGTATTGATTGCCCTC | 68 | 1926 |
| 455633 | 37026 | 37045 | AGTAAAAGCAGTGGCTGACG | 60 | 1927 |
| 455634 | 37086 | 37105 | CACCTGCCACAGGACAAATG | 28 | 1928 |
| 455635 | 37755 | 37774 | TTGCCCCAATTAGGCCAATA | 76 | 1929 |
| 455636 | 37822 | 37841 | AAGGGCTTAAATTCCACTGG | 73 | 1930 |
| 455637 | 37873 | 37892 | GTACTTTACATGTGCAGCAC | 81 | 1931 |
| 455638 | 38268 | 38287 | AATATATCCAAAATGTTATT | 8 | 1932 |
| 455639 | 38694 | 38713 | GCAGCATCCAACAGAAATAG | 62 | 1933 |
| 455640 | 39294 | 39313 | GAGACTGAACACACGCAAAC | 65 | 1934 |
| 455641 | 39324 | 39343 | GTTCTCTGGGATAGTGAGAA | 49 | 1935 |
| 455642 | 39792 | 39811 | GAGAAACCCAGCCAGCTAAT | 69 | 1936 |
| 455643 | 39937 | 39956 | GGAAGATCTGCCTGAGATTC | 46 | 1937 |
| 455644 | 40132 | 40151 | TACAGCATCCAGCTCAGTGC | 63 | 1938 |
| 455645 | 40633 | 40652 | CCCAGTTTAGAACAATACAA | 65 | 1939 |
| 455646 | 40866 | 40885 | GTAGCCATTGCCCAACACAG | 63 | 1940 |
| 455647 | 40901 | 40920 | CACCACAAGTCCCAGTAGGG | 58 | 1941 |
| 455648 | 40923 | 40942 | TAAACCAAAGTGTGCATATG | 11 | 1942 |
| 455649 | 41087 | 41106 | AAGGACTTACCAATCTTGAC | 7 | 1943 |
| 455650 | 41114 | 41133 | ACCTAACAATTTGGAGAGTC | 44 | 1944 |
| 455651 | 41239 | 41258 | TTACAAGACCAAAGGGTGCC | 68 | 1945 |
| 455652 | 41329 | 41348 | AAATCAACCTTCAAGACATC | 13 | 1946 |
| 455653 | 41397 | 41416 | AAAAATATGTCTACCACATC | 52 | 1947 |
| 455654 | 41431 | 41450 | AAGTTCTAGCTATGACAGAA | 23 | 1948 |
| 455655 | 41575 | 41594 | AGCCTGCAGAACTATGAGCC | 48 | 1949 |
| 455656 | 41629 | 41648 | ATTGGAAGCTTGCTGAGGCC | 44 | 1950 |
| 455657 | 41644 | 41663 | CTGCCTTCCGCCATGATTGG | 48 | 1951 |
| 455658 | 41747 | 41766 | CGAGACAGTGAGTTCTTGTG | 64 | 1952 |
| 455659 | 42067 | 42086 | CTGGCCCTTCACCAAATCAG | 62 | 1953 |
| 455660 | 42139 | 42158 | GGTCAGATTTATTAGTACAA | 65 | 1954 |
| 455661 | 42904 | 42923 | ATCATACCTGAAGAAACTGC | 16 | 1955 |
| 455662 | 43059 | 43078 | ATACAGAGCTTTGAGAAAGG | 38 | 1956 |
| 455663 | 43194 | 43213 | TGTAACAGTGAGAGTCATCT | 71 | 1957 |
| 455664 | 43284 | 43303 | TCTGAGTCTTTACACAGTAT | 72 | 1958 |
| 455665 | 43724 | 43743 | TTCATCAAGGAAAGCATTTA | 31 | 1959 |
| 455666 | 43765 | 43784 | TGGAGATGTGGACTGAACTG | 19 | 1960 |
| 455667 | 43908 | 43927 | CCTGGGCCGCAGTGGCTGCA | 63 | 1961 |
| 455668 | 43926 | 43945 | GTTTTGTCTCAGGTCTCACC | 75 | 1962 |
| 455669 | 43941 | 43960 | CCAGACCAGGGATTTGTTTT | 34 | 1963 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455670 | 43974 | 43993 | CTCATTATAAAGTTGTTTGA | 55 | 1964 |
| 455671 | 44507 | 44526 | TGTACTATGAAAGTTTGTCA | 80 | 1965 |
| 455672 | 44525 | 44544 | AATGATATTGGAATAATCTG | 26 | 1966 |
| 455673 | 44540 | 44559 | CTTTGGAAAAGTTTGAATGA | 26 | 1967 |
| 455674 | 44583 | 44602 | CAGCCTCATAAAATAAGCTG | 19 | 1968 |
| 455675 | 45414 | 45433 | TACTGAGAATAGTGTTTCAC | 71 | 1969 |
| 455676 | 45440 | 45459 | AAGACATCCTTATCTTTTGC | 75 | 1970 |
| 455677 | 45512 | 45531 | TTCCAATATTTGTACCCTCA | 87 | 1971 |
| 455678 | 45626 | 45645 | TACAATGGCCTTTCTAAACC | 64 | 1972 |
| 455679 | 45712 | 45731 | AGATCTTTACTTTCATTACA | 54 | 1973 |
| 455680 | 46058 | 46077 | TATGCAAATTGCATACATTT | 59 | 1974 |
| 455681 | 46091 | 46110 | TTTCCAGATATTTTCCCATA | 88 | 1975 |
| 455682 | 46241 | 46260 | GTGTATTTCACCACAATTTT | 78 | 1976 |
| 455683 | 46571 | 46590 | TGTCTTTGAACATGATCTTC | 67 | 1977 |
| 455684 | 46676 | 46695 | GCATGACTAATTAAAACATC | 58 | 1978 |
| 455685 | 46759 | 46778 | CAGAGCAAGTGGCAGGGCTG | 69 | 1979 |
| 455686 | 46791 | 46810 | CAGAGAGAGTAAAAATTGTT | 49 | 1980 |
| 455687 | 46905 | 46924 | CAGCAGAAAGCAGTTAAATT | 56 | 1981 |
| 455688 | 46941 | 46960 | CAGTAATGGTGAGGGTGATG | 28 | 1982 |
| 455689 | 46956 | 46975 | GGTCCCCATTTCCTACAGTA | 67 | 1983 |
| 455690 | 47307 | 47326 | ACACCTGAGCATATCAGTTT | 67 | 1984 |
| 455691 | 47400 | 47419 | CAGAAAATCCTAGTGCTGCC | 62 | 1985 |
| 455692 | 47424 | 47443 | ATAAAATACAAAGGTTTTCC | 23 | 1986 |
| 455693 | 47467 | 47486 | TCCAAATTGACTTAAACCAC | 74 | 1987 |
| 455694 | 47528 | 47547 | TTGAAAACATCCTTGGGATA | 44 | 1988 |
| 455695 | 47579 | 47598 | CAGGCTGGATTTGGGCCACG | 76 | 1989 |
| 455696 | 47649 | 47668 | GCCACAGATAATGCATAAAT | 39 | 1990 |
| 455697 | 47795 | 47814 | CTGGGTTGAGGCCACAAATA | 78 | 1991 |
| 455698 | 47929 | 47948 | GTTTGTGTACTTATAATCCC | 75 | 1992 |
| 455699 | 47974 | 47993 | GACAAAATGACACACATCCT | 72 | 1993 |
| 455700 | 48188 | 48207 | TTTCACACAATTGATAACTT | 57 | 1994 |
| 455701 | 48208 | 48227 | CAGGCCAACACAGAAAGCTG | 70 | 1995 |
| 455702 | 48277 | 48296 | AGAAACCCACCTCTAATACC | 31 | 1996 |
| 455703 | 48402 | 48421 | GCCACACTTTCCATTCTAGT | 90 | 1997 |
| 455704 | 48417 | 48436 | TGGTTACCAGCTCAAGCCAC | 72 | 1998 |
| 455705 | 48566 | 48585 | CAGGTCTAGAGGCCTATCCC | 73 | 1999 |
| 455706 | 48665 | 48684 | TCTTCAAAGAACCCAGCACC | 63 | 2000 |
| 455707 | 48697 | 48716 | AGATGGAGAGAAAGACTCTG | 61 | 2001 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455708 | 48728 | 48747 | CCCACAGTGACAGTGACTCA | 89 | 2002 |
| 455709 | 48768 | 48787 | CTTAGAAGTTTTGGGAAGGT | 60 | 2003 |
| 455710 | 48802 | 48821 | ATGGTCCCTATCCAAGCCCA | 81 | 2004 |
| 455711 | 48828 | 48847 | ATGGGCAACCATTCTCTTCC | 80 | 2005 |
| 455712 | 49754 | 49773 | GTTGGATGTCTACTTAAACG | 63 | 2006 |
| 455713 | 49845 | 49864 | GACCACATGTTCAGCTAAGA | 68 | 2007 |
| 455714 | 49923 | 49942 | AAACAGAGGCAGTGGTGCTG | 62 | 2008 |
| 455715 | 50053 | 50072 | CCAAAAAGGAGGTCAATGCA | 30 | 2009 |
| 455716 | 50522 | 50541 | GTATCCCCAAGAGAAGGCTC | 59 | 2010 |
| 455717 | 50571 | 50590 | TCAAATGAAGCCAAAACCTC | 63 | 2011 |
| 455718 | 50774 | 50793 | CACTTTCTAGAGATTTTAAC | 1 | 2012 |
| 455719 | 51623 | 51642 | TCAGATCTTGCATGTCTGCG | 2 | 2013 |
| 455720 | 51753 | 51772 | CCGCAAGTGAGCGAGACACA | 49 | 2014 |
| 455721 | 51827 | 51846 | CCACATTCTTTAGTCAACTC | 59 | 2015 |
| 455722 | 51856 | 51875 | CAGAAAACATTTCCTCAGAC | 3 | 2016 |
| 455723 | 52033 | 52052 | ACCAGTTTTCTAGCCGATCT | 90 | 2017 |
| 455724 | 52056 | 52075 | AGGAAAAGCTTCTTTCATCC | 34 | 2018 |
| 455725 | 52071 | 52090 | GCTTTCGAGAAAGAAAGGAA | 44 | 2019 |
| 455726 | 53203 | 53222 | TGGATGAAGGTAAAAGTGCA | 42 | 2020 |
| 455727 | 53246 | 53265 | TCACTATAGGGCCTTGCACA | 53 | 2021 |
| 455728 | 53262 | 53281 | AGCTGGTGCAACATGCTCAC | 69 | 2022 |
| 455729 | 53329 | 53348 | GCATTCTCATGTAGAGTTGC | 0 | 2023 |
| 455730 | 53344 | 53363 | GATATGAATAGACAGGCATT | 63 | 2024 |
| 455731 | 53431 | 53450 | ATTCCCAGAACTTAAGCTTC | 40 | 2025 |
| 455732 | 53571 | 53590 | ATTCCATCATTCTTTGATGG | 47 | 2026 |
| 455733 | 53900 | 53919 | TGCACAAGGAATAAGTGAAT | 51 | 2027 |
| 455734 | 54378 | 54397 | AGAAGGGCTTGAACTACATG | 15 | 2028 |
| 455735 | 54577 | 54596 | GAGCCCAGATATGCAGAACA | 58 | 2029 |
| 455736 | 54592 | 54611 | AAATGACAAGCATCTGAGCC | 16 | 2030 |
| 455737 | 54632 | 54651 | ATTTATACCACTAGGAGGCA | 52 | 2031 |
| 455738 | 55241 | 55260 | TTCAGTGACATTAAGAAAAG | 28 | 2032 |
| 455739 | 55256 | 55275 | ATCTTAAGTTTACAGTTCAG | 64 | 2033 |
| 455740 | 55277 | 55296 | GCATGAAATTTACAATTTTT | 26 | 2034 |
| 455741 | 55418 | 55437 | TCCTGCCAATAAATTAAGAA | 0 | 2035 |
| 455742 | 55657 | 55676 | GAAGTCAGCCCGCCTCTCAC | 33 | 2036 |
| 455743 | 55841 | 55860 | GTGTCCCTCAGTAAAATCTC | 53 | 2037 |
| 455744 | 55877 | 55896 | ATGACCCTGGCCACCAACTC | 63 | 2038 |
| 455745 | 55961 | 55980 | CAGAATCAGAGAGCAAGCAG | 56 | 2039 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455746 | 56125 | 56144 | CCTTAAAATCCACAGGGAAG | 5 | 2040 |
| 455747 | 56151 | 56170 | TCCCCATCACTAAGCCTTAC | 31 | 2041 |
| 455748 | 56203 | 56222 | TAACACCTCACCCTACAGGC | 56 | 2042 |
| 455749 | 56287 | 56306 | ACACCATACTAAGTTTCTGA | 68 | 2043 |
| 455750 | 57995 | 58014 | CTTGTCAATGCACACTTTAA | 80 | 2044 |
| 455751 | 58074 | 58093 | TCTAGTTCAAATGATGTCTG | 66 | 2045 |
| 455752 | 58089 | 58108 | AATAAAGACAGAGTCTCTAG | 30 | 2046 |
| 455753 | 58106 | 58125 | CAAAATGAAGATCTCTGAAT | 23 | 2047 |
| 455754 | 58173 | 58192 | AGCTTTGTGGCTTTGTTCAG | 60 | 2048 |
| 455755 | 58259 | 58278 | TGAATGACATGTACAAGTAA | 52 | 2049 |
| 455756 | 58377 | 58396 | TGTGTAAGGACTATATACTC | 64 | 2050 |
| 455757 | 58471 | 58490 | TTCAGCACAGTAACATACTG | 41 | 2051 |
| 455758 | 58496 | 58515 | AGATGTGTTACAATTGCCTA | 76 | 2052 |
| 455759 | 58696 | 58715 | TTTACATCCTGAAAGGTATT | 51 | 2053 |
| 455760 | 59471 | 59490 | ATATGTACTTATTAAACCTA | 18 | 2054 |
| 455761 | 59748 | 59767 | ACAAAAGGAAGCCTCTAGGC | 0 | 2055 |
| 455762 | 59913 | 59932 | CCAAGTGTTTGAATTCTGCA | 83 | 2056 |
| 455763 | 60155 | 60174 | CAGGTTGATGTTTCTAATTC | 60 | 2057 |
| 455764 | 60170 | 60189 | CTACAGCTGAAAGAACAGGT | 76 | 2058 |
| 455765 | 60249 | 60268 | ATGTTCCAAGCCAGAGAGCT | 54 | 2059 |
| 455766 | 60323 | 60342 | GGTGTGGAGAACAACTCAGC | 72 | 2060 |
| 455767 | 60373 | 60392 | GGGAATTTGGAAAGCCCCAG | 0 | 2061 |
| 455768 | 60392 | 60411 | CAGCCGCAGGAGCTGGATGG | 42 | 2062 |
| 455769 | 60407 | 60426 | GGAGCCAAGCAGGGTCAGCC | 73 | 2063 |
| 455770 | 60433 | 60452 | GGAGAGAAAAACAGGGCACT | 69 | 2064 |
| 455771 | 60448 | 60467 | TATCCCACCTCAGTGGGAGA | 1 | 2065 |
| 455772 | 60602 | 60621 | TCTGAATCAATGAAAAGCAG | 79 | 2066 |
| 455773 | 60703 | 60722 | CATCACAATTTTTAAAAATG | 0 | 2067 |
| 455774 | 61216 | 61235 | GTATTTTTAAAACACATATA | 0 | 2068 |
| 455775 | 61251 | 61270 | CTTAATATACATATGAATAC | 14 | 2069 |
| 455786 | 61340 | 61359 | CAAATATCACAGAGACAGTC | 88 | 2070 |
| 455787 | 61758 | 61777 | GTACAGCAACCTTATTTTAA | 5 | 2071 |
| 455788 | 61853 | 61872 | TTAAATCCTGGGAATGGCAC | 83 | 2072 |
| 455789 | 61959 | 61978 | CTAATGTTGATGGGTATTTA | 60 | 2073 |
| 455790 | 62043 | 62062 | CATGGTTATGTGTATCTGCA | 89 | 2074 |
| 455791 | 62067 | 62086 | TTCACTTGATGTGAAATGAA | 18 | 2075 |
| 455792 | 62500 | 62519 | TGCCAGGGACACAACTTGCT | 82 | 2076 |
| 455793 | 62595 | 62614 | ATGGCATTCAGTACTAACAG | 59 | 2077 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455794 | 62610 | 62629 | TTTTCCTCAGAGAGAATGGC | 67 | 2078 |
| 455795 | 63284 | 63303 | AGTCACAATCAGGGAAGCCT | 77 | 2079 |
| 455796 | 63449 | 63468 | AGTAATCATTCCACCTTCTC | 70 | 2080 |
| 455797 | 63464 | 63483 | CAGTGTTAAGCAAACAGTAA | 41 | 2081 |
| 455798 | 63554 | 63573 | ATACACACATCTTCTAAGCA | 48 | 2082 |
| 455799 | 63576 | 63595 | TCAAGTTTGCTGAAAGCTGA | 48 | 2083 |
| 455800 | 63591 | 63610 | ATAGAGATTTTCATATCAAG | 41 | 2084 |
| 455801 | 64070 | 64089 | ACAGGGAGGTCTCAGGAATC | 77 | 2085 |
| 455802 | 64122 | 64141 | TTTAAGACCTTGGAGGCATT | 36 | 2086 |
| 455803 | 64586 | 64605 | AGGGATGGTGCTCATTGTCT | 20 | 2087 |
| 455804 | 64810 | 64829 | GCCGGATCCCTTTTCTGGGC | 64 | 2088 |
| 455805 | 64955 | 64974 | TGATCACCTCGACTGAAAAC | 65 | 2089 |
| 455806 | 65058 | 65077 | GTGCCACCTTCCAACACACA | 74 | 2090 |
| 455807 | 65530 | 65549 | CAGACAGGTGTATTTGGTGG | 65 | 2091 |
| 455808 | 65895 | 65914 | ACTTTGCAAAATTTAGCCCA | 77 | 2092 |
| 455809 | 65928 | 65947 | TCCCATTCCCACGAGAATTT | 76 | 2093 |
| 455810 | 65972 | 65991 | GCCTTCAAGCCAGAGCCCTC | 76 | 2094 |
| 455811 | 65987 | 66006 | GACCAAGAGTTCAGGGCCTT | 59 | 2095 |
| 455812 | 66099 | 66118 | GTAATGGGAAAGCCAAGTCT | 51 | 2096 |
| 455813 | 66128 | 66147 | TTGCCAGCCATGTTTTCCTG | 67 | 2097 |
| 455814 | 66283 | 66302 | AGGGCATCCATCCCCTGCCA | 7 | 2098 |
| 455815 | 66664 | 66683 | TCACTGGAGCAAGCAAAACA | 64 | 2099 |
| 455816 | 66775 | 66794 | GGTCATAGAAAATAAACTTG | 62 | 2100 |
| 455817 | 66863 | 66882 | AGTGTTGAGACCCTGAACAC | 53 | 2101 |
| 455818 | 66918 | 66937 | AGAGAAAACTGCCCATTTTT | 71 | 2102 |
| 455819 | 66948 | 66967 | AGATCATGGAACCTACAGCT | 18 | 2103 |
| 455820 | 66963 | 66982 | GGACATGGGAAGGAAAGATC | 27 | 2104 |
| 455821 | 67191 | 67210 | CAACAACTACCTGGGTCAGC | 51 | 2105 |
| 455822 | 67271 | 67290 | AGGCATTTGCCTATCTATCC | 58 | 2106 |
| 455823 | 67334 | 67353 | CCAACAAAAGCACTCACTAC | 56 | 2107 |
| 455824 | 67773 | 67792 | TGAAATCTGGGCCTCAAACC | 78 | 2108 |
| 455825 | 67843 | 67862 | GAAACCCTTTCTTCAGACCA | 79 | 2109 |
| 455826 | 68621 | 68640 | TCAAAACAGCAAGTGCTGAA | 60 | 2110 |
| 455827 | 69053 | 69072 | AACCCTAAAGGATCACATTA | 43 | 2111 |
| 455828 | 69357 | 69376 | CAAAGAGCCGTGTGGCAGGG | 65 | 2112 |
| 455829 | 69395 | 69414 | GACCAGCCGTGGGACCCCAA | 84 | 2113 |
| 455830 | 69473 | 69492 | CCACAGGAAGGGCGATGGTA | 58 | 2114 |
| 455831 | 69498 | 69517 | GCAGGAAAGGACCTGGCCTC | 45 | 2115 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides having 5-10-5 MOE wings and deoxy gap targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS NO | Human Start Site | Human Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455832 | 70567 | 70586 | TTAGGGAGCTGACACCCTAG | 56 | 2116 |
| 455833 | 70645 | 70664 | CAATTCAGTGCAGAATTCAA | 80 | 2117 |
| 455834 | 70675 | 70694 | TCTGAGTTTACTTTGGGCCA | 75 | 2118 |
| 455835 | 70725 | 70744 | CATGATGACCATGTGAAAGA | 82 | 2119 |
| 455836 | 70890 | 70909 | CTGAATGCTTACACCAAGAG | 83 | 2120 |
| 455837 | 70973 | 70992 | CCAATTTTCTATGAGCTTTG | 85 | 2121 |
| 455838 | 71013 | 71032 | CTTTTATGTATAAAATAAGA | 6 | 2122 |
| 455839 | 71573 | 71592 | CCAGGTACATCTTCAATAGC | 75 | 2123 |
| 455840 | 71610 | 71629 | GTACAATTGCTTCAACTAGA | 87 | 2124 |
| 455841 | 71698 | 71717 | ACATTTTTGGATGAGGGCAT | 81 | 2125 |
| 455842 | 71750 | 71769 | AAAGCCAAAGGTTATATCTC | 77 | 2126 |
| 455843 | 71765 | 71784 | AATGCTTGTGGTTCCAAAGC | 79 | 2127 |
| 455844 | 71929 | 71948 | TGTAAAAGTTTAACAGCCTC | 70 | 2128 |
| 455845 | 71992 | 72011 | CATAACCTTTTCCCACCTGA | 79 | 2129 |
| 455846 | 72036 | 72055 | CAGTTCTTTGCACAAAGCTG | 76 | 2130 |
| 455847 | 72127 | 72146 | CAAGATTGTCTGGAAAGCTC | 76 | 2131 |
| 455848 | 72202 | 72221 | TCGCATTCAGTAAGCAGAGC | 47 | 2132 |
| 455849 | 72229 | 72248 | AAACCAGTTTTCTTACTGAC | 17 | 2133 |
| 455850 | 72285 | 72304 | CGGTGTCACACAGATAAACT | 73 | 2134 |
| 455851 | 72367 | 72386 | TTAACTCTCACCCAGTGTCC | 61 | 2135 |
| 455852 | 72406 | 72425 | GTACTAAACATAGCCCAGGG | 78 | 2136 |
| 455853 | 72687 | 72706 | AAATACTCACCAAACTGCCC | 4 | 2137 |
| 455854 | 72768 | 72787 | GTGACCAGCTCTCGGTGTGT | 10 | 2138 |
| 455855 | 73340 | 73359 | GATTTGGTTTGTCCAAACTG | 49 | 2139 |
| 455856 | 73530 | 73549 | GTCAGAAAAGCCAGATTTAC | 46 | 2140 |
| 455857 | 73621 | 73640 | GCAACTGGCAGGCCACGCCC | 39 | 2141 |
| 455858 | 73636 | 73655 | AGTTGTCCACCCTCTGCAAC | 0 | 2142 |
| 455859 | 73683 | 73702 | TGTCAAAGGTGAGGGACTCT | 57 | 2143 |
| 455860 | 74018 | 74037 | ACACAAGACATTTCCTTTTT | 64 | 1544 |

**Example 33: Dose-dependent antisense inhibition of human STAT3 in HuVEC cells**

**[0374]** Gapmers from the study described in Example 32 exhibiting significant *in vitro* inhibition of STAT3 were tested at various doses in HuVEC cells. Cells were plated at a density of 5,000 cells per well and transfected using LipofectAMINE2000® reagent with 1.1 nM, 3.3 nM, 10.0 nM, and 30.0 nM concentrations of antisense oligonucleotide, as specified in Table 54. After a treatment period of approximately 16 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199 (forward sequence ACATGCCACTTTGGTGTTTCATAA, designated herein as SEQ ID NO:

6; reverse sequence TCTTCGTAGATTGTGCTGATAGAGAAC, designated herein as SEQ ID NO: 7; probe sequence CAGTATAGCCGCTTCCTGCAAGAGTCGAA, designated herein as SEQ ID NO: 8) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0375]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 54 and was calculated by plotting the concentrations of oligonucleotides used versus the percent inhibition of STAT3 mRNA expression achieved at each concentration, and noting the concentration of oligonucleotide at which 50% inhibition of STAT3 mRNA expression was achieved compared to the control. As illustrated in Table 54, STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 54**

| Do se-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 1.1 nM | 3.3 nM | 10.0 nM | 30.0 nM | $IC_{50}$ (nM) |
| 337332 | 7 | 19 | 46 | 80 | 10.4 |
| 345785 | 8 | 22 | 46 | 74 | 11.3 |
| 455265 | 20 | 43 | 64 | 85 | 5.0 |
| 455267 | 16 | 30 | 62 | 79 | 6.7 |
| 455269 | 23 | 49 | 72 | 84 | 4.0 |
| 455270 | 3 | 28 | 60 | 79 | 8.1 |
| 455271 | 16 | 40 | 71 | 86 | 4.9 |
| 455272 | 28 | 30 | 57 | 86 | 5.7 |
| 455282 | 18 | 28 | 55 | 80 | 7.4 |
| 455291 | 21 | 45 | 75 | 85 | 4.1 |
| 455370 | 6 | 23 | 53 | 78 | 9.0 |
| 455371 | 15 | 46 | 73 | 90 | 4.5 |
| 455391 | 10 | 30 | 54 | 75 | 8.5 |
| 455393 | 6 | 33 | 62 | 81 | 7.0 |
| 455394 | 5 | 33 | 63 | 85 | 6.7 |
| 455398 | 7 | 25 | 56 | 76 | 8.8 |
| 455411 | 10 | 21 | 58 | 82 | 7.9 |
| 455412 | 15 | 27 | 50 | 79 | 8.4 |
| 455429 | 17 | 43 | 67 | 81 | 5.2 |
| 455438 | 20 | 43 | 66 | 83 | 5.0 |
| 455439 | 10 | 41 | 67 | 84 | 5.7 |
| 455447 | 7 | 23 | 53 | 87 | 7.7 |
| 455457 | 9 | 24 | 52 | 79 | 8.8 |
| 455458 | 8 | 34 | 62 | 83 | 6.7 |
| 455463 | 6 | 37 | 63 | 85 | 6.3 |
| 455471 | 11 | 42 | 67 | 78 | 5.9 |
| 455525 | 0 | 9 | 42 | 72 | 13.4 |
| 455527 | 0 | 21 | 60 | 87 | 7.8 |
| 455530 | 11 | 26 | 62 | 83 | 7.1 |
| 455536 | 5 | 21 | 62 | 85 | 7.6 |

| Do se-dependent antisense inhibition of human STAT3 in HuVEC cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 1.1 nM | 3.3 nM | 10.0 nM | 30.0 nM | $IC_{50}$ (nM) |
| 455540 | 8 | 28 | 65 | 87 | 6.5 |
| 455547 | 6 | 19 | 45 | 67 | 13.4 |
| 455548 | 0 | 41 | 68 | 90 | 5.8 |
| 455551 | 0 | 3 | 33 | 72 | 15.9 |
| 455553 | 0 | 29 | 64 | 87 | 7.2 |
| 455565 | 0 | 19 | 54 | 86 | 8.8 |
| 455566 | 13 | 28 | 45 | 76 | 9.6 |
| 455569 | 0 | 16 | 47 | 76 | 11.1 |
| 455581 | 0 | 19 | 62 | 85 | 8.6 |
| 455582 | 0 | 26 | 70 | 89 | 6.9 |
| 455591 | 7 | 17 | 47 | 68 | 12.8 |
| 455594 | 0 | 16 | 48 | 76 | 10.9 |
| 455611 | 14 | 43 | 68 | 81 | 5.4 |
| 455637 | 10 | 22 | 56 | 76 | 8.9 |
| 455677 | 0 | 18 | 46 | 72 | 11.9 |
| 455681 | 16 | 19 | 42 | 69 | 13.0 |
| 455703 | 9 | 40 | 72 | 92 | 5.1 |
| 455708 | 11 | 15 | 45 | 77 | 10.7 |
| 455723 | 3 | 9 | 33 | 68 | 17.0 |
| 455762 | 0 | 9 | 42 | 70 | 14.1 |
| 455786 | 21 | 32 | 50 | 79 | 7.4 |
| 455790 | 13 | 19 | 56 | 84 | 7.8 |
| 455840 | 17 | 30 | 52 | 77 | 7.9 |

**Example 34: Antisense inhibition of human STAT3 in HuVEC cells by oligonucleotides designed by microwalk**

**[0376]** Additional gapmers were designed based on the gapmers presented in Example 1 that demonstrated an inhibition of at least 50%. These gapmers were designed by creating gapmers shifted slightly upstream and downstream (i.e., "microwalk") of the original gapmers. These gapmers were tested *in vitro.* ISIS 337332 was also included in the assay as a comparator. Cultured HuVEC cells at a density of 5,000 cells per well were transfected using LipofectAMINE 2000® reagent with 30 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. The human primer probe set RTS199, described hereinabove, was used to measure STAT3 mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells. The results are presented in Table 55.

**[0377]** The chimeric antisense oligonucleotides in Table 55 were designed as 5-10-5 MOE gapmers. The gapmers designated with an asterisk (*) in Table 55 are the original gapmers from which gapmers, ISIS 465226-466744, were designed via microwalk. The 5-10-5 gapmers are 20 nucleosides in length, wherein the

central gap segment is comprised of ten 2'-deoxynucleosides and is flanked on both sides (in the 5' and 3' directions) by wings 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. "Target start site" indicates the 5'-most nucleoside to which the gapmer is targeted. "Target stop site" indicates the 3'-most nucleoside to which the gapmer is targeted. Each gapmer listed in Table 55 is targeted to the target region spanning nucleobases 2313-76017 of SEQ ID NO: 2 (the complement of GENBANK Accession No. NT_010755.14 truncated from nucleotides 4185000 to 4264000).

**Table 55**

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 466646 | 2313 | 2332 | CACACTATACACATTTTTAA | 3 | 2144 |
| 466647 | 2314 | 2333 | ACACACTATACACATTTTTA | 11 | 2145 |
| 466648 | 2315 | 2334 | TACACACTATACACATTTTT | 8 | 2146 |
| 455525* | 2316 | 2335 | GTACACACTATACACATTTT | 47 | 1824 |
| 466649 | 2317 | 2336 | GGTACACACTATACACATTT | 46 | 2147 |
| 466650 | 2318 | 2337 | AGGTACACACTATACACATT | 46 | 2148 |
| 466651 | 2319 | 2338 | CAGGTACACACTATACACAT | 54 | 2149 |
| 466652 | 2320 | 2339 | GCAGGTACACACTATACACA | 68 | 2150 |
| 466653 | 2321 | 2340 | AGCAGGTACACACTATACAC | 43 | 2151 |
| 466654 | 2322 | 2341 | CAGCAGGTACACACTATACA | 56 | 2152 |
| 466655 | 2323 | 2342 | CCAGCAGGTACACACTATAC | 72 | 2153 |
| 466656 | 2324 | 2343 | ACCAGCAGGTACACACTATA | 52 | 2154 |
| 466657 | 2325 | 2344 | GACCAGCAGGTACACACTAT | 69 | 2155 |
| 466658 | 2326 | 2345 | AGACCAGCAGGTACACACTA | 15 | 2156 |
| 466659 | 2327 | 2346 | AAGACCAGCAGGTACACACT | 49 | 2157 |
| 466660 | 2328 | 2347 | TAAGACCAGCAGGTACACAC | 59 | 2158 |
| 466661 | 2329 | 2348 | GTAAGACCAGCAGGTACACA | 73 | 2159 |
| 466662 | 2330 | 2349 | AGTAAGACCAGCAGGTACAC | 65 | 2160 |
| 466663 | 2331 | 2350 | CAGTAAGACCAGCAGGTACA | 64 | 2161 |
| 466664 | 2332 | 2351 | ACAGTAAGACCAGCAGGTAC | 53 | 2162 |
| 466665 | 2333 | 2352 | TACAGTAAGACCAGCAGGTA | 67 | 2163 |
| 466666 | 2334 | 2353 | ATACAGTAAGACCAGCAGGT | 75 | 2164 |
| 466667 | 2335 | 2354 | CATACAGTAAGACCAGCAGG | 66 | 2165 |
| 466668 | 2336 | 2355 | ACATACAGTAAGACCAGCAG | 55 | 2166 |
| 466669 | 2337 | 2356 | CACATACAGTAAGACCAGCA | 71 | 2167 |
| 466670 | 2338 | 2357 | GCACATACAGTAAGACCAGC | 83 | 2168 |
| 466671 | 2339 | 2358 | TGCACATACAGTAAGACCAG | 28 | 2169 |
| 466672 | 2340 | 2359 | TTGCACATACAGTAAGACCA | 70 | 2170 |
| 466673 | 2341 | 2360 | GTTGCACATACAGTAAGACC | 39 | 2171 |
| 466674 | 2342 | 2361 | AGTTGCACATACAGTAAGAC | 53 | 2172 |
| 466675 | 2343 | 2362 | TAGTTGCACATACAGTAAGA | 43 | 2173 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455527* | 2383 | 2402 | GCCAAAAATTTACAACCCAT | 48 | 1826 |
| 465806 | 2384 | 2403 | AGCCAAAAATTTACAACCCA | 29 | 2174 |
| 465807 | 2385 | 2404 | CAGCCAAAAATTTACAACCC | 7 | 2175 |
| 465808 | 2386 | 2405 | CCAGCCAAAAATTTACAACC | 35 | 2176 |
| 465809 | 2387 | 2406 | GCCAGCCAAAAATTTACAAC | 10 | 2177 |
| 465810 | 2388 | 2407 | AGCCAGCCAAAAATTTACAA | 37 | 2178 |
| 465811 | 2389 | 2408 | CAGCCAGCCAAAAATTTACA | 29 | 2179 |
| 465812 | 2390 | 2409 | ACAGCCAGCCAAAAATTTAC | 3 | 2180 |
| 465813 | 2391 | 2410 | CACAGCCAGCCAAAAATTTA | 6 | 2181 |
| 465814 | 2392 | 2411 | GCACAGCCAGCCAAAAATTT | 35 | 2182 |
| 465815 | 2393 | 2412 | AGCACAGCCAGCCAAAAATT | 22 | 2183 |
| 465816 | 2394 | 2413 | CAGCACAGCCAGCCAAAAAT | 23 | 2184 |
| 465817 | 2395 | 2414 | TCAGCACAGCCAGCCAAAAA | 33 | 2185 |
| 465818 | 2396 | 2415 | ATCAGCACAGCCAGCCAAAA | 32 | 2186 |
| 465819 | 2397 | 2416 | TATCAGCACAGCCAGCCAAA | 48 | 2187 |
| 465820 | 2398 | 2417 | TTATCAGCACAGCCAGCCAA | 32 | 2188 |
| 465821 | 2399 | 2418 | TTTATCAGCACAGCCAGCCA | 0 | 2189 |
| 465822 | 2400 | 2419 | CTTTATCAGCACAGCCAGCC | 49 | 2190 |
| 465823 | 2401 | 2420 | GCTTTATCAGCACAGCCAGC | 69 | 2191 |
| 465824 | 2402 | 2421 | TGCTTTATCAGCACAGCCAG | 48 | 2192 |
| 465825 | 2403 | 2422 | ATGCTTTATCAGCACAGCCA | 74 | 2193 |
| 465826 | 2404 | 2423 | AATGCTTTATCAGCACAGCC | 62 | 2194 |
| 465827 | 2405 | 2424 | CAATGCTTTATCAGCACAGC | 67 | 2195 |
| 465828 | 2406 | 2425 | CCAATGCTTTATCAGCACAG | 71 | 2196 |
| 465829 | 2407 | 2426 | CCCAATGCTTTATCAGCACA | 47 | 2197 |
| 465830 | 2408 | 2427 | GCCCAATGCTTTATCAGCAC | 81 | 2198 |
| 465831 | 2409 | 2428 | AGCCCAATGCTTTATCAGCA | 75 | 2199 |
| 465832 | 2410 | 2429 | AAGCCCAATGCTTTATCAGC | 57 | 2200 |
| 465349 | 2655 | 2674 | AGGCTCCAACCTCTAAAACA | 41 | 2201 |
| 465350 | 2656 | 2675 | AAGGCTCCAACCTCTAAAAC | 34 | 2202 |
| 465351 | 2657 | 2676 | CAAGGCTCCAACCTCTAAAA | 43 | 2203 |
| 465352 | 2658 | 2677 | TCAAGGCTCCAACCTCTAAA | 51 | 2204 |
| 465353 | 2659 | 2678 | ATCAAGGCTCCAACCTCTAA | 38 | 2205 |
| 465354 | 2660 | 2679 | AATCAAGGCTCCAACCTCTA | 29 | 2206 |
| 465355 | 2661 | 2680 | AAATCAAGGCTCCAACCTCT | 56 | 2207 |
| 465356 | 2662 | 2681 | AAAATCAAGGCTCCAACCTC | 24 | 2208 |
| 465357 | 2663 | 2682 | TAAAATCAAGGCTCCAACCT | 46 | 2209 |
| 465358 | 2664 | 2683 | CTAAAATCAAGGCTCCAACC | 45 | 2210 |
| 465359 | 2665 | 2684 | ACTAAAATCAAGGCTCCAAC | 50 | 2211 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465366 | 2666 | 2685 | GACTAAAATCAAGGCTCCAA | 51 | 2212 |
| 465367 | 2667 | 2686 | AGACTAAAATCAAGGCTCCA | 64 | 2213 |
| 465368 | 2668 | 2687 | GAGACTAAAATCAAGGCTCC | 76 | 2214 |
| 455530* | 2669 | 2688 | AGAGACTAAAATCAAGGCTC | 74 | 1829 |
| 455536* | 5000 | 5019 | AGAACTGAAATTCCTTGGTC | 52 | 1835 |
| 465833 | 5001 | 5020 | CAGAACTGAAATTCCTTGGT | 81 | 2215 |
| 465834 | 5002 | 5021 | ACAGAACTGAAATTCCTTGG | 81 | 2216 |
| 465835 | 5003 | 5022 | AACAGAACTGAAATTCCTTG | 48 | 2217 |
| 465836 | 5004 | 5023 | GAACAGAACTGAAATTCCTT | 46 | 2218 |
| 465837 | 5005 | 5024 | AGAACAGAACTGAAATTCCT | 39 | 2219 |
| 465838 | 5006 | 5025 | AAGAACAGAACTGAAATTCC | 22 | 2220 |
| 465839 | 5007 | 5026 | AAAGAACAGAACTGAAATTC | 3 | 2221 |
| 465840 | 5008 | 5027 | AAAAGAACAGAACTGAAATT | 0 | 2222 |
| 465841 | 5009 | 5028 | CAAAAGAACAGAACTGAAAT | 0 | 2223 |
| 465842 | 5010 | 5029 | ACAAAAGAACAGAACTGAAA | 0 | 2224 |
| 465843 | 5011 | 5030 | TACAAAAGAACAGAACTGAA | 3 | 2225 |
| 465844 | 5012 | 5031 | CTACAAAAGAACAGAACTGA | 0 | 2226 |
| 465845 | 5013 | 5032 | CCTACAAAAGAACAGAACTG | 13 | 2227 |
| 465846 | 5014 | 5033 | CCCTACAAAAGAACAGAACT | 0 | 2228 |
| 465847 | 5015 | 5034 | CCCCTACAAAAGAACAGAAC | 7 | 2229 |
| 465848 | 5016 | 5035 | TCCCCTACAAAAGAACAGAA | 33 | 2230 |
| 465849 | 5017 | 5036 | TTCCCCTACAAAAGAACAGA | 18 | 2231 |
| 465850 | 5018 | 5037 | CTTCCCCTACAAAAGAACAG | 0 | 2232 |
| 465851 | 5019 | 5038 | GCTTCCCCTACAAAAGAACA | 43 | 2233 |
| 465852 | 5020 | 5039 | AGCTTCCCCTACAAAAGAAC | 32 | 2234 |
| 465853 | 5021 | 5040 | AAGCTTCCCCTACAAAAGAA | 0 | 2235 |
| 465854 | 5022 | 5041 | AAAGCTTCCCCTACAAAAGA | 15 | 2236 |
| 465855 | 5023 | 5042 | AAAAGCTTCCCCTACAAAAG | 14 | 2237 |
| 465856 | 5024 | 5043 | TAAAAGCTTCCCCTACAAAA | 4 | 2238 |
| 465857 | 5025 | 5044 | TTAAAAGCTTCCCCTACAAA | 0 | 2239 |
| 465858 | 5026 | 5045 | TTTAAAAGCTTCCCCTACAA | 11 | 2240 |
| 465859 | 5027 | 5046 | TTTTAAAAGCTTCCCCTACA | 11 | 2241 |
| 465860 | 5688 | 5707 | CAGTGGTTTTTATAAATGAC | 29 | 2242 |
| 465861 | 5689 | 5708 | TCAGTGGTTTTTATAAATGA | 19 | 2243 |
| 465862 | 5690 | 5709 | TTCAGTGGTTTTTATAAATG | 4 | 2244 |
| 465863 | 5691 | 5710 | TTTCAGTGGTTTTTATAAAT | 0 | 2245 |
| 465864 | 5692 | 5711 | CTTTCAGTGGTTTTTATAAA | 0 | 2246 |
| 465865 | 5693 | 5712 | TCTTTCAGTGGTTTTTATAA | 0 | 2247 |
| 465866 | 5694 | 5713 | CTCTTTCAGTGGTTTTTATA | 35 | 2248 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465867 | 5695 | 5714 | ACTCTTTCAGTGGTTTTTAT | 67 | 2249 |
| 465868 | 5696 | 5715 | TACTCTTTCAGTGGTTTTTA | 60 | 2250 |
| 465886 | 5697 | 5716 | GTACTCTTTCAGTGGTTTTT | 85 | 2251 |
| 465887 | 5698 | 5717 | AGTACTCTTTCAGTGGTTTT | 62 | 2252 |
| 455540* | 5699 | 5718 | AAGTACTCTTTCAGTGGTTT | 76 | 1839 |
| 465888 | 5700 | 5719 | CAAGTACTCTTTCAGTGGTT | 80 | 2253 |
| 465906 | 5701 | 5720 | TCAAGTACTCTTTCAGTGGT | 74 | 2254 |
| 465926 | 5702 | 5721 | CTCAAGTACTCTTTCAGTGG | 80 | 2255 |
| 465927 | 5703 | 5722 | CCTCAAGTACTCTTTCAGTG | 71 | 2256 |
| 465928 | 5704 | 5723 | CCCTCAAGTACTCTTTCAGT | 54 | 2257 |
| 465929 | 5705 | 5724 | TCCCTCAAGTACTCTTTCAG | 33 | 2258 |
| 465930 | 5706 | 5725 | GTCCCTCAAGTACTCTTTCA | 56 | 2259 |
| 465931 | 5707 | 5726 | TGTCCCTCAAGTACTCTTTC | 43 | 2260 |
| 465932 | 5708 | 5727 | ATGTCCCTCAAGTACTCTTT | 33 | 2261 |
| 465486 | 7674 | 7693 | AAAGGGCTGCAAAAAATCTG | 39 | 2262 |
| 465487 | 7675 | 7694 | GAAAGGGCTGCAAAAAATCT | 11 | 2263 |
| 465488 | 7676 | 7695 | AGAAAGGGCTGCAAAAAATC | 28 | 2264 |
| 465489 | 7677 | 7696 | CAGAAAGGGCTGCAAAAAAT | 39 | 2265 |
| 465490 | 7678 | 7697 | ACAGAAAGGGCTGCAAAAAA | 29 | 2266 |
| 465506 | 7679 | 7698 | AACAGAAAGGGCTGCAAAAA | 36 | 2267 |
| 465507 | 7680 | 7699 | AAACAGAAAGGGCTGCAAAA | 35 | 2268 |
| 465508 | 7681 | 7700 | TAAACAGAAAGGGCTGCAAA | 47 | 2269 |
| 455547* | 7682 | 7701 | GTAAACAGAAAGGGCTGCAA | 72 | 1846 |
| 465509 | 7683 | 7702 | GGTAAACAGAAAGGGCTGCA | 70 | 2270 |
| 465510 | 7684 | 7703 | TGGTAAACAGAAAGGGCTGC | 63 | 2271 |
| 465511 | 7685 | 7704 | CTGGTAAACAGAAAGGGCTG | 60 | 2272 |
| 465526 | 7686 | 7705 | CCTGGTAAACAGAAAGGGCT | 65 | 2273 |
| 465527 | 7687 | 7706 | ACCTGGTAAACAGAAAGGGC | 26 | 2274 |
| 465528 | 7688 | 7707 | AACCTGGTAAACAGAAAGGG | 53 | 2275 |
| 465529 | 7689 | 7708 | TAACCTGGTAAACAGAAAGG | 35 | 2276 |
| 465530 | 7690 | 7709 | ATAACCTGGTAAACAGAAAG | 3 | 2277 |
| 465531 | 7691 | 7710 | GATAACCTGGTAAACAGAAA | 17 | 2278 |
| 465532 | 7692 | 7711 | AGATAACCTGGTAAACAGAA | 14 | 2279 |
| 465533 | 7693 | 7712 | AAGATAACCTGGTAAACAGA | 26 | 2280 |
| 455548* | 8078 | 8097 | GGGCAGATTTACCTTCCTTA | 77 | 1847 |
| 466722 | 8241 | 8260 | AATAGCAATCACCTTAGGAA | 53 | 2281 |
| 466723 | 8242 | 8261 | CAATAGCAATCACCTTAGGA | 62 | 2282 |
| 466724 | 8243 | 8262 | ACAATAGCAATCACCTTAGG | 48 | 2283 |
| 455551* | 8244 | 8263 | TACAATAGCAATCACCTTAG | 65 | 1850 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 466725 | 8245 | 8264 | CTACAATAGCAATCACCTTA | 15 | 2284 |
| 466726 | 8246 | 8265 | ACTACAATAGCAATCACCTT | 45 | 2285 |
| 466727 | 8247 | 8266 | AACTACAATAGCAATCACCT | 42 | 2286 |
| 466728 | 8248 | 8267 | AAACTACAATAGCAATCACC | 26 | 2287 |
| 466729 | 8249 | 8268 | AAAACTACAATAGCAATCAC | 14 | 2288 |
| 466730 | 8250 | 8269 | CAAAACTACAATAGCAATCA | 0 | 2289 |
| 466731 | 8251 | 8270 | TCAAAACTACAATAGCAATC | 29 | 2290 |
| 466732 | 8252 | 8271 | TTCAAAACTACAATAGCAAT | 20 | 2291 |
| 466733 | 8253 | 8272 | TTTCAAAACTACAATAGCAA | 14 | 2292 |
| 466734 | 8254 | 8273 | GTTTCAAAACTACAATAGCA | 58 | 2293 |
| 466735 | 8255 | 8274 | TGTTTCAAAACTACAATAGC | 28 | 2294 |
| 466736 | 8256 | 8275 | GTGTTTCAAAACTACAATAG | 42 | 2295 |
| 466737 | 8257 | 8276 | AGTGTTTCAAAACTACAATA | 13 | 2296 |
| 466738 | 8258 | 8277 | AAGTGTTTCAAAACTACAAT | 18 | 2297 |
| 466739 | 8259 | 8278 | CAAGTGTTTCAAAACTACAA | 30 | 2298 |
| 466740 | 8260 | 8279 | CCAAGTGTTTCAAAACTACA | 49 | 2299 |
| 466741 | 8261 | 8280 | ACCAAGTGTTTCAAAACTAC | 46 | 2300 |
| 466742 | 8262 | 8281 | AACCAAGTGTTTCAAAACTA | 41 | 2301 |
| 466743 | 8263 | 8282 | CAACCAAGTGTTTCAAAACT | 13 | 2302 |
| 455553* | 9123 | 9142 | ACCTGCCCCTATGTATAAGC | 75 | 1852 |
| | 11261 | 11280 | | | |
| 466744 | 9124 | 9143 | CACCTGCCCCTATGTATAAG | 67 | 2303 |
| | 11262 | 11281 | | | |
| 466745 | 9125 | 9144 | CCACCTGCCCCTATGTATAA | 69 | 2304 |
| | 11263 | 11282 | | | |
| 466746 | 9126 | 9145 | TCCACCTGCCCCTATGTATA | 68 | 2305 |
| | 11264 | 11283 | | | |
| 466747 | 9127 | 9146 | TTCCACCTGCCCCTATGTAT | 69 | 2306 |
| | 11265 | 11284 | | | |
| 466748 | 9128 | 9147 | ATTCCACCTGCCCCTATGTA | 58 | 2307 |
| | 11266 | 11285 | | | |
| 466749 | 9129 | 9148 | TATTCCACCTGCCCCTATGT | 38 | 2308 |
| | 11267 | 11286 | | | |
| 466750 | 9130 | 9149 | TTATTCCACCTGCCCCTATG | 47 | 309 |
| | 11268 | 11287 | | | |
| 466751 | 9131 | 9150 | TTTATTCCACCTGCCCCTAT | 54 | 2310 |
| 466752 | 9132 | 9151 | TTTTATTCCACCTGCCCCTA | 50 | 2311 |
| 466753 | 9133 | 9152 | GTTTTATTCCACCTGCCCCT | 58 | 2312 |
| 466754 | 9134 | 9153 | TGTTTTATTCCACCTGCCCC | 53 | 2313 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 466755 | 9135 | 9154 | ATGTTTTATTCCACCTGCCC | 69 | 2314 |
| 466756 | 9136 | 9155 | TATGTTTTATTCCACCTGCC | 3 | 2315 |
| 466757 | 9137 | 9156 | TTATGTTTTATTCCACCTGC | 48 | 2316 |
| 466758 | 9138 | 9157 | ATTATGTTTTATTCCACCTG | 53 | 2317 |
| 466759 | 9139 | 9158 | AATTATGTTTTATTCCACCT | 24 | 2318 |
| 466760 | 9140 | 9159 | TAATTATGTTTTATTCCACC | 10 | 2319 |
| 466761 | 9141 | 9160 | CTAATTATGTTTTATTCCAC | 13 | 2320 |
| 466762 | 9142 | 9161 | CCTAATTATGTTTTATTCCA | 23 | 2321 |
| 466763 | 9143 | 9162 | TCCTAATTATGTTTTATTCC | 27 | 2322 |
| 466764 | 9144 | 9163 | CTCCTAATTATGTTTTATTC | 21 | 2323 |
| 466765 | 9145 | 9164 | CCTCCTAATTATGTTTTATT | 30 | 2324 |
| 465740 | 9862 | 9881 | TGGCTTCTTCCTGAGACACA | 81 | 2325 |
| | 12345 | 12364 | | | |
| 465741 | 9863 | 9882 | TTGGCTTCTTCCTGAGACAC | 68 | 2326 |
| | 12346 | 12365 | | | |
| 465742 | 9864 | 9883 | GTTGGCTTCTTCCTGAGACA | 81 | 2327 |
| | 12347 | 12366 | | | |
| 465743 | 9865 | 9884 | TGTTGGCTTCTTCCTGAGAC | 68 | 2328 |
| | 12348 | 12367 | | | |
| 465744 | 9866 | 9885 | CTGTTGGCTTCTTCCTGAGA | 44 | 2329 |
| | 12349 | 12368 | | | |
| 465745 | 9867 | 9886 | CCTGTTGGCTTCTTCCTGAG | 73 | 2330 |
| | 12350 | 12369 | | | |
| 465746 | 9868 | 9887 | TCCTGTTGGCTTCTTCCTGA | 61 | 2331 |
| | 12351 | 12370 | | | |
| 465747 | 9869 | 9888 | CTCCTGTTGGCTTCTTCCTG | 53 | 2332 |
| | 12352 | 12371 | | | |
| 465748 | 9870 | 9889 | CCTCCTGTTGGCTTCTTCCT | 78 | 2333 |
| | 12353 | 12372 | | | |
| 465749 | 9871 | 9890 | TCCTCCTGTTGGCTTCTTCC | 73 | 2334 |
| | 12354 | 12373 | | | |
| 465750 | 9872 | 9891 | TTCCTCCTGTTGGCTTCTTC | 70 | 2335 |
| | 12355 | 12374 | | | |
| 465751 | 9873 | 9892 | GTTCCTCCTGTTGGCTTCTT | 89 | 2336 |
| | 12356 | 12375 | | | |
| 465752 | 9874 | 9893 | GGTTCCTCCTGTTGGCTTCT | 86 | 2337 |
| | 12357 | 12376 | | | |
| 465753 | 9875 | 9894 | AGGTTCCTCCTGTTGGCTTC | 73 | 2338 |
| | 12358 | 12377 | | | |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465754 | 9876 | 9895 | AAGGTTCCTCCTGTTGGCTT | 85 | 2339 |
| | 12359 | 12378 | | | |
| 465755 | 9877 | 9896 | TAAGGTTCCTCCTGTTGGCT | 82 | 2340 |
| | 12360 | 12379 | | | |
| 465756 | 9878 | 9897 | ATAAGGTTCCTCCTGTTGGC | 72 | 2341 |
| | 12361 | 12380 | | | |
| 465757 | 9879 | 9898 | AATAAGGTTCCTCCTGTTGG | 61 | 2342 |
| | 12362 | 12381 | | | |
| 465758 | 9880 | 9899 | AAATAAGGTTCCTCCTGTTG | 40 | 2343 |
| | 12363 | 12382 | | | |
| 465759 | 9881 | 9900 | AAAATAAGGTTCCTCCTGTT | 41 | 2344 |
| | 12364 | 12383 | | | |
| 465760 | 9882 | 9901 | CAAAATAAGGTTCCTCCTGT | 20 | 2345 |
| | 12365 | 12384 | | | |
| 465761 | 9883 | 9902 | TCAAAATAAGGTTCCTCCTG | 57 | 2346 |
| | 12366 | 12385 | | | |
| 465762 | 9884 | 9903 | CTCAAAATAAGGTTCCTCCT | 48 | 2347 |
| | 12367 | 12386 | | | |
| 465763 | 9885 | 9904 | ACTCAAAATAAGGTTCCTCC | 52 | 2348 |
| | 12368 | 12387 | | | |
| 455566* | 9886 | 9905 | GACTCAAAATAAGGTTCCTC | 59 | 1855 |
| | 12369 | 12388 | | | |
| 465764 | 9887 | 9906 | TGACTCAAAATAAGGTTCCT | 54 | 2349 |
| | 12370 | 12389 | | | |
| 465765 | 9888 | 9907 | CTGACTCAAAATAAGGTTCC | 47 | 2350 |
| | 12371 | 12390 | | | |
| 465766 | 9889 | 9908 | CCTGACTCAAAATAAGGTTC | 55 | 2351 |
| | 12372 | 12391 | | | |
| 465767 | 9890 | 9909 | ACCTGACTCAAAATAAGGTT | 48 | 2352 |
| | 12373 | 12382 | | | |
| 455553* | 9123 | 9142 | ACCTGCCCCTATGTATAAGC | 75 | 1852 |
| | 11261 | 11280 | | | |
| 466744 | 9124 | 9143 | CACCTGCCCCTATGTATAAG | 67 | 2303 |
| | 11262 | 11281 | | | |
| 466745 | 9125 | 9144 | CCACCTGCCCCTATGTATAA | 69 | 2304 |
| | 11263 | 11282 | | | |
| 466746 | 9126 | 9145 | TCCACCTGCCCCTATGTATA | 68 | 2305 |
| | 11264 | 11283 | | | |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 466747 | 9127 | 9146 | TTCCACCTGCCCCTATGTAT | 69 | 2306 |
| | 11265 | 11284 | | | |
| 466748 | 9128 | 9147 | ATTCCACCTGCCCCTATGTA | 58 | 2307 |
| | 11266 | 11285 | | | |
| 466749 | 9129 | 9148 | TATTCCACCTGCCCCTATGT | 38 | 2308 |
| | 11267 | 11286 | | | |
| 466750 | 9130 | 9149 | TTATTCCACCTGCCCCTATG | 47 | 2309 |
| | 11268 | 11287 | | | |
| 465726 | 11695 | 11714 | TTAATCTTTCCTAGGCAAAG | 19 | 2353 |
| 465727 | 11696 | 11715 | ATTAATCTTTCCTAGGCAAA | 22 | 2354 |
| 465728 | 11697 | 11716 | CATTAATCTTTCCTAGGCAA | 43 | 2355 |
| 465729 | 11698 | 11717 | GCATTAATCTTTCCTAGGCA | 68 | 2356 |
| 465730 | 11699 | 11718 | AGCATTAATCTTTCCTAGGC | 80 | 2357 |
| 455565* | 11700 | 11719 | TAGCATTAATCTTTCCTAGG | 74 | 1864 |
| 465731 | 11701 | 11720 | TTAGCATTAATCTTTCCTAG | 42 | 2358 |
| 465732 | 11702 | 11721 | ATTAGCATTAATCTTTCCTA | 22 | 2359 |
| 465733 | 11703 | 11722 | GATTAGCATTAATCTTTCCT | 40 | 2360 |
| 465734 | 11704 | 11723 | AGATTAGCATTAATCTTTCC | 0 | 2361 |
| 465735 | 11705 | 11724 | AAGATTAGCATTAATCTTTC | 10 | 2362 |
| 465736 | 11706 | 11725 | TAAGATTAGCATTAATCTTT | 3 | 2363 |
| 465737 | 12342 | 12361 | CTTCTTCCTGAGACACAGCC | 71 | 2364 |
| 465738 | 12343 | 12362 | GCTTCTTCCTGAGACACAGC | 74 | 2365 |
| 465739 | 12344 | 12363 | GGCTTCTTCCTGAGACACAG | 83 | 2366 |
| 465740 | 9862 | 9881 | TGGCTTCTTCCTGAGACACA | 81 | 2325 |
| | 12345 | 12364 | | | |
| 465741 | 9863 | 9882 | TTGGCTTCTTCCTGAGACAC | 68 | 2326 |
| | 12346 | 12365 | | | |
| 465742 | 9864 | 9883 | GTTGGCTTCTTCCTGAGACA | 81 | 2327 |
| | 12347 | 12366 | | | |
| 465743 | 9865 | 9884 | TGTTGGCTTCTTCCTGAGAC | 68 | 2328 |
| | 12348 | 12367 | | | |
| 465744 | 9866 | 9885 | CTGTTGGCTTCTTCCTGAGA | 44 | 2329 |
| | 12349 | 12368 | | | |
| 465745 | 9867 | 9886 | CCTGTTGGCTTCTTCCTGAG | 73 | 2330 |
| | 12350 | 12369 | | | |
| 465746 | 9868 | 9887 | TCCTGTTGGCTTCTTCCTGA | 61 | 2331 |
| | 12351 | 12370 | | | |
| 465747 | 9869 | 9888 | CTCCTGTTGGCTTCTTCCTG | 53 | 2332 |
| | 12352 | 12371 | | | |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465748 | 9870 | 9889 | CCTCCTGTTGGCTTCTTCCT | 78 | 2333 |
| | 12353 | 12372 | | | |
| 465749 | 9871 | 9890 | TCCTCCTGTTGGCTTCTTCC | 73 | 2334 |
| | 12354 | 12373 | | | |
| 465750 | 9872 | 9891 | TTCCTCCTGTTGGCTTCTTC | 70 | 2335 |
| | 12355 | 12374 | | | |
| 465751 | 9873 | 9892 | GTTCCTCCTGTTGGCTTCTT | 89 | 2336 |
| | 12356 | 12375 | | | |
| 465752 | 9874 | 9893 | GGTTCCTCCTGTTGGCTTCT | 86 | 2337 |
| | 12357 | 12376 | | | |
| 465753 | 9875 | 9894 | AGGTTCCTCCTGTTGGCTTC | 73 | 2338 |
| | 12358 | 12377 | | | |
| 465754 | 9876 | 9895 | AAGGTTCCTCCTGTTGGCTT | 85 | 2339 |
| | 12359 | 12378 | | | |
| 465755 | 9877 | 9896 | TAAGGTTCCTCCTGTTGGCT | 82 | 2340 |
| | 12360 | 12379 | | | |
| 465756 | 9878 | 9897 | ATAAGGTTCCTCCTGTTGGC | 72 | 2341 |
| | 12361 | 12380 | | | |
| 465757 | 9879 | 9898 | AATAAGGTTCCTCCTGTTGG | 61 | 2342 |
| | 12362 | 12381 | | | |
| 465758 | 9880 | 9899 | AAATAAGGTTCCTCCTGTTG | 40 | 2343 |
| | 12363 | 12382 | | | |
| 465759 | 9881 | 9900 | AAAATAAGGTTCCTCCTGTT | 41 | 2344 |
| | 12364 | 12383 | | | |
| 465760 | 9882 | 9901 | CAAAATAAGGTTCCTCCTGT | 20 | 2345 |
| | 12365 | 12384 | | | |
| 465761 | 9883 | 9902 | TCAAAATAAGGTTCCTCCTG | 57 | 2346 |
| | 12366 | 12385 | | | |
| 465762 | 9884 | 9903 | CTCAAAATAAGGTTCCTCCT | 48 | 2347 |
| | 12367 | 12386 | | | |
| 465763 | 9885 | 9904 | ACTCAAAATAAGGTTCCTCC | 52 | 2348 |
| | 12368 | 12387 | | | |
| 455566* | 9886 | 9905 | GACTCAAAATAAGGTTCCTC | 59 | 1865 |
| | 12369 | 12388 | | | |
| 465764 | 9887 | 9906 | TGACTCAAAATAAGGTTCCT | 54 | 2349 |
| | 12370 | 12389 | | | |
| 465765 | 9888 | 9907 | CTGACTCAAAATAAGGTTCC | 47 | 2350 |
| | 12371 | 12390 | | | |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465766 | 9889 | 9908 | CCTGACTCAAAATAAGGTTC | 55 | 2351 |
| | 12372 | 12391 | | | |
| 465767 | 9890 | 9909 | ACCTGACTCAAAATAAGGTT | 48 | 2352 |
| | 12373 | 12392 | | | |
| 465369 | 14101 | 14120 | TGAGGATGACCCCAGATAAA | 64 | 2367 |
| 465370 | 14102 | 14121 | GTGAGGATGACCCCAGATAA | 60 | 2368 |
| 465371 | 14103 | 14122 | TGTGAGGATGACCCCAGATA | 47 | 2369 |
| 465372 | 14104 | 14123 | CTGTGAGGATGACCCCAGAT | 68 | 2370 |
| 465373 | 14105 | 14124 | CCTGTGAGGATGACCCCAGA | 67 | 2371 |
| 465374 | 14106 | 14125 | GCCTGTGAGGATGACCCCAG | 70 | 2372 |
| 465375 | 14107 | 14126 | TGCCTGTGAGGATGACCCCA | 75 | 2373 |
| 465376 | 14108 | 14127 | ATGCCTGTGAGGATGACCCC | 72 | 2374 |
| 465377 | 14109 | 14128 | TATGCCTGTGAGGATGACCC | 58 | 2375 |
| 465378 | 14110 | 14129 | CTATGCCTGTGAGGATGACC | 56 | 2376 |
| 465379 | 14111 | 14130 | GCTATGCCTGTGAGGATGAC | 65 | 2377 |
| 465380 | 14112 | 14131 | TGCTATGCCTGTGAGGATGA | 23 | 2378 |
| 465386 | 14113 | 14132 | CTGCTATGCCTGTGAGGATG | 64 | 2379 |
| 465387 | 14114 | 14133 | TCTGCTATGCCTGTGAGGAT | 66 | 2380 |
| 465388 | 14115 | 14134 | ATCTGCTATGCCTGTGAGGA | 69 | 2381 |
| 465389 | 14116 | 14135 | TATCTGCTATGCCTGTGAGG | 59 | 2382 |
| 465390 | 14117 | 14136 | ATATCTGCTATGCCTGTGAG | 51 | 2383 |
| 465391 | 14118 | 14137 | AATATCTGCTATGCCTGTGA | 57 | 2384 |
| 465392 | 14119 | 14138 | GAATATCTGCTATGCCTGTG | 60 | 2385 |
| 465393 | 14120 | 14139 | AGAATATCTGCTATGCCTGT | 53 | 2386 |
| 465394 | 14121 | 14140 | CAGAATATCTGCTATGCCTG | 55 | 2387 |
| 465395 | 14122 | 14141 | TCAGAATATCTGCTATGCCT | 64 | 2388 |
| 465396 | 14123 | 14142 | ATCAGAATATCTGCTATGCC | 43 | 2389 |
| 465397 | 14124 | 14143 | AATCAGAATATCTGCTATGC | 37 | 2390 |
| 465398 | 14125 | 14144 | GAATCAGAATATCTGCTATG | 22 | 2391 |
| 465399 | 14126 | 14145 | TGAATCAGAATATCTGCTAT | 33 | 2392 |
| 465400 | 14127 | 14146 | CTGAATCAGAATATCTGCTA | 58 | 2393 |
| 465401 | 14128 | 14147 | TCTGAATCAGAATATCTGCT | 77 | 2394 |
| 455569* | 14129 | 14148 | ATCTGAATCAGAATATCTGC | 67 | 1868 |
| 465406 | 14130 | 14149 | CATCTGAATCAGAATATCTG | 45 | 2395 |
| 465407 | 14131 | 14150 | CCATCTGAATCAGAATATCT | 47 | 2396 |
| 465408 | 14132 | 14151 | ACCATCTGAATCAGAATATC | 55 | 2397 |
| 465409 | 14133 | 14152 | GACCATCTGAATCAGAATAT | 72 | 2398 |
| 465410 | 14134 | 14153 | GGACCATCTGAATCAGAATA | 70 | 2399 |
| 465411 | 14135 | 14154 | AGGACCATCTGAATCAGAAT | 67 | 2400 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465426 | 14136 | 14155 | AAGGACCATCTGAATCAGAA | 71 | 2401 |
| 465427 | 14137 | 14156 | CAAGGACCATCTGAATCAGA | 73 | 2402 |
| 465428 | 14138 | 14157 | CCAAGGACCATCTGAATCAG | 64 | 2403 |
| 465429 | 14139 | 14158 | ACCAAGGACCATCTGAATCA | 54 | 2404 |
| 465446 | 14140 | 14159 | GACCAAGGACCATCTGAATC | 65 | 2405 |
| 465447 | 14141 | 14160 | GGACCAAGGACCATCTGAAT | 72 | 2406 |
| 465448 | 14142 | 14161 | AGGACCAAGGACCATCTGAA | 68 | 2407 |
| 465449 | 14143 | 14162 | AAGGACCAAGGACCATCTGA | 78 | 2408 |
| 465450 | 14144 | 14163 | TAAGGACCAAGGACCATCTG | 37 | 2409 |
| 465451 | 14145 | 14164 | CTAAGGACCAAGGACCATCT | 73 | 2410 |
| 465452 | 14146 | 14165 | ACTAAGGACCAAGGACCATC | 65 | 2411 |
| 465453 | 14147 | 14166 | AACTAAGGACCAAGGACCAT | 54 | 2412 |
| 465454 | 14148 | 14167 | AAACTAAGGACCAAGGACCA | 49 | 2413 |
| 465455 | 14149 | 14168 | CAAACTAAGGACCAAGGACC | 61 | 2414 |
| 465456 | 14150 | 14169 | TCAAACTAAGGACCAAGGAC | 53 | 2415 |
| 465457 | 14151 | 14170 | CTCAAACTAAGGACCAAGGA | 59 | 2416 |
| 465534 | 16802 | 16821 | CAACAGAGTGAAATGTAATG | 16 | 2417 |
| 465535 | 16803 | 16822 | TCAACAGAGTGAAATGTAAT | 12 | 2418 |
| 465536 | 16804 | 16823 | CTCAACAGAGTGAAATGTAA | 52 | 2419 |
| 465537 | 16805 | 16824 | GCTCAACAGAGTGAAATGTA | 74 | 2420 |
| 465538 | 16806 | 16825 | TGCTCAACAGAGTGAAATGT | 17 | 2421 |
| 465539 | 16807 | 16826 | ATGCTCAACAGAGTGAAATG | 37 | 2422 |
| 465540 | 16808 | 16827 | AATGCTCAACAGAGTGAAAT | 14 | 2423 |
| 465541 | 16809 | 16828 | GAATGCTCAACAGAGTGAAA | 30 | 2424 |
| 465542 | 16810 | 16829 | AGAATGCTCAACAGAGTGAA | 23 | 2425 |
| 465543 | 16811 | 16830 | TAGAATGCTCAACAGAGTGA | 43 | 2426 |
| 465544 | 16812 | 16831 | ATAGAATGCTCAACAGAGTG | 38 | 2427 |
| 465545 | 16813 | 16832 | CATAGAATGCTCAACAGAGT | 38 | 2428 |
| 465546 | 16814 | 16833 | CCATAGAATGCTCAACAGAG | 56 | 2429 |
| 465547 | 16815 | 16834 | TCCATAGAATGCTCAACAGA | 37 | 2430 |
| 465548 | 16816 | 16835 | ATCCATAGAATGCTCAACAG | 48 | 2431 |
| 465549 | 16817 | 16836 | AATCCATAGAATGCTCAACA | 24 | 2432 |
| 465550 | 16818 | 16837 | AAATCCATAGAATGCTCAAC | 34 | 2433 |
| 465551 | 16819 | 16838 | AAAATCCATAGAATGCTCAA | 30 | 2434 |
| 465552 | 16820 | 16839 | CAAAATCCATAGAATGCTCA | 32 | 2435 |
| 465553 | 16821 | 16840 | TCAAAATCCATAGAATGCTC | 46 | 2436 |
| 465554 | 16822 | 16841 | GTCAAAATCCATAGAATGCT | 57 | 2437 |
| 465555 | 16823 | 16842 | TGTCAAAATCCATAGAATGC | 32 | 2438 |
| 465556 | 16824 | 16843 | TTGTCAAAATCCATAGAATG | 5 | 2439 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465557 | 16825 | 16844 | TTTGTCAAAATCCATAGAAT | 2 | 2440 |
| 465558 | 16826 | 16845 | ATTTGTCAAAATCCATAGAA | 17 | 2441 |
| 465559 | 16827 | 16846 | CATTTGTCAAAATCCATAGA | 17 | 2442 |
| 465560 | 16828 | 16847 | ACATTTGTCAAAATCCATAG | 31 | 2443 |
| 465561 | 16829 | 16848 | CACATTTGTCAAAATCCATA | 43 | 2444 |
| 465562 | 16830 | 16849 | ACACATTTGTCAAAATCCAT | 42 | 2445 |
| 465563 | 16831 | 16850 | CACACATTTGTCAAAATCCA | 56 | 2446 |
| 455581* | 16832 | 16851 | TCACACATTTGTCAAAATCC | 55 | 1880 |
| 465564 | 16833 | 16852 | ATCACACATTTGTCAAAATC | 34 | 2447 |
| 465565 | 16834 | 16853 | CATCACACATTTGTCAAAAT | 40 | 2448 |
| 465566 | 16835 | 16854 | TCATCACACATTTGTCAAAA | 41 | 2449 |
| 465567 | 16836 | 16855 | ATCATCACACATTTGTCAAA | 37 | 2450 |
| 465568 | 16837 | 16856 | CATCATCACACATTTGTCAA | 44 | 2451 |
| 465569 | 16838 | 16857 | ACATCATCACACATTTGTCA | 60 | 2452 |
| 465570 | 16839 | 16858 | TACATCATCACACATTTGTC | 9 | 2453 |
| 465571 | 16840 | 16859 | ATACATCATCACACATTTGT | 48 | 2454 |
| 465572 | 16841 | 16860 | TATACATCATCACACATTTG | 46 | 2455 |
| 465573 | 16842 | 16861 | ATATACATCATCACACATTT | 28 | 2456 |
| 455582* | 16863 | 16882 | TATATAATTGTGTACTGGCA | 79 | 1881 |
| 465458 | 16864 | 16883 | TTATATAATTGTGTACTGGC | 83 | 2457 |
| 465459 | 16865 | 16884 | TTTATATAATTGTGTACTGG | 22 | 2458 |
| 465460 | 16866 | 16885 | TTTTATATAATTGTGTACTG | 8 | 2459 |
| 465461 | 16867 | 16886 | ATTTTATATAATTGTGTACT | 0 | 2460 |
| 465462 | 16868 | 16887 | TATTTTATATAATTGTGTAC | 1 | 2461 |
| 465463 | 16869 | 16888 | CTATTTTATATAATTGTGTA | 9 | 2462 |
| 465464 | 16870 | 16889 | ACTATTTTATATAATTGTGT | 0 | 2463 |
| 465465 | 16871 | 16890 | AACTATTTTATATAATTGTG | 7 | 2464 |
| 465466 | 16872 | 16891 | AAACTATTTTATATAATTGT | 13 | 2465 |
| 465606 | 21187 | 21206 | TAATGAGACTTTAGCACTCT | 67 | 2466 |
| 455591* | 21188 | 21207 | ATAATGAGACTTTAGCACTC | 62 | 1890 |
| 465607 | 21189 | 21208 | AATAATGAGACTTTAGCACT | 41 | 2467 |
| 465608 | 21190 | 21209 | CAATAATGAGACTTTAGCAC | 54 | 2468 |
| 465609 | 21191 | 21210 | GCAATAATGAGACTTTAGCA | 6 | 2469 |
| 465610 | 21193 | 21212 | CTGCAATAATGAGACTTTAG | 77 | 2470 |
| 465611 | 21194 | 21213 | ACTGCAATAATGAGACTTTA | 53 | 2471 |
| 465612 | 21195 | 21214 | AACTGCAATAATGAGACTTT | 39 | 2472 |
| 465266 | 21638 | 21657 | ATTTGAATAAATGAATGAAA | 0 | 2473 |
| 465267 | 21639 | 21658 | TATTTGAATAAATGAATGAA | 0 | 2474 |
| 465268 | 21640 | 21659 | ATATTTGAATAAATGAATGA | 0 | 2475 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465269 | 21641 | 21660 | AATATTTGAATAAATGAATG | 0 | 2476 |
| 465270 | 21642 | 21661 | AAATATTTGAATAAATGAAT | 0 | 2477 |
| 465271 | 21643 | 21662 | CAAATATTTGAATAAATGAA | 0 | 2478 |
| 465272 | 21644 | 21663 | TCAAATATTTGAATAAATGA | 0 | 2479 |
| 465273 | 21645 | 21664 | CTCAAATATTTGAATAAATG | 0 | 2480 |
| 465274 | 21646 | 21665 | GCTCAAATATTTGAATAAAT | 0 | 2481 |
| 465275 | 21647 | 21666 | TGCTCAAATATTTGAATAAA | 6 | 2482 |
| 465276 | 21648 | 21667 | ATGCTCAAATATTTGAATAA | 0 | 2483 |
| 465277 | 21649 | 21668 | AATGCTCAAATATTTGAATA | 0 | 2484 |
| 465278 | 21650 | 21669 | GAATGCTCAAATATTTGAAT | 19 | 2485 |
| 465279 | 21651 | 21670 | AGAATGCTCAAATATTTGAA | 0 | 2486 |
| 465280 | 21652 | 21671 | CAGAATGCTCAAATATTTGA | 5 | 2487 |
| 465281 | 21653 | 21672 | ACAGAATGCTCAAATATTTG | 9 | 2488 |
| 465282 | 21654 | 21673 | TACAGAATGCTCAAATATTT | 1 | 2489 |
| 465283 | 21655 | 21674 | CTACAGAATGCTCAAATATT | 0 | 2490 |
| 465284 | 21656 | 21675 | ACTACAGAATGCTCAAATAT | 0 | 2491 |
| 465285 | 21657 | 21676 | AACTACAGAATGCTCAAATA | 2 | 2492 |
| 465286 | 21658 | 21677 | CAACTACAGAATGCTCAAAT | 12 | 2493 |
| 465287 | 21659 | 21678 | GCAACTACAGAATGCTCAAA | 26 | 2494 |
| 465288 | 21660 | 21679 | AGCAACTACAGAATGCTCAA | 39 | 2495 |
| 465289 | 21661 | 21680 | CAGCAACTACAGAATGCTCA | 53 | 2496 |
| 465290 | 21662 | 21681 | CCAGCAACTACAGAATGCTC | 26 | 2497 |
| 465291 | 21663 | 21682 | CCCAGCAACTACAGAATGCT | 42 | 2498 |
| 465292 | 21664 | 21683 | CCCCAGCAACTACAGAATGC | 40 | 2499 |
| 465293 | 21665 | 21684 | TCCCCAGCAACTACAGAATG | 13 | 2500 |
| 465294 | 21666 | 21685 | TTCCCCAGCAACTACAGAAT | 30 | 2501 |
| 465295 | 21667 | 21686 | TTTCCCCAGCAACTACAGAA | 16 | 2502 |
| 465296 | 21668 | 21687 | ATTTCCCCAGCAACTACAGA | 5 | 2503 |
| 465297 | 21669 | 21688 | TATTTCCCCAGCAACTACAG | 7 | 2504 |
| 465298 | 21670 | 21689 | CTATTTCCCCAGCAACTACA | 20 | 2505 |
| 465299 | 21671 | 21690 | GCTATTTCCCCAGCAACTAC | 7 | 2506 |
| 465300 | 21672 | 21691 | TGCTATTTCCCCAGCAACTA | 25 | 2507 |
| 465301 | 21673 | 21692 | CTGCTATTTCCCCAGCAACT | 31 | 2508 |
| 465302 | 21674 | 21693 | ACTGCTATTTCCCCAGCAAC | 14 | 2509 |
| 455594* | 21675 | 21694 | CACTGCTATTTCCCCAGCAA | 43 | 1893 |
| 465303 | 21676 | 21695 | TCACTGCTATTTCCCCAGCA | 23 | 2510 |
| 465304 | 21677 | 21696 | TTCACTGCTATTTCCCCAGC | 45 | 2511 |
| 465305 | 21678 | 21697 | GTTCACTGCTATTTCCCCAG | 11 | 2512 |
| 465306 | 21679 | 21698 | AGTTCACTGCTATTTCCCCA | 62 | 2513 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465307 | 21680 | 21699 | CAGTTCACTGCTATTTCCCC | 52 | 2514 |
| 465308 | 21681 | 21700 | TCAGTTCACTGCTATTTCCC | 40 | 2515 |
| 465309 | 21682 | 21701 | TTCAGTTCACTGCTATTTCC | 29 | 2516 |
| 465310 | 21683 | 21702 | CTTCAGTTCACTGCTATTTC | 40 | 2517 |
| 465311 | 21684 | 21703 | TCTTCAGTTCACTGCTATTT | 25 | 2518 |
| 465312 | 21685 | 21704 | TTCTTCAGTTCACTGCTATT | 18 | 2519 |
| 465313 | 21686 | 21705 | ATTCTTCAGTTCACTGCTAT | 7 | 2520 |
| 465314 | 21687 | 21706 | CATTCTTCAGTTCACTGCTA | 33 | 2521 |
| 465315 | 21688 | 21707 | ACATTCTTCAGTTCACTGCT | 39 | 2522 |
| 465316 | 21689 | 21708 | GACATTCTTCAGTTCACTGC | 49 | 2523 |
| 465317 | 21690 | 21709 | AGACATTCTTCAGTTCACTG | 50 | 2524 |
| 465318 | 21691 | 21710 | AAGACATTCTTCAGTTCACT | 37 | 2525 |
| 465319 | 21692 | 21711 | AAAGACATTCTTCAGTTCAC | 26 | 2526 |
| 465320 | 21693 | 21712 | CAAAGACATTCTTCAGTTCA | 13 | 2527 |
| 465321 | 21694 | 21713 | ACAAAGACATTCTTCAGTTC | 0 | 2528 |
| 465322 | 21695 | 21714 | AACAAAGACATTCTTCAGTT | 11 | 2529 |
| 465323 | 21696 | 21715 | GAACAAAGACATTCTTCAGT | 10 | 2530 |
| 465324 | 21697 | 21716 | AGAACAAAGACATTCTTCAG | 14 | 2531 |
| 465325 | 21698 | 21717 | AAGAACAAAGACATTCTTCA | 7 | 2532 |
| 465326 | 21699 | 21718 | TAAGAACAAAGACATTCTTC | 13 | 2533 |
| 465327 | 21700 | 21719 | ATAAGAACAAAGACATTCTT | 1 | 2534 |
| 465328 | 21701 | 21720 | CATAAGAACAAAGACATTCT | 16 | 2535 |
| 465329 | 21702 | 21721 | CCATAAGAACAAAGACATTC | 38 | 2536 |
| 465330 | 21703 | 21722 | CCCATAAGAACAAAGACATT | 11 | 2537 |
| 465331 | 21704 | 21723 | CCCCATAAGAACAAAGACAT | 0 | 2538 |
| 465332 | 21705 | 21724 | GCCCCATAAGAACAAAGACA | 30 | 2539 |
| 465333 | 21706 | 21725 | AGCCCCATAAGAACAAAGAC | 22 | 2540 |
| 465334 | 21707 | 21726 | AAGCCCCATAAGAACAAAGA | 21 | 2541 |
| 465613 | 26034 | 26053 | TCTCCAGCCTACAGATGACT | 32 | 2542 |
| 465614 | 26035 | 26054 | CTCTCCAGCCTACAGATGAC | 31 | 2543 |
| 465615 | 26036 | 26055 | TCTCTCCAGCCTACAGATGA | 29 | 2544 |
| 465616 | 26037 | 26056 | CTCTCTCCAGCCTACAGATG | 22 | 2545 |
| 465617 | 26038 | 26057 | CCTCTCTCCAGCCTACAGAT | 44 | 2546 |
| 465618 | 26039 | 26058 | TCCTCTCTCCAGCCTACAGA | 41 | 2547 |
| 465619 | 26040 | 26059 | TTCCTCTCTCCAGCCTACAG | 32 | 2548 |
| 465620 | 26041 | 26060 | GTTCCTCTCTCCAGCCTACA | 0 | 2549 |
| 465621 | 26042 | 26061 | AGTTCCTCTCTCCAGCCTAC | 44 | 2550 |
| 465622 | 26043 | 26062 | CAGTTCCTCTCTCCAGCCTA | 39 | 2551 |
| 465623 | 26044 | 26063 | CCAGTTCCTCTCTCCAGCCT | 47 | 2552 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465624 | 26045 | 26064 | TCCAGTTCCTCTCTCCAGCC | 49 | 2553 |
| 465625 | 26046 | 26065 | TTCCAGTTCCTCTCTCCAGC | 46 | 2554 |
| 465626 | 26047 | 26066 | CTTCCAGTTCCTCTCTCCAG | 47 | 2555 |
| 465627 | 26048 | 26067 | CCTTCCAGTTCCTCTCTCCA | 28 | 2556 |
| 465628 | 26049 | 26068 | CCCTTCCAGTTCCTCTCTCC | 28 | 2557 |
| 465629 | 26050 | 26069 | CCCCTTCCAGTTCCTCTCTC | 21 | 2558 |
| 465630 | 26051 | 26070 | GCCCCTTCCAGTTCCTCTCT | 65 | 2559 |
| 465631 | 26052 | 26071 | AGCCCCTTCCAGTTCCTCTC | 60 | 2560 |
| 465632 | 26053 | 26072 | TAGCCCCTTCCAGTTCCTCT | 56 | 2561 |
| 465633 | 26054 | 26073 | TTAGCCCCTTCCAGTTCCTC | 52 | 2562 |
| 465634 | 26055 | 26074 | TTTAGCCCCTTCCAGTTCCT | 53 | 2563 |
| 465635 | 26056 | 26075 | CTTTAGCCCCTTCCAGTTCC | 39 | 2564 |
| 465636 | 26057 | 26076 | ACTTTAGCCCCTTCCAGTTC | 31 | 2565 |
| 465637 | 26058 | 26077 | AACTTTAGCCCCTTCCAGTT | 46 | 2566 |
| 465638 | 26059 | 26078 | CAACTTTAGCCCCTTCCAGT | 37 | 2567 |
| 465639 | 26060 | 26079 | CCAACTTTAGCCCCTTCCAG | 48 | 2568 |
| 455611* | 26061 | 26080 | GCCAACTTTAGCCCCTTCCA | 62 | 1870 |
| 465640 | 26062 | 26081 | AGCCAACTTTAGCCCCTTCC | 71 | 2569 |
| 465641 | 26063 | 26082 | CAGCCAACTTTAGCCCCTTC | 70 | 2570 |
| 465642 | 26064 | 26083 | TCAGCCAACTTTAGCCCCTT | 66 | 2571 |
| 465643 | 26065 | 26084 | CTCAGCCAACTTTAGCCCCT | 35 | 2572 |
| 465644 | 26066 | 26085 | ACTCAGCCAACTTTAGCCCC | 49 | 2573 |
| 465645 | 26067 | 26086 | TACTCAGCCAACTTTAGCCC | 33 | 2574 |
| 465646 | 26068 | 26087 | CTACTCAGCCAACTTTAGCC | 28 | 2575 |
| 465647 | 26069 | 26088 | ACTACTCAGCCAACTTTAGC | 12 | 2576 |
| 465648 | 26070 | 26089 | AACTACTCAGCCAACTTTAG | 34 | 2577 |
| 465649 | 26071 | 26090 | TAACTACTCAGCCAACTTTA | 26 | 2578 |
| 455637* | 37873 | 37892 | GTACTTTACATGTGCAGCAC | 78 | 1931 |
| 465650 | 37874 | 37893 | TGTACTTTACATGTGCAGCA | 71 | 2579 |
| 465651 | 37875 | 37894 | GTGTACTTTACATGTGCAGC | 75 | 2580 |
| 465652 | 37876 | 37895 | TGTGTACTTTACATGTGCAG | 65 | 2581 |
| 465653 | 37877 | 37896 | CTGTGTACTTTACATGTGCA | 65 | 2582 |
| 465654 | 37878 | 37897 | CCTGTGTACTTTACATGTGC | 60 | 2583 |
| 465655 | 37879 | 37898 | TCCTGTGTACTTTACATGTG | 51 | 2584 |
| 465656 | 37880 | 37899 | CTCCTGTGTACTTTACATGT | 48 | 2585 |
| 465657 | 37881 | 37900 | TCTCCTGTGTACTTTACATG | 25 | 2586 |
| 465658 | 37882 | 37901 | ATCTCCTGTGTACTTTACAT | 33 | 2587 |
| 465659 | 37883 | 37902 | AATCTCCTGTGTACTTTACA | 23 | 2588 |
| 465660 | 37884 | 37903 | AAATCTCCTGTGTACTTTAC | 24 | 2589 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465661 | 37885 | 37904 | TAAATCTCCTGTGTACTTTA | 26 | 2590 |
| 465666 | 37886 | 37905 | CTAAATCTCCTGTGTACTTT | 16 | 2591 |
| 465667 | 37887 | 37906 | TCTAAATCTCCTGTGTACTT | 27 | 2592 |
| 465668 | 37888 | 37907 | TTCTAAATCTCCTGTGTACT | 30 | 2593 |
| 465669 | 37889 | 37908 | TTTCTAAATCTCCTGTGTAC | 30 | 2594 |
| 465670 | 37890 | 37909 | TTTTCTAAATCTCCTGTGTA | 11 | 2595 |
| 465671 | 37891 | 37910 | GTTTTCTAAATCTCCTGTGT | 37 | 2596 |
| 465672 | 37892 | 37911 | AGTTTTCTAAATCTCCTGTG | 49 | 2597 |
| 465686 | 37893 | 37912 | AAGTTTTCTAAATCTCCTGT | 19 | 2598 |
| 465687 | 37894 | 37913 | GAAGTTTTCTAAATCTCCTG | 46 | 2599 |
| 465688 | 37895 | 37914 | CGAAGTTTTCTAAATCTCCT | 53 | 2600 |
| 465689 | 37896 | 37915 | ACGAAGTTTTCTAAATCTCC | 45 | 2601 |
| 465690 | 37897 | 37916 | TACGAAGTTTTCTAAATCTC | 9 | 2602 |
| 465706 | 37898 | 37917 | CTACGAAGTTTTCTAAATCT | 14 | 2603 |
| 465707 | 37899 | 37918 | GCTACGAAGTTTTCTAAATC | 32 | 2604 |
| 455677* | 45512 | 45531 | TTCCAATATTTGTACCCTCA | 49 | 1971 |
| 465574 | 45513 | 45532 | TTTCCAATATTTGTACCCTC | 43 | 2605 |
| 465575 | 45514 | 45533 | CTTTCCAATATTTGTACCCT | 50 | 2606 |
| 465576 | 45515 | 45534 | GCTTTCCAATATTTGTACCC | 58 | 2607 |
| 465577 | 45516 | 45535 | TGCTTTCCAATATTTGTACC | 35 | 2608 |
| 465578 | 45517 | 45536 | TTGCTTTCCAATATTTGTAC | 31 | 2609 |
| 465579 | 45518 | 45537 | CTTGCTTTCCAATATTTGTA | 29 | 2610 |
| 465580 | 45519 | 45538 | CCTTGCTTTCCAATATTTGT | 35 | 2611 |
| 465581 | 45520 | 45539 | CCCTTGCTTTCCAATATTTG | 26 | 2612 |
| 465582 | 45521 | 45540 | TCCCTTGCTTTCCAATATTT | 34 | 2613 |
| 465583 | 45522 | 45541 | GTCCCTTGCTTTCCAATATT | 39 | 2614 |
| 465584 | 45523 | 45542 | TGTCCCTTGCTTTCCAATAT | 44 | 2615 |
| 465585 | 45524 | 45543 | CTGTCCCTTGCTTTCCAATA | 60 | 2616 |
| 465586 | 45525 | 45544 | TCTGTCCCTTGCTTTCCAAT | 59 | 2617 |
| 465587 | 45526 | 45545 | TTCTGTCCCTTGCTTTCCAA | 47 | 2618 |
| 455681* | 46091 | 46110 | TTTCCAGATATTTTCCCATA | 48 | 1975 |
| 465335 | 46092 | 46111 | GTTTCCAGATATTTTCCCAT | 71 | 2619 |
| 465336 | 46093 | 46112 | TGTTTCCAGATATTTTCCCA | 53 | 2620 |
| 466676 | 48396 | 48415 | CTTTCCATTCTAGTTTTACC | 1 | 2621 |
| 466677 | 48397 | 48416 | ACTTTCCATTCTAGTTTTAC | 19 | 2622 |
| 466678 | 48398 | 48417 | CACTTTCCATTCTAGTTTTA | 23 | 2623 |
| 466679 | 48399 | 48418 | ACACTTTCCATTCTAGTTTT | 9 | 2624 |
| 466680 | 48400 | 48419 | CACACTTTCCATTCTAGTTT | 31 | 2625 |
| 466681 | 48401 | 48420 | CCACACTTTCCATTCTAGTT | 64 | 2626 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455703* | 48402 | 48421 | GCCACACTTTCCATTCTAGT | 75 | 1997 |
| 466682 | 48403 | 48422 | AGCCACACTTTCCATTCTAG | 56 | 2627 |
| 466683 | 48404 | 48423 | AAGCCACACTTTCCATTCTA | 40 | 2628 |
| 466684 | 48405 | 48424 | CAAGCCACACTTTCCATTCT | 24 | 2629 |
| 466685 | 48406 | 48425 | TCAAGCCACACTTTCCATTC | 39 | 2630 |
| 466686 | 48407 | 48426 | CTCAAGCCACACTTTCCATT | 38 | 2631 |
| 466687 | 48408 | 48427 | GCTCAAGCCACACTTTCCAT | 53 | 2632 |
| 466688 | 48409 | 48428 | AGCTCAAGCCACACTTTCCA | 59 | 2633 |
| 466689 | 48410 | 48429 | CAGCTCAAGCCACACTTTCC | 51 | 2634 |
| 466690 | 48411 | 48430 | CCAGCTCAAGCCACACTTTC | 43 | 2635 |
| 466691 | 48412 | 48431 | ACCAGCTCAAGCCACACTTT | 30 | 2636 |
| 466692 | 48413 | 48432 | TACCAGCTCAAGCCACACTT | 35 | 2637 |
| 466693 | 48414 | 48433 | TTACCAGCTCAAGCCACACT | 32 | 2638 |
| 466694 | 48415 | 48434 | GTTACCAGCTCAAGCCACAC | 53 | 2639 |
| 466695 | 48416 | 48435 | GGTTACCAGCTCAAGCCACA | 54 | 2640 |
| 455704* | 48417 | 48436 | TGGTTACCAGCTCAAGCCAC | 61 | 1998 |
| 455708* | 48728 | 48747 | CCCACAGTGACAGTGACTCA | 58 | 2002 |
| 465708 | 48729 | 48748 | TCCCACAGTGACAGTGACTC | 61 | 2641 |
| 465709 | 48730 | 48749 | TTCCCACAGTGACAGTGACT | 60 | 2642 |
| 465710 | 48731 | 48750 | CTTCCCACAGTGACAGTGAC | 55 | 2643 |
| 455723* | 52033 | 52052 | ACCAGTTTTCTAGCCGATCT | 24 | 2017 |
| 466696 | 52034 | 52053 | TACCAGTTTTCTAGCCGATC | 54 | 2644 |
| 466697 | 52035 | 52054 | TTACCAGTTTTCTAGCCGAT | 41 | 2645 |
| 466698 | 52036 | 52055 | TTTACCAGTTTTCTAGCCGA | 37 | 2646 |
| 466699 | 52037 | 52056 | CTTTACCAGTTTTCTAGCCG | 17 | 2647 |
| 466700 | 52038 | 52057 | CCTTTACCAGTTTTCTAGCC | 11 | 2648 |
| 466701 | 52039 | 52058 | TCCTTTACCAGTTTTCTAGC | 24 | 2649 |
| 466702 | 52040 | 52059 | ATCCTTTACCAGTTTTCTAG | 1 | 2650 |
| 466703 | 52041 | 52060 | CATCCTTTACCAGTTTTCTA | 7 | 2651 |
| 466704 | 52042 | 52061 | TCATCCTTTACCAGTTTTCT | 0 | 2652 |
| 466705 | 52043 | 52062 | TTCATCCTTTACCAGTTTTC | 15 | 2653 |
| 466706 | 52044 | 52063 | TTTCATCCTTTACCAGTTTT | 0 | 2654 |
| 466707 | 52045 | 52064 | CTTTCATCCTTTACCAGTTT | 9 | 2655 |
| 466708 | 52046 | 52065 | TCTTTCATCCTTTACCAGTT | 0 | 2656 |
| 466709 | 52047 | 52066 | TTCTTTCATCCTTTACCAGT | 8 | 2657 |
| 466710 | 52048 | 52067 | CTTCTTTCATCCTTTACCAG | 11 | 2658 |
| 466711 | 52049 | 52068 | GCTTCTTTCATCCTTTACCA | 8 | 2659 |
| 466712 | 52050 | 52069 | AGCTTCTTTCATCCTTTACC | 6 | 2660 |
| 466713 | 52051 | 52070 | AAGCTTCTTTCATCCTTTAC | 0 | 2661 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 466714 | 52052 | 52071 | AAAGCTTCTTTCATCCTTTA | 18 | 2662 |
| 466715 | 52053 | 52072 | AAAAGCTTCTTTCATCCTTT | 2 | 2663 |
| 466716 | 52054 | 52073 | GAAAAGCTTCTTTCATCCTT | 9 | 2664 |
| 466717 | 52055 | 52074 | GGAAAAGCTTCTTTCATCCT | 1 | 2665 |
| 455724* | 52056 | 52075 | AGGAAAAGCTTCTTTCATCC | 0 | 2018 |
| 455762* | 59913 | 59932 | CCAAGTGTTTGAATTCTGCA | 36 | 2056 |
| 466766 | 59914 | 59933 | ACCAAGTGTTTGAATTCTGC | 58 | 2666 |
| 466767 | 59915 | 59934 | TACCAAGTGTTTGAATTCTG | 32 | 2667 |
| 466768 | 59916 | 59935 | ATACCAAGTGTTTGAATTCT | 21 | 2668 |
| 466769 | 59917 | 59936 | CATACCAAGTGTTTGAATTC | 9 | 2669 |
| 466770 | 59918 | 59937 | ACATACCAAGTGTTTGAATT | 14 | 2670 |
| 466771 | 59919 | 59938 | CACATACCAAGTGTTTGAAT | 26 | 2671 |
| 466772 | 59920 | 59939 | CCACATACCAAGTGTTTGAA | 8 | 2672 |
| 466773 | 59921 | 59940 | CCCACATACCAAGTGTTTGA | 19 | 2673 |
| 466774 | 59922 | 59941 | TCCCACATACCAAGTGTTTG | 5 | 2674 |
| 466775 | 59923 | 59942 | CTCCCACATACCAAGTGTTT | 25 | 2675 |
| 466776 | 59924 | 59943 | CCTCCCACATACCAAGTGTT | 32 | 2676 |
| 466777 | 59925 | 59944 | TCCTCCCACATACCAAGTGT | 12 | 2677 |
| 466778 | 59926 | 59945 | CTCCTCCCACATACCAAGTG | 10 | 2678 |
| 466779 | 59927 | 59946 | GCTCCTCCCACATACCAAGT | 15 | 2679 |
| 466780 | 59928 | 59947 | AGCTCCTCCCACATACCAAG | 5 | 2680 |
| 466781 | 59929 | 59948 | GAGCTCCTCCCACATACCAA | 23 | 2681 |
| 465768 | 61325 | 61344 | CAGTCTAGAATAGCCATGGA | 71 | 2682 |
| 465769 | 61326 | 61345 | ACAGTCTAGAATAGCCATGG | 72 | 2683 |
| 465770 | 61327 | 61346 | GACAGTCTAGAATAGCCATG | 78 | 2684 |
| 465771 | 61328 | 61347 | AGACAGTCTAGAATAGCCAT | 74 | 2685 |
| 465772 | 61329 | 61348 | GAGACAGTCTAGAATAGCCA | 70 | 2686 |
| 465773 | 61330 | 61349 | AGAGACAGTCTAGAATAGCC | 70 | 2687 |
| 465774 | 61331 | 61350 | CAGAGACAGTCTAGAATAGC | 63 | 2688 |
| 465775 | 61332 | 61351 | ACAGAGACAGTCTAGAATAG | 55 | 2689 |
| 465776 | 61333 | 61352 | CACAGAGACAGTCTAGAATA | 64 | 2690 |
| 465777 | 61334 | 61353 | TCACAGAGACAGTCTAGAAT | 71 | 2691 |
| 465778 | 61335 | 61354 | ATCACAGAGACAGTCTAGAA | 79 | 2692 |
| 465779 | 61336 | 61355 | TATCACAGAGACAGTCTAGA | 66 | 2693 |
| 465780 | 61337 | 61356 | ATATCACAGAGACAGTCTAG | 64 | 2694 |
| 465781 | 61338 | 61357 | AATATCACAGAGACAGTCTA | 48 | 2695 |
| 465782 | 61339 | 61358 | AAATATCACAGAGACAGTCT | 65 | 2696 |
| 455786* | 61340 | 61359 | CAAATATCACAGAGACAGTC | 63 | 2070 |
| 465783 | 61341 | 61360 | GCAAATATCACAGAGACAGT | 69 | 2697 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465786 | 61342 | 61361 | TGCAAATATCACAGAGACAG | 78 | 2698 |
| 465787 | 61343 | 61362 | ATGCAAATATCACAGAGACA | 72 | 2699 |
| 465788 | 61344 | 61363 | AATGCAAATATCACAGAGAC | 59 | 2700 |
| 465789 | 61345 | 61364 | AAATGCAAATATCACAGAGA | 23 | 2701 |
| 465790 | 61346 | 61365 | AAAATGCAAATATCACAGAG | 28 | 2702 |
| 465791 | 61347 | 61366 | TAAAATGCAAATATCACAGA | 0 | 2703 |
| 465792 | 61348 | 61367 | TTAAAATGCAAATATCACAG | 12 | 2704 |
| 465793 | 61349 | 61368 | TTTAAAATGCAAATATCACA | 3 | 2705 |
| 465794 | 61350 | 61369 | GTTTAAAATGCAAATATCAC | 2 | 2706 |
| 465795 | 61351 | 61370 | AGTTTAAAATGCAAATATCA | 0 | 2707 |
| 465796 | 61352 | 61371 | CAGTTTAAAATGCAAATATC | 13 | 2708 |
| 465797 | 61353 | 61372 | TCAGTTTAAAATGCAAATAT | 0 | 2709 |
| 465798 | 61354 | 61373 | TTCAGTTTAAAATGCAAATA | 0 | 2710 |
| 465799 | 61355 | 61374 | ATTCAGTTTAAAATGCAAAT | 1 | 2711 |
| 465800 | 61356 | 61375 | TATTCAGTTTAAAATGCAAA | 0 | 2712 |
| 465801 | 61357 | 61376 | ATATTCAGTTTAAAATGCAA | 0 | 2713 |
| 455790* | 62043 | 62062 | CATGGTTATGTGTATCTGCA | 69 | 2074 |
| 465337 | 62044 | 62063 | ACATGGTTATGTGTATCTGC | 69 | 2714 |
| 465338 | 62045 | 62064 | CACATGGTTATGTGTATCTG | 40 | 2715 |
| 465339 | 62046 | 62065 | CCACATGGTTATGTGTATCT | 32 | 2716 |
| 337332 | 66135 | 66154 | GAAGCCCTTGCCAGCCATGT | 79 | 1541 |
| 455840* | 71610 | 71629 | GTACAATTGCTTCAACTAGA | 81 | 2124 |
| 466782 | 71611 | 71630 | AGTACAATTGCTTCAACTAG | 54 | 2717 |
| 466783 | 71612 | 71631 | CAGTACAATTGCTTCAACTA | 68 | 2718 |
| 466784 | 71613 | 71632 | GCAGTACAATTGCTTCAACT | 72 | 2719 |
| 465588 | 71614 | 71633 | GGCAGTACAATTGCTTCAAC | 69 | 2720 |
| 455264* | 74768 | 74787 | TCCTTAAACCTTCCTATTTC | 26 | 1563 |
| 465226 | 74769 | 74788 | CTCCTTAAACCTTCCTATTT | 45 | 2721 |
| 455265* | 74770 | 74789 | TCTCCTTAAACCTTCCTATT | 57 | 1564 |
| 465227 | 74771 | 74790 | TTCTCCTTAAACCTTCCTAT | 54 | 2722 |
| 455266* | 74772 | 74791 | ATTCTCCTTAAACCTTCCTA | 52 | 1565 |
| 465228 | 74773 | 74792 | GATTCTCCTTAAACCTTCCT | 64 | 2723 |
| 455267* | 74774 | 74793 | AGATTCTCCTTAAACCTTCC | 60 | 1566 |
| 465229 | 74775 | 74794 | TAGATTCTCCTTAAACCTTC | 22 | 2724 |
| 455268* | 74776 | 74795 | TTAGATTCTCCTTAAACCTT | 55 | 1567 |
| 465230 | 74777 | 74796 | CTTAGATTCTCCTTAAACCT | 69 | 2725 |
| 455269* | 74778 | 74797 | GCTTAGATTCTCCTTAAACC | 84 | 1568 |
| 465231 | 74779 | 74798 | TGCTTAGATTCTCCTTAAAC | 64 | 2726 |
| 455270* | 74780 | 74799 | ATGCTTAGATTCTCCTTAAA | 50 | 1569 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 465232 | 74781 | 74800 | AATGCTTAGATTCTCCTTAA | 71 | 2727 |
| 455271* | 74782 | 74801 | AAATGCTTAGATTCTCCTTA | 69 | 1570 |
| 465233 | 74783 | 74802 | AAAATGCTTAGATTCTCCTT | 69 | 2728 |
| 455272* | 74784 | 74803 | TAAAATGCTTAGATTCTCCT | 56 | 1571 |
| 455281* | 74872 | 74891 | CAAGGTTGTAAGCACCCTCT | 63 | 1580 |
| 465234 | 74873 | 74892 | TCAAGGTTGTAAGCACCCTC | 54 | 2729 |
| 455282* | 74874 | 74893 | GTCAAGGTTGTAAGCACCCT | 8 | 1581 |
| 465235 | 74875 | 74894 | AGTCAAGGTTGTAAGCACCC | 65 | 2730 |
| 455283* | 74876 | 74895 | GAGTCAAGGTTGTAAGCACC | 48 | 1582 |
| 455290* | 74900 | 74919 | GCAGATCAAGTCCAGGGAGA | 77 | 1589 |
| 465236 | 74901 | 74920 | AGCAGATCAAGTCCAGGGAG | 80 | 2731 |
| 455291* | 74902 | 74921 | CAGCAGATCAAGTCCAGGGA | 82 | 1590 |
| 465237 | 74903 | 74922 | ACAGCAGATCAAGTCCAGGG | 82 | 2732 |
| 455292* | 74904 | 74923 | AACAGCAGATCAAGTCCAGG | 69 | 1591 |
| 455369* | 75418 | 75437 | GGTGTTCCCATACGCACAGG | 75 | 1668 |
| 465238 | 75419 | 75438 | AGGTGTTCCCATACGCACAG | 68 | 2733 |
| 455370* | 75420 | 75439 | TAGGTGTTCCCATACGCACA | 67 | 1669 |
| 465239 | 75421 | 75440 | CTAGGTGTTCCCATACGCAC | 82 | 2734 |
| 455371* | 75422 | 75441 | GCTAGGTGTTCCCATACGCA | 85 | 1670 |
| 465240 | 75423 | 75442 | TGCTAGGTGTTCCCATACGC | 77 | 2735 |
| 455372* | 75424 | 75443 | GTGCTAGGTGTTCCCATACG | 72 | 1671 |
| 455390* | 75616 | 75635 | AACTGTCTCCAGGCAGGAGG | 65 | 1689 |
| 465241 | 75617 | 75636 | CAACTGTCTCCAGGCAGGAG | 51 | 2736 |
| 455391* | 75618 | 75637 | TCAACTGTCTCCAGGCAGGA | 52 | 1690 |
| 465242 | 75619 | 75638 | ATCAACTGTCTCCAGGCAGG | 76 | 2737 |
| 455392* | 75620 | 75639 | CATCAACTGTCTCCAGGCAG | 63 | 1691 |
| 465243 | 75621 | 75640 | ACATCAACTGTCTCCAGGCA | 70 | 2738 |
| 455393* | 75622 | 75641 | CACATCAACTGTCTCCAGGC | 75 | 1692 |
| 465244 | 75623 | 75642 | ACACATCAACTGTCTCCAGG | 61 | 2739 |
| 455394* | 75624 | 75643 | GACACATCAACTGTCTCCAG | 69 | 1693 |
| 455397* | 75662 | 75681 | TACTGAAGAGTGTTGCTGGA | 77 | 1696 |
| 465245 | 75663 | 75682 | GTACTGAAGAGTGTTGCTGG | 84 | 2740 |
| 455398* | 75664 | 75683 | TGTACTGAAGAGTGTTGCTG | 76 | 1697 |
| 465246 | 75665 | 75684 | ATGTACTGAAGAGTGTTGCT | 72 | 2741 |
| 455399* | 75666 | 75685 | TATGTACTGAAGAGTGTTGC | 70 | 1698 |
| 455411* | 75726 | 75745 | AACCCAATGGTAAGCCCAAG | 77 | 1710 |
| 465247 | 75727 | 75746 | AAACCCAATGGTAAGCCCAA | 61 | 2742 |
| 455412* | 75728 | 75747 | TAAACCCAATGGTAAGCCCA | 72 | 1711 |
| 465248 | 75729 | 75748 | TTAAACCCAATGGTAAGCCC | 69 | 2743 |

| Inhibition of human STAT3 mRNA levels by chimeric antisense oligonucleotides targeted to SEQ ID NO: 2 | | | | | |
|---|---|---|---|---|---|
| ISIS No | Start Site | Stop Site | Sequence | % inhibition | SEQ ID NO |
| 455413* | 75730 | 75749 | TTTAAACCCAATGGTAAGCC | 38 | 1712 |
| 455428* | 75829 | 75848 | TACAATCAGAGTTAAGACCA | 58 | 1727 |
| 465249 | 75830 | 75849 | CTACAATCAGAGTTAAGACC | 58 | 2744 |
| 455429* | 75831 | 75850 | GCTACAATCAGAGTTAAGAC | 71 | 1728 |
| 465250 | 75832 | 75851 | TGCTACAATCAGAGTTAAGA | 59 | 2745 |
| 455430* | 75833 | 75852 | TTGCTACAATCAGAGTTAAG | 47 | 1729 |
| 455437* | 75847 | 75866 | TCCTCTCAGAACTTTTGCTA | 36 | 1736 |
| 465251 | 75848 | 75867 | CTCCTCTCAGAACTTTTGCT | 47 | 2746 |
| 455438* | 75849 | 75868 | GCTCCTCTCAGAACTTTTGC | 75 | 1737 |
| 465252 | 75850 | 75869 | AGCTCCTCTCAGAACTTTTG | 71 | 2747 |
| 455439* | 75851 | 75870 | CAGCTCCTCTCAGAACTTTT | 68 | 1738 |
| 465253 | 75852 | 75871 | TCAGCTCCTCTCAGAACTTT | 62 | 2748 |
| 455440* | 75853 | 75872 | CTCAGCTCCTCTCAGAACTT | 58 | 1739 |
| 455446* | 75965 | 75984 | GTAGGTAAGCAACCCACGGG | 69 | 1745 |
| 465254 | 75966 | 75985 | GGTAGGTAAGCAACCCACGG | 79 | 2749 |
| 455447* | 75967 | 75986 | AGGTAGGTAAGCAACCCACG | 80 | 1476 |
| 465255 | 75968 | 75987 | TAGGTAGGTAAGCAACCCAC | 84 | 2750 |
| 455448* | 75969 | 75988 | ATAGGTAGGTAAGCAACCCA | 71 | 1474 |
| 455456* | 75985 | 76004 | GCTTATAAACCACCTTATAG | 37 | 1755 |
| 465256 | 75986 | 76005 | AGCTTATAAACCACCTTATA | 43 | 2751 |
| 455457* | 75987 | 76006 | CAGCTTATAAACCACCTTAT | 57 | 1756 |
| 465257 | 75988 | 76007 | GCAGCTTATAAACCACCTTA | 73 | 2752 |
| 455458* | 75989 | 76008 | AGCAGCTTATAAACCACCTT | 75 | 1757 |
| 465258 | 75990 | 76009 | CAGCAGCTTATAAACCACCT | 65 | 2753 |
| 455459* | 75991 | 76010 | ACAGCAGCTTATAAACCACC | 46 | 1758 |
| 455462* | 75997 | 76016 | GCCAGGACAGCAGCTTATAA | 70 | 1761 |
| 466718 | 75998 | 76017 | GGCCAGGACAGCAGCTTATA | 87 | 2754 |
| 455463* | 75999 | 76018 | TGGCCAGGACAGCAGCTTAT | 83 | 1762 |
| 466719 | 76000 | 76019 | GTGGCCAGGACAGCAGCTTA | 76 | 2755 |
| 455464* | 76001 | 76020 | AGTGGCCAGGACAGCAGCTT | 82 | 1763 |
| 455470* | 76013 | 76032 | GAATTTGAATGCAGTGGCCA | 75 | 1769 |
| 466720 | 76014 | 76033 | GGAATTTGAATGCAGTGGCC | 87 | 2756 |
| 455471* | 76015 | 76034 | TGGAATTTGAATGCAGTGGC | 75 | 1770 |
| 466721 | 76016 | 76035 | TTGGAATTTGAATGCAGTGG | 72 | 2757 |
| 455472* | 76017 | 76036 | ATTGGAATTTGAATGCAGTG | 60 | 1771 |

**Example 35: Dose-dependent antisense inhibition of human STAT3 in HuVEC cells**

**[0378]** Gapmers from the study described in Example 3 exhibiting significant *in vitro* inhibition of STAT3 were tested at various doses in HuVEC cells. Cells were plated at a density of 5,000 cells per well and transfected using LipofectAMINE2000® reagent with 8.8 nM, 17.5 nM, 35.0 nM, and 70.0 nM concentrations of antisense oligonucleotide, as specified in Table 56. After a treatment period of approximately 16 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0379]** As illustrated in Table 56, STAT3 mRNA levels were reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 56**

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells using LipofectAMINE 2000® reagent | | | | |
|---|---|---|---|---|
| ISIS No | 8.8 nM | 17.5 nM | 35.0 nM | 70.0 nM |
| 337332 | 50 | 71 | 81 | 88 |
| 455269 | 62 | 69 | 79 | 82 |
| 455291 | 72 | 81 | 87 | 88 |
| 455371 | 71 | 83 | 88 | 90 |
| 455447 | 53 | 70 | 81 | 79 |
| 455463 | 68 | 79 | 84 | 87 |
| 455464 | 69 | 78 | 84 | 86 |
| 455471 | 62 | 82 | 88 | 90 |
| 455547 | 43 | 64 | 75 | 87 |
| 455565 | 41 | 73 | 83 | 92 |
| 455582 | 50 | 67 | 81 | 87 |
| 455637 | 50 | 65 | 79 | 85 |
| 455703 | 45 | 65 | 81 | 85 |
| 455840 | 58 | 70 | 80 | 85 |
| 465236 | 62 | 76 | 81 | 85 |
| 465237 | 67 | 81 | 86 | 90 |
| 465239 | 64 | 77 | 85 | 92 |
| 465240 | 50 | 66 | 76 | 83 |
| 465245 | 70 | 81 | 87 | 87 |
| 465254 | 54 | 75 | 81 | 86 |
| 465255 | 63 | 74 | 84 | 85 |
| 465335 | 46 | 62 | 74 | 80 |
| 465449 | 49 | 71 | 84 | 84 |
| 465458 | 54 | 73 | 84 | 88 |
| 465509 | 66 | 80 | 86 | 83 |
| 465510 | 48 | 66 | 76 | 82 |
| 465511 | 56 | 68 | 75 | 79 |
| 465526 | 53 | 68 | 76 | 76 |
| 465537 | 41 | 60 | 77 | 85 |

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells using LipofectAMINE 2000® reagent | | | | |
|---|---|---|---|---|
| ISIS No | 8.8 nM | 17.5 nM | 35.0 nM | 70.0 nM |
| 465588 | 52 | 73 | 76 | 79 |
| 465610 | 35 | 57 | 71 | 79 |
| 465730 | 51 | 75 | 85 | 87 |
| 465739 | 72 | 81 | 88 | 90 |
| 465740 | 70 | 81 | 86 | 89 |
| 465742 | 63 | 76 | 87 | 88 |
| 465748 | 48 | 62 | 67 | 74 |
| 465751 | 70 | 81 | 87 | 87 |
| 465752 | 76 | 82 | 88 | 89 |
| 465754 | 70 | 83 | 86 | 87 |
| 465755 | 70 | 81 | 85 | 89 |
| 465770 | 52 | 69 | 77 | 77 |
| 465771 | 40 | 55 | 64 | 75 |
| 465778 | 40 | 69 | 75 | 77 |
| 465786 | 56 | 71 | 76 | 83 |
| 465830 | 66 | 77 | 83 | 82 |
| 465833 | 50 | 67 | 79 | 86 |
| 465834 | 42 | 67 | 77 | 81 |
| 465886 | 58 | 73 | 83 | 87 |
| 465888 | 49 | 68 | 82 | 12 |
| 465926 | 43 | 64 | 76 | 82 |
| 466661 | 47 | 63 | 80 | 84 |
| 466666 | 39 | 66 | 80 | 86 |
| 466670 | 73 | 83 | 89 | 90 |
| 466718 | 73 | 78 | 84 | 85 |
| 466719 | 63 | 73 | 83 | 83 |
| 466720 | 80 | 87 | 86 | 86 |

**Example 36: Dose-dependent antisense inhibition of human STAT3 in HuVEC cells**

**[0380]** Gapmers from the study described in Example 3 were further tested at various doses in HuVEC cells. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 187.5 nM, 375.0 nM, 750.0 nM, 1,500.0 nM, 3,000.0 nM, and 6,000.0 nM concentrations of antisense oligonucleotide, as specified in Table 57. After a treatment period of approximately 16 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0381]** As illustrated in Table 57, STAT3 mRNA levels were significantly reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

**Table 57**

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells using electroporation | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 187.5 nM | 375.0 nM | 750.0 nM | 1500.0 nM | 3000.0 nM | 6000.0 nM | $IC_{50}$ (μM) |
| 337332 | 35 | 51 | 73 | 84 | 97 | 98 | 0.3 |
| 455269 | 64 | 76 | 87 | 89 | 92 | 90 | <0.2 |
| 455291 | 63 | 79 | 88 | 90 | 90 | 93 | <0.2 |
| 455371 | 50 | 81 | 90 | 94 | 96 | 95 | <0.2 |
| 455447 | 37 | 49 | 61 | 91 | 94 | 96 | 0.3 |
| 455463 | 57 | 78 | 89 | 93 | 95 | 94 | <0.2 |
| 455464 | 57 | 67 | 78 | 80 | 79 | 87 | <0.2 |
| 455471 | 50 | 73 | 81 | 86 | 91 | 92 | <0.2 |
| 455547 | 19 | 49 | 63 | 82 | 92 | 94 | 0.5 |
| 455582 | 42 | 62 | 82 | 92 | 97 | 97 | 0.2 |
| 455637 | 44 | 60 | 63 | 87 | 91 | 92 | 0.2 |
| 455840 | 39 | 58 | 75 | 81 | 88 | 89 | 0.2 |
| 465236 | 56 | 67 | 71 | 83 | 91 | 92 | <0.2 |
| 465237 | 56 | 75 | 87 | 92 | 94 | 93 | <0.2 |
| 465239 | 60 | 78 | 88 | 95 | 99 | 99 | <0.2 |
| 465240 | 49 | 67 | 80 | 85 | 94 | 95 | 0.1 |
| 465245 | 54 | 67 | 81 | 86 | 90 | 90 | <0.2 |
| 465254 | 28 | 50 | 63 | 76 | 91 | 92 | 0.4 |
| 465255 | 46 | 55 | 78 | 89 | 92 | 94 | 0.2 |
| 465335 | 25 | 52 | 65 | 89 | 95 | 95 | 0.4 |
| 465449 | 28 | 56 | 78 | 72 | 96 | 96 | 0.3 |
| 465458 | 19 | 68 | 84 | 91 | 96 | 97 | 0.3 |
| 465509 | 42 | 68 | 77 | 84 | 88 | 88 | 0.1 |
| 465510 | 15 | 43 | 60 | 73 | 85 | 88 | 0.6 |
| 465511 | 19 | 39 | 47 | 68 | 79 | 86 | 0.8 |
| 465526 | 15 | 39 | 54 | 64 | 82 | 84 | 0.8 |
| 465537 | 44 | 65 | 82 | 90 | 95 | 90 | 0.1 |
| 465565 | 12 | 45 | 62 | 80 | 93 | 97 | 0.6 |
| 465588 | 44 | 66 | 82 | 85 | 85 | 87 | 0.1 |
| 465610 | 33 | 56 | 72 | 89 | 96 | 97 | 0.3 |
| 465730 | 48 | 51 | 72 | 91 | 94 | 91 | 0.2 |
| 465739 | 42 | 78 | 85 | 93 | 96 | 92 | 0.9 |
| 465740 | 54 | 69 | 80 | 96 | 98 | 98 | <0.2 |
| 465742 | 67 | 55 | 91 | 93 | 87 | 93 | <0.2 |
| 465748 | 49 | 67 | 88 | 96 | 98 | 99 | 0.1 |
| 465751 | 56 | 63 | 82 | 91 | 98 | 98 | 0.1 |
| 465752 | 62 | 79 | 84 | 93 | 96 | 90 | <0.2 |

| Dose-dependent antisense inhibition of human STAT3 in HuVEC cells using electroporation | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 187.5 nM | 375.0 nM | 750.0 nM | 1500.0 nM | 3000.0 nM | 6000.0 nM | $IC_{50}$ (μM) |
| 465754 | 41 | 69 | 84 | 63 | 94 | 93 | <0.2 |
| 465755 | 47 | 56 | 67 | 83 | 93 | 97 | 0.2 |
| 465770 | 52 | 54 | 70 | 85 | 88 | 83 | 0.2 |
| 465771 | 38 | 62 | 76 | 83 | 84 | 86 | 0.2 |
| 465778 | 40 | 58 | 79 | 84 | 96 | 96 | 0.2 |
| 465786 | 41 | 68 | 88 | 94 | 95 | 93 | 0.1 |
| 465830 | 50 | 73 | 89 | 93 | 88 | 92 | <0.2 |
| 465833 | 27 | 44 | 76 | 89 | 88 | 97 | 0.4 |
| 465834 | 8 | 27 | 57 | 80 | 93 | 97 | 0.7 |
| 465886 | 58 | 79 | 90 | 97 | 98 | 96 | <0.2 |
| 465888 | 39 | 60 | 65 | 90 | 94 | 97 | 0.3 |
| 465926 | 23 | 50 | 41 | 85 | 93 | 94 | 0.5 |
| 466661 | 31 | 58 | 76 | 90 | 95 | 96 | 0.3 |
| 466666 | 44 | 55 | 79 | 92 | 96 | 97 | 0.2 |
| 466670 | 50 | 54 | 82 | 96 | 96 | 96 | 0.2 |
| 466718 | 55 | 79 | 90 | 93 | 95 | 96 | <0.2 |
| 466719 | 44 | 52 | 73 | 65 | 87 | 91 | 0.3 |
| 466720 | 48 | 78 | 90 | 90 | 90 | 90 | <0.2 |

**Example 37: Tolerability of antisense oligonucleotides targeting human STAT3 in CD1 mice**

**[0382]** Thirty-nine antisense oligonucleotides exhibiting a high level of potency were further tested for in vivo tolerability.

**[0383]** Groups of eight male CD1 mice were injected subcutaneously twice a week for 6 weeks with 50 mg/kg of ISIS antisense oligonucleotides. One group of eight male CD1 mice was injected subcutaneously twice a week for 6 weeks with PBS. This group served as the control group. Three days after the last dose mice were euthanized and organs and plasma were harvested for further analysis. Liver, spleen, and kidney weights were measured at the end of the study and were compared to PBS treated mice.

**[0384]** To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma concentrations of transaminases were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). Plasma concentrations of ALT (alanine transaminase) and AST (aspartate transaminase) were measured.

**[0385]** To evaluate the effect of ISIS oligonucleotides on kidney function, plasma concentrations of blood urea nitrogen (BUN) were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY).

**[0386]** Blood obtained from all mice groups were sent to Antech Diagnostics for hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) measurements and analyses, as well as measurements of the differential blood cell

counts, such as that of WBC, RBC, and total hemoglobin content.

**[0387]** Among the 39 antisense oligonucleotides tested, certain antisense oligonucleotides, including ISIS 455265, ISIS 455269, ISIS 455271, ISIS 455272, ISIS 455291, ISIS 455371, ISIS 455394, ISIS 455703, ISIS 455429, ISIS 455471, ISIS 455527, ISIS 455530, ISIS 455536, ISIS 455548, ISIS 455611, ISIS 465236, ISIS 465237, ISIS 465588, ISIS 465740, ISIS 465754, ISIS 465830, ISIS 466670, and ISIS 466720 met tolerability thresholds for organ weight, ALT, AST, BUN, and hematological parameters.

**Example 38: Measurement of half-life of antisense oligonucleotide in CD1 mouse liver**

**[0388]** CD1 mice were treated with ISIS antisense oligonucleotides described and the oligonucleotide half-life in the liver was evaluated.

***Treatment***

**[0389]** Groups of twelve CD1 mice each were injected subcutaneously twice per week for 2 weeks with 50 mg/kg of ISIS 455265, ISIS 455269, ISIS 455271, ISIS 455272, ISIS 455291, ISIS 455371, ISIS 455393, ISIS 455553, ISIS 455582, ISIS 455703, ISIS 455394, ISIS 455429, ISIS 455438, ISIS 455471, ISIS 455527, ISIS 455530, ISIS 455536, ISIS 455540, ISIS 455548, ISIS 455611, ISIS 455429, ISIS 455463, ISIS 455464, ISIS 455471, ISIS 455527, ISIS 455611, ISIS 465236, ISIS 465237, ISIS 465239, ISIS 465588, ISIS 465740, ISIS 465742, ISIS 465751, ISIS 465752, ISIS 465754, ISIS 465830, ISIS 466670, ISIS 466718, and ISIS 466720. Four mice from each group were sacrificed 3 days, 28 days, and 56 days following the final dose. Livers were harvested for analysis.

***Measurement of oligonucleotide concentration***

**[0390]** The concentration of the full-length oligonucleotide as well as the total oligonucleotide concentration (including the degraded form) was measured. The method used is a modification of previously published methods (Leeds et al., 1996; Geary et al., 1999), which includes a phenol-chloroform (liquid-liquid) extraction followed by a solid phase extraction. An internal standard (ISIS 355868, a 27-mer 2'-O-methoxyethyl modified phosphorothioate oligonucleotide, GCGTTTGCTCTTCTTCTTGCGTTTTTT, designated herein as SEQ ID NO: 2758) was added prior to extraction. Tissue sample concentrations were calculated using calibration curves, with a lower limit of quantitation (LLOQ) of approximately 1.14 µg/g. Half-lives were then calculated using WinNonlin software (PHARSIGHT).

**[0391]** The half-life of each oligonucleotide is presented in Table 58. Antisense oligonucleotides with half-lives within 11-34 days were chosen for further studies.

**Table 58**

| Half-life of ISIS oligonucleotides in the liver of CD1 mice | |
|---|---|
| ISIS No | Half-life (days) |
| 455265 | 12 |
| 455269 | 48 |
| 455271 | 16 |
| 455272 | 16 |
| 455291 | 19 |
| 455371 | 28 |

| Half-life of ISIS oligonucleotides in the liver of CD1 mice | |
|---|---|
| ISIS No | Half-life (days) |
| 455394 | 17 |
| 455703 | 27 |
| 455429 | 15 |
| 455471 | 15 |
| 455527 | 13 |
| 455530 | 12 |
| 455536 | 20 |
| 455548 | 13 |
| 455611 | 37 |
| 465236 | 22 |
| 465237 | 17 |
| 465588 | 14 |
| 465740 | 15 |
| 465754 | 23 |
| 465830 | 23 |
| 466670 | 11 |
| 466720 | 17 |

**Example 39: Tolerability of antisense oligonucleotides targeting human STAT3 in Sprague-Dawley rats**

**[0392]** Twenty-three antisense oligonucleotides exhibiting a high level of potency were further tested for in vivo tolerability.

**[0393]** Groups of four Sprague-Dawley rats were injected subcutaneously twice a week for 6 weeks with 50 mg/kg of ISIS antisense oligonucleotides. One group of rats was injected subcutaneously twice a week for 6 weeks with PBS. This group served as the control group. Three days after the last dose rats were euthanized and organs and plasma were harvested for further analysis. Liver, spleen, and kidney weights were measured at the end of the study and were compared to PBS treated rats

**[0394]** To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma concentrations of transaminases were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY). Plasma concentrations of AST (aspartate transaminase) and total bilirubin were measured.

**[0395]** To evaluate the effect of ISIS oligonucleotides on kidney function, BUN, total urine protein, and creatinine were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, NY).

**[0396]** Among the 23 antisense oligonucleotides tested, certain antisense oligonucleotides, including ISIS 455269, ISIS 455291, ISIS 455371, ISIS 455703, ISIS 455429, ISIS 465236, ISIS 465237, ISIS 465754, ISIS 465830, and ISIS 466670 met tolerability thresholds for organ weight, AST, bilirubin, BUN, total urine protein, and creatinine.

**Example 40: Measurement of half-life of antisense oligonucleotide in Sprague-Dawley rat liver and**

**kidney**

**[0397]** Sprague Dawley rats were treated with ISIS antisense oligonucleotides and the oligonucleotide half-life as well as the elapsed time for oligonucleotide degradation and elimination from the liver and kidney was evaluated.

***Treatment***

**[0398]** Groups of four Sprague Dawley rats each were injected subcutaneously twice a week for 2 weeks with 20 mg/kg of ISIS 455265, ISIS 455269, ISIS 455271, ISIS 455272, ISIS 455291, ISIS 455371, ISIS 455394, ISIS 455703, ISIS 455429, ISIS 455471, ISIS 455527, ISIS 455530, ISIS 455536, ISIS 455548, ISIS 455611, ISIS 465236, ISIS 465237, ISIS 465588, ISIS 465740, ISIS 465754, ISIS 465830, ISIS 466670, and ISIS 466720. Three days after the last dose, the rats were sacrificed and livers and kidneys were collected for analysis.

***Measurement of oligonucleotide concentration***

**[0399]** The concentration of the full-length oligonucleotide as well as the total oligonucleotide concentration (including the degraded form) was measured. The method used is a modification of previously published methods (Leeds et al., 1996; Geary et al., 1999), which includes a phenol-chloroform (liquid-liquid) extraction followed by a solid phase extraction. An internal standard (ISIS 355868, a 27-mer 2'-O-methoxyethyl modified phosphorothioate oligonucleotide, GCGTTTGCTCTTCTTCTTGCGTTTTTT, designated herein as SEQ ID NO: 2758) was added prior to extraction. Tissue sample concentrations were calculated using calibration curves, with a lower limit of quantitation (LLOQ) of approximately 1.14 µg/g. The kidney to liver ratio of the full-length oligonucleotide concentration, as well as that for the total oligonucleotide concentration were calculated. The results are presented in Table 59.

**Table 59**

| Kidney to liver ratio of full-length and total oligonucleotide concentrations in Sprague-Dawley rats | | |
|---|---|---|
| ISIS No | Full length | Total |
| 455265 | 3.6 | 3.8 |
| 455269 | 2.1 | 2.4 |
| 455271 | 3.1 | 3.0 |
| 455272 | 2.9 | 3.1 |
| 455291 | 2.7 | 3.3 |
| 455371 | 2.2 | 2.4 |
| 455394 | 1.8 | 2.2 |
| 455703 | 2.3 | 2.8 |
| 455429 | 3.8 | 3.9 |
| 455471 | 2.7 | 2.9 |
| 455527 | 5.0 | 3.9 |
| 455530 | 3.9 | 2.9 |
| 455536 | 3.5 | 3.6 |
| 455548 | 2.5 | 2.9 |

| Kidney to liver ratio of full-length and total oligonucleotide concentrations in Sprague-Dawley rats | | |
|---|---|---|
| ISIS No | Full length | Total |
| 455611 | 2.3 | 2.3 |
| 465236 | 2.3 | 3.3 |
| 465237 | 2.4 | 2.7 |
| 465588 | 2.8 | 2.6 |
| 465740 | 2.4 | 2.6 |
| 465754 | 1.6 | 1.8 |
| 465830 | 5.1 | 2.6 |
| 466670 | 3.1 | 4.4 |
| 466720 | 2.3 | 2.6 |

**Example 41: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in SK-BR-3 cells**

**[0400]** Gapmers from the rodent tolerability studies described in Examples 6-9 were tested at various doses in SK-BR-3 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated without any transfection reagent with 0.02 µM, 0.10 µM, 0.50 µM, 1.00 µM. 2.50 µM, and 10.00 µM concentrations of antisense oligonucleotide, as specified in Table 60. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, as described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0401]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 60.

**Table 60**

| Dose-dependent antisense inhibition of human STAT3 by free-uptake of ISIS oligonucleotide by SK-BR-3 cells | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 0.02 µM | 0.1 µM | 0.5 µM | 1 µM | 2.5 µM | 10 µM | $IC_{50}$ (µM) |
| 455265 | 22 | 14 | 25 | 19 | 30 | 37 | >10.0 |
| 455269 | 17 | 17 | 21 | 45 | 64 | 67 | 1.3 |
| 455271 | 0 | 0 | 0 | 11 | 16 | 53 | 9.0 |
| 455272 | 0 | 0 | 0 | 5 | 12 | 51 | 9.6 |
| 455291 | 9 | 15 | 31 | 45 | 58 | 76 | 1.2 |
| 455371 | 16 | 20 | 34 | 37 | 54 | 70 | 1.7 |
| 455394 | 0 | 2 | 14 | 6 | 30 | 55 | 8.3 |
| 455429 | 0 | 0 | 0 | 12 | 29 | 57 | 7.9 |
| 455471 | 0 | 16 | 28 | 24 | 42 | 58 | 2.9 |
| 455527 | 5 | 15 | 14 | 21 | 35 | 45 | >10.0 |
| 455530 | 0 | 14 | 12 | 14 | 28 | 36 | >10.0 |
| 455536 | 0 | 0 | 0 | 1 | 8 | 26 | >10.0 |
| 455548 | 16 | 14 | 17 | 17 | 20 | 44 | >10.0 |
| 455611 | 19 | 1 | 3 | 21 | 35 | 38 | >10.0 |

| Dose-dependent antisense inhibition of human STAT3 by free-uptake of ISIS oligonucleotide by SK-BR-3 cells | | | | | | | |
|---|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 1 μM | 2.5 μM | 10 μM | $IC_{50}$ (μM) |
| 455703 | 0 | 0 | 0 | 0 | 3 | 33 | >10.0 |
| 465236 | 0 | 7 | 15 | 19 | 37 | 60 | 3.8 |
| 465237 | 2 | 13 | 22 | 29 | 50 | 67 | 2.3 |
| 465588 | 5 | 3 | 21 | 18 | 42 | 44 | >10.0 |
| 465740 | 1 | 14 | 0 | 19 | 14 | 39 | >10.0 |
| 465754 | 0 | 0 | 4 | 15 | 39 | 55 | 7.7 |
| 465830 | 6 | 18 | 23 | 17 | 42 | 67 | 3.0 |
| 466670 | 21 | 19 | 33 | 35 | 58 | 71 | 1.6 |
| 466720 | 0 | 0 | 11 | 13 | 27 | 53 | 8.7 |

**Example 42: Measurement of viscosity of ISIS antisense oligonucleotides targeting human STAT3**

**[0402]** The viscosity of antisense oligonucleotides selected from the studies described in Examples 6-10 was measured with the aim of screening out antisense oligonucleotides which have a viscosity more than 40 cP. Oligonucleotides having a viscosity greater than 40 cP would be too viscous to be administered to any subject.

**[0403]** ISIS oligonucleotides (32-35 mg) were weighed into a glass vial, 120 μL of water was added and the antisense oligonucleotide was dissolved into solution by heating the vial at 50°C. Part of (75 μL) the pre-heated sample was pipetted to a micro-viscometer (Cambridge). The temperature of the micro-viscometter was set to 25°C and the viscosity of the sample was measured. Another part (20 μL) of the pre-heated sample was pipetted into 10 mL of water for UV reading at 260 nM at 85°C (Cary UV instrument). The results are presented in Table 61 and indicate that all the antisense oligonucleotides solutions are optimal in their viscosity under the criterion stated above.

**Table 61**

| Viscosity of ISIS antisense oligonucleotides targeting human STAT3 | |
|---|---|
| ISIS No | Viscosity |
| 455269 | 6.1 |
| 455291 | 13.6 |
| 466371 | 7.2 |
| 455703 | 17.6 |
| 455429 | 9.3 |
| 465237 | 26.2 |
| 465754 | 19.7 |
| 465830 | 8.1 |
| 466670 | 15.9 |

**Example 43: Effect of ISIS antisense oligonucleotides targeting human STAT3 in cynomolgus monkeys**

**[0404]** Nine antisense oligonucleotides exhibiting a high level of potency were further tested for in cynomolgus monkeys. Antisense oligonucleotide tolerability and pharmacokinetic profile in the liver and kidney was evaluated.

**[0405]** The study was conducted at the Korea Institute of Toxicology, Republic of Korea. Prior to the study, the monkeys were kept in quarantine for a 30-day time period, during which standard panels of serum chemistry and hematology, examination of fecal samples for ova and parasites, and a tuberculosis test, were conducted to screen out abnormal or ailing monkeys. Nine groups of four randomly assigned male cynomolgus monkeys each were injected subcutaneously thrice per week for the first week, and subsequently twice a week for the next 7 weeks, with 25 mg/kg of ISIS antisense oligonucleotides. A control group of 4 cynomolgus monkeys was injected with PBS subcutaneously thrice per week for the first week, and subsequently twice a week for the next 7 weeks. Terminal sacrifices of all groups were conducted on day 55, which was 48 hours after the last dose.

**[0406]** During the study period, the monkeys were observed daily for signs of illness or distress. Any animal showing adverse effects to the treatment was removed and referred to the veterinarian and Study Director.

**[0407]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, spleen heart, kidney, liver, and gall bladder weights were measured at day 55. Organ weights were measured and treatment group weights were compared to the corresponding PBS control weights

**[0408]** To evaluate the effect of ISIS oligonucleotides on hepatic and kidney function, blood samples were collected from all the study groups. The monkeys were fasted overnight prior to blood collection. Approximately, 1 mL each of blood samples was collected in tubes without any anticoagulant for serum separation. The tubes were kept at room temperature for 90 min and then centrifuged (3000 rpm for 10 min at room temperature) to obtain serum. Concentrations of transaminases were measured using a Toshiba 200FR NEO chemistry analyzer (Toshiba Co., Japan). Plasma concentrations of ALT (alanine transaminase), AST (aspartate transaminase), and BUN were measured on day 55. C-reactive protein (CRP), which is synthesized in the liver and which serves as a marker of inflammation, was also similarly measured on day 55.

**[0409]** To evaluate the effect of ISIS oligonucleotides on factors involved in inflammation, blood was collected on day 55 from all animals for analyses of complement C3 levels, MIP-1β cytokine levels, and platelet number.

**[0410]** For complement C3 analysis, approximately 0.5 mL each of blood sample was collected in tubes without anticoagulant for serum separation. For cytokine level analyses, approximately 2 mL each of blood sample was collected in tubes without anticoagulant for serum separation. The tubes were kept at room temperature for 90 min and then centrifuged (3000 rpm for 10 min at room temperature) to obtain serum. Complement C3 was measured using an automatic analyzer (Toshiba 200 FR NEO chemistry analyzer, Toshiba co., Japan). Serum was utilized for cytokine analysis using a nine-panel Searchlight Multiplex Array.

**[0411]** For platelet count, approximately 0.5 mL each of blood samples was collected in tubes containing potassium salt of EDTA. Samples were analyzed for platelet count using an ADVIA120 hematology analyzer (Bayer, USA).

**[0412]** The concentration of oligonucleotide was measured in the liver and kidney on day 55. The method used is a modification of previously published methods (Leeds et al., 1996; Geary et al., 1999), which includes a phenol-chloroform (liquid-liquid) extraction followed by a solid phase extraction. An internal standard (ISIS 355868, a 27-mer 2'-O-methoxyethyl modified phosphorothioate oligonucleotide, GCGTTTGCTCTTCTTCTTGCGTTTTTT, designated herein as SEQ ID NO: 2758) was added prior to extraction. Tissue sample concentrations were calculated using calibration curves, with a lower limit of quantitation (LLOQ) of approximately 1.14 µg/g.

**[0413]** Among the 9 antisense oligonucleotides tested, certain antisense oligonucleotides, including ISIS 455269, ISIS 455371, ISIS 455429, and ISIS 455670 met tolerability thresholds for organ weight, ALT, AST, BUN, and hematological parameters.

**Example 44: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in MDA-MB-231 cells**

**[0414]** ISIS oligonucleotides from the study described in Example 12 were further tested at different doses in MDA-MB-231 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated without any transfection reagent with 0.02 μM, 0.20 μM, 1.00 μM, 5.00 μM, and 10.00 μM concentrations of antisense oligonucleotide, as specified in Table 62. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, as described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells. The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 62.

**Table 62**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by MDA-MB-231 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.20 μM | 1.00 μM | 5.00 μM | 10.00 μM | $IC_{50}$ (μM) |
| 455269 | 0 | 3 | 30 | 47 | 59 | 6.4 |
| 455291 | 1 | 3 | 13 | 41 | 47 | 8.3 |
| 455371 | 5 | 0 | 10 | 34 | 43 | >10.0 |
| 455429 | 0 | 0 | 22 | 31 | 43 | >10.0 |
| 455703 | 0 | 5 | 13 | 28 | 39 | >10.0 |
| 465237 | 0 | 0 | 22 | 39 | 41 | >10.0 |
| 465754 | 5 | 1 | 22 | 30 | 46 | >10.0 |
| 465830 | 0 | 0 | 17 | 43 | 52 | 7.5 |
| 466670 | 4 | 7 | 18 | 49 | 56 | 6.5 |

**Example 45: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in U251-MG cells**

**[0415]** ISIS oligonucleotides from the study described in Example 12 were further tested at different doses in U251-MG cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated without any transfection reagent with 0.1 μM, 1.0 μM, 5.0 μM, 10.0 μM, and 20.0 μM concentrations of antisense oligonucleotide, as specified in Table 63. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, as described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells. The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 63.

**Table 63**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by U251-MG cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.1 μM | 1.0 μM | 5.0 μM | 10.0 μM | 20.0 μM | $IC_{50}$ (μM) |
| 455269 | 3 | 16 | 31 | 47 | 56 | 11.9 |
| 455291 | 0 | 11 | 29 | 42 | 51 | 14.1 |
| 455371 | 3 | 0 | 25 | 33 | 39 | >20.0 |
| 455429 | 6 | 0 | 25 | 33 | 39 | >20.0 |
| 455703 | 5 | 2 | 13 | 33 | 36 | >20.0 |
| 465237 | 2 | 0 | 7 | 2 | 6 | >20.0 |
| 465754 | 0 | 0 | 8 | 16 | 4 | >20.0 |
| 465830 | 0 | 0 | 18 | 2 | 10 | >20.0 |
| 466670 | 0 | 0 | 18 | 25 | 37 | >20.0 |

**Example 46: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in A431 cells**

**[0416]** ISIS oligonucleotides from the study described in Example 12 were further tested at different doses in A431 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated without any transfection reagent with 0.02 μM, 0.2 μM, 1.0 μM, 5.0 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 64. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, as described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0417]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 64. As illustrated in Table 64, the ISIS oligonucleotides were able to penetrate the cell membrane and significantly reduce STAT3 mRNA levels in a dose-dependent manner.

**Table 64**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by A431 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.2 μM | 1.0 μM | 5.0 μM | 10.0 μM | $IC_{50}$ (μM) |
| 455269 | 41 | 64 | 86 | 86 | 89 | 0.15 |
| 455291 | 25 | 61 | 83 | 85 | 86 | 0.17 |
| 455371 | 30 | 65 | 82 | 88 | 92 | 0.15 |
| 455429 | 15 | 73 | 84 | 87 | 88 | 0.19 |
| 455703 | 12 | 55 | 72 | 82 | 82 | 0.13 |
| 465237 | 23 | 72 | 82 | 86 | 87 | 0.13 |
| 465754 | 0 | 67 | 73 | 79 | 83 | 0.15 |
| 465830 | 0 | 50 | 67 | 71 | 78 | 0.21 |
| 466670 | 36 | 79 | 88 | 93 | 94 | 0.03 |

**Example 47: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense**

**oligonucleotide in H460 cells**

**[0418]** ISIS oligonucleotides from the study described in Example 12 were further tested at different doses in H460 cells. Cells were plated at a density of 4,000 cells per well. Cells were incubated without any transfection reagent with 0.02 µM, 0.20 µM, 1.00 µM, 5.00 µM, and 10.00 µM concentrations of antisense oligonucleotide, as specified in Table 65. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS199, as described hereinabove, was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0419]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 65. As illustrated in Table 65, the ISIS oligonucleotides were able to penetrate the cell membrane and significantly reduce STAT3 mRNA levels in a dose-dependent manner.

**Table 65**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by H460 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 µM | 0.20 µM | 1.00 µM | 5.00 µM | 10.00 µM | $IC_{50}$ (µM) |
| 455269 | 3 | 69 | 81 | 92 | 94 | 0.1 |
| 455291 | 0 | 29 | 79 | 88 | 92 | 0.3 |
| 455371 | 0 | 20 | 63 | 85 | 89 | 0.8 |
| 455429 | 3 | 37 | 75 | 87 | 88 | 0.6 |
| 455703 | 4 | 24 | 69 | 87 | 92 | 0.3 |
| 465237 | 0 | 20 | 72 | 87 | 89 | 0.6 |
| 465754 | 10 | 45 | 80 | 91 | 92 | 0.2 |
| 465830 | 10 | 28 | 65 | 82 | 89 | 0.7 |
| 466670 | 15 | 32 | 71 | 90 | 93 | 0.3 |

**Example 48: Effect of ISIS oligonucleotides targeting STAT3 in the treatment of U251 human glioma cancer xenograft model**

**[0420]** BALB/c nude mice inoculated with human U251 glioma tumor cells were treated with ISIS oligonucleotides from the study described in Example 12. The effect of the treatment on tumor growth in the mice was evaluated.

***Treatment***

**[0421]** BALB/c nude mice were subcutaneously implanted with 1 x $10^6$ tumor cells. On day 4 of the implantation, groups of 4 mice each were administered 50 mg/kg injected intraperitoneally five times a week for 3 and a half weeks of ISIS 455269, ISIS 455291, ISIS 455371, ISIS 455703, ISIS 455429, ISIS 465237, ISIS 465754, ISIS 465830, or ISIS 466670. One group of mice was administered 50 mg/kg injected intraperitoneally five times a week for 3 and a half weeks of the control oligonucleotide, ISIS 141923. One group of mice was administered PBS injected intraperitoneally five times a week for 3 and a half weeks.

***Effect on tumor growth***

**[0422]** Tumor size was measured twice weekly in two dimensions using a caliper, and tumor volumes were calculated using the formula: $V = 0.5 \times a \times b^2$, where *a* and *b* are the long and short diameters of the tumor, respectively. The results are presented in Table 66. The data indicates that treatment with ISIS oligonucleotides significantly impeded tumor growth. 'n/a' indicates that the data points for that time point are not available.

**Table 66**

| Effect of antisense inhibition of STAT3 on tumor growth in the U251 xenograft model | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day 10 | Day 14 | Day 17 | Day 21 | Day 23 | Day 29 | Day 32 | Day 35 |
| PBS | 205 | 216 | 285 | 381 | 519 | 771 | 937 | 1,141 |
| ISIS 141923 | 175 | 178 | 296 | 404 | 544 | 719 | 923 | 1,027 |
| ISIS 455269 | 157 | 151 | 227 | 307 | 349 | 418 | 486 | 542 |
| ISIS 455291 | 149 | 169 | 193 | 238 | 297 | 429 | 635 | 610 |
| ISIS 455371 | 141 | 169 | 253 | 379 | 375 | 598 | 838 | 912 |
| ISIS 455429 | 180 | 160 | 251 | 337 | 427 | 546 | 807 | 897 |
| ISIS 455703 | 156 | 161 | 246 | 342 | 414 | 615 | 872 | 991 |
| ISIS 465237 | 149 | 166 | 245 | 326 | 350 | 551 | 703 | 744 |
| ISIS 465830 | 173 | 205 | 287 | 346 | 383 | 696 | 844 | 825 |
| ISIS 466670 | 112 | 172 | 208 | 254 | 274 | 492 | 462 | 669 |

**Example 49: Effect of ISIS 455291 targeting STAT3 in the treatment of an MDA-MB-231 human breast cancer xenograft model**

**[0423]** BALB/c nude mice inoculated with human breast cancer cells MDA-MB-231 were treated with ISIS 455291. The effect of the treatment on tumor growth and tolerability in the mice was evaluated.

***Treatment***

**[0424]** The study was conducted at Pharmaron Inc (Beijing, P.R. China). The BALB/c nude mice were obtained from Beijing HFK Bio-Technology Co., Ltd. MDA-MB-231 human breast cancer cells were maintained in vitro as a monolayer culture in Leibovitz's L-15 medium supplemented with 10% heat-inactivated fetal calf serum, 100 U/mL penicillin, 100 µg/mL streptomycin, and 2 mM L-glutamine. The cells were maintained at 37°C in an atmosphere of 5% $CO_2$ in air. The tumor cells were routinely sub-cultured twice weekly with trypsin-EDTA treatment. Cells growing an exponential growth phase were harvested and counted for tumor inoculation.

**[0425]** Two groups of eight randomly assigned 6-8 week-old female BALB/c nude mice each were inoculated at the right flank with the MDA-MB-231 tumor fragments (3 mm x 2 mm x 2 mm, which were generated from tumor inoculation passage) for tumor development. Antisense oligonucleotide treatment started at day 11 after tumor inoculation when the mean tumor size reached approximately 100 $mm^3$. One of the groups was injected intraperitoneally twice a week for 3 weeks with 50 mg/kg of ISIS 455291. The other group of mice was injected intraperitoneally twice a week for 3 weeks with PBS, and served as the control group.

**[0426]** All procedures related to animal handling, care, and treatment, were performed according to the guidelines approved by the Institutional Animal Care and Use Committee (IACUC). At the time of routine monitoring, the animals were checked for any effects of tumor growth on normal behavior, such as mobility, food consumption, body weight changes and any other abnormal effect.

***RNA analysis***

**[0427]** RNA was extracted from tumor tissue for real-time PCR analysis of human STAT3 mRNA levels using primer probe set RTS199, described hereinabove. Murine STAT3 mRNA levels were also measured using primer probe set mSTAT3_LTS00664 (forward sequence CGACAGCTTCCCCATGGA, designated herein as SEQ ID NO: 1513; reverse sequence ATGCCCAGTCTTGACTCTCAATC, designated herein as SEQ ID NO: 1514; probe sequence CTGCGGCAGTTCCTGGCACCTT, designated herein as SEQ ID NO: 1515). Results are presented as percent inhibition of STAT3, relative to PBS control, normalized to cyclophilin. As shown in Table 67, treatment with ISIS 455291 resulted in reduction of both human and murine STAT3 mRNA in comparison to the PBS control.

**Table 67**

| Inhibition of STAT3 mRNA in the treatment groups relative to the PBS control in the MDA-MB-231 xenograft model | |
|---|---|
| | % inhibition |
| Human STAT3 | 91 |
| Murine STAT3 | 94 |

***Effect on tumor growth***

**[0428]** Tumor size was measured twice weekly in two dimensions using a caliper, and tumor volumes were calculated using the formula: $V = 0.536 \times a \times b^2$, where *a* and *b* are the long and short diameters of the tumor, respectively. The tumor size was utilized for calculations of the T-C and $T_V/C_V$ values. T-C was calculated with T as the median time (in days) required for the tumors in the treatment groups to reach a pre-determined size (900 $mm^3$), and C as the median time (in days) for the tumors in the control group to reach the same size. The $T_V/C_V$ value (expressed as percentage) is an indication of the anti-tumor effectiveness of the ISIS oligonucleotides, where $T_V$ and $C_V$ were the mean volume of the treated and control groups, respectively, on a given day (day 32).

**[0429]** The results are presented in Tables 68 and 69. The data indicates that inhibition of STAT3 mRNA significantly impeded tumor growth.

**Table 68**

| Effect of antisense inhibition of STAT3 on tumor growth in the MDA-MB-231 xenograft model | | |
|---|---|---|
| Days | PBS | ISIS 455291 |
| 11 | 103 | 103 |
| 15 | 185 | 156 |
| 18 | 292 | 205 |
| 22 | 519 | 320 |
| 25 | 745 | 437 |

| Effect of antisense inhibition of STAT3 on tumor growth in the MDA-MB-231 xenograft model | | |
|---|---|---|
| Days | PBS | ISIS 455291 |
| 29 | 1,332 | 792 |
| 32 | 1,741 | 1,075 |

**Table 69**

| Effect of antisense inhibition of STAT3 on tumor growth inhibition in the MDA-MB-231 xenograft model | | | |
|---|---|---|---|
| Treatment | Tumor Size ($mm^3$) at day 32 | $T_V/C_V$ (%) | T-C at 900 $mm^3$ |
| PBS | 1,741 | - | - |
| ISIS 455291 | 1,075 | 62 | 4 |

***Body weight measurements***

**[0430]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were measured on a regular basis during the treatment period. The data is presented in Table 70 and indicate that treatment with ISIS 455291 does not affect the overall body weight of the mice.

**Table 70**

| Body weight measurements of mice in the MDA-MB-231 xenograft model | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Day 11 | Day 15 | Day 18 | Day 22 | Day 25 | Day 29 | Day 32 |
| PBS | 22 | 22 | 23 | 23 | 23 | 23 | 24 |
| ISIS 455291 | 22 | 22 | 23 | 23 | 24 | 24 | 25 |

**Example 50: Effect of ISIS 455291 targeting STAT3 in the treatment of an A431 human epidermoid carcinoma xenograft model**

**[0431]** BALB/c nude mice inoculated with human epidermoid cancer cells A431 were treated with ISIS 455291. The effect of the treatment on tumor growth and tolerability in the mice was evaluated.

***Treatment***

**[0432]** The study was conducted at Pharmaron Inc (Beijing, P.R. China). The BALB/c nude mice were obtained from Beijing HFK Bio-Technology Co., Ltd. A431 human epidermoid carcinoma cells were maintained in vitro as a monolayer culture in DMEM medium supplemented with 10% heat-inactivated fetal calf serum, 100 U/mL penicillin, 100 µg/mL streptomycin, and 2 mM L-glutamine. The cells were maintained at 37°C in an atmosphere of 5% $CO_2$ in air. The tumor cells were routinely sub-cultured twice weekly with trypsin-EDTA treatment. Cells growing in an exponential growth phase were harvested and counted for tumor inoculation.

**[0433]** Two groups of eight randomly assigned 6-8 week-old female BALB/c nude mice each were inoculated subcutaneously with 5 x $10^6$ A431 tumor cells for tumor development. Antisense oligonucleotide treatment started at day 8 after tumor inoculation when the mean tumor size reached approximately 95 $mm^3$. One of the groups was injected intraperitoneally twice a week for 4 weeks with 50 mg/kg of ISIS 455291. The other group

of mice was injected intraperitoneally twice a week for 3 weeks with PBS, and served as the control group.

**[0434]** All procedures related to animal handling, care, and treatment, were performed according to the guidelines approved by the Institutional Animal Care and Use Committee (IACUC). At the time of routine monitoring, the animals were checked for any effects of tumor growth on normal behavior, such as mobility, food consumption, body weight changes and any other abnormal effect.

***RNA analysis***

**[0435]** RNA was extracted from tumor tissue for real-time PCR analysis of human STAT3 mRNA levels using primer probe set RTS199, described hereinabove. Murine STAT3 mRNA levels were also measured using primer probe set mSTAT3_LTS00664. Results are presented as percent inhibition of STAT3, relative to PBS control, normalized to cyclophilin. As shown in Table 71, treatment with ISIS 455291 resulted in reduction of both human and murine STAT3 mRNA in comparison to the PBS control.

**Table 71**

| Inhibition of STAT3 mRNA in the treatment groups relative to the PBS control in the A431 xenograft model | |
|---|---|
| | % inhibition |
| Human STAT3 | 67 |
| Murine STAT3 | 92 |

***Effect on tumor growth***

**[0436]** Tumor size was measured twice weekly in two dimensions using a caliper, and tumor volumes were calculated using the formula: $V = 0.5 \times a \times b^2$, where *a* and *b* are the long and short diameters of the tumor, respectively. The tumor size was utilized for calculations of the T-C and $T_V/C_V$ values. T-C was calculated with T as the median time (in days) required for the tumors in the treatment groups to reach a pre-determined size (800 $mm^3$), and C as the median time (in days) for the tumors in the control group to reach the same size. The $T_V/C_V$ value (expressed as percentage) is an indication of the anti-tumor effectiveness of the ISIS oligonucleotides, where $T_V$ and $C_V$ were the mean volume of the treated and control groups, respectively, on a given day (day 33).

**[0437]** The results are presented in Tables 72 and 73. The data indicates that inhibition of STAT3 mRNA impeded tumor growth.

**Table 72**

| Effect of antisense inhibition of STAT3 on tumor growth in the A431 xenograft model | | |
|---|---|---|
| Days | PBS | ISIS 455291 |
| 8 | 94 | 95 |
| 14 | 178 | 173 |
| 17 | 308 | 242 |
| 21 | 528 | 393 |
| 24 | 682 | 572 |
| 28 | 875 | 759 |
| 31 | 1,071 | 984 |

| Effect of antisense inhibition of STAT3 on tumor growth in the A431 xenograft model | | |
|---|---|---|
| Days | PBS | ISIS 455291 |
| 33 | 1,210 | 1,112 |

**Table 73**

| Effect of antisense inhibition of STAT3 on tumor growth inhibition in the A431 xenograft model | | | |
|---|---|---|---|
| Treatment | Tumor Size ($mm^3$) at day 33 | $T_V/C_V$ (%) | T-C at 800 $mm^3$ |
| PBS | 1,210 | - | - |
| ISIS 455291 | 1,112 | 92 | 2 |

***Body weight measurements***

**[0438]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were measured on a regular basis during the treatment period. The data is presented in Table 74 and indicate that treatment with ISIS 455291 does not affect the overall body weight of the mice.

**Table 74**

| Body weight measurements of mice in the A431 xenograft model | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day 8 | Day 14 | Day 17 | Day 21 | Day 24 | Day 28 | Day 31 | Day 33 |
| PBS | 20 | 20 | 20 | 21 | 21 | 21 | 22 | 22 |
| ISIS 455291 | 20 | 21 | 21 | 22 | 22 | 22 | 23 | 23 |

**Example 51: Effect of ISIS 455291 targeting STAT3 in the treatment of an NCI-H460 human non-small cell lung cancer (NSCLC) xenograft model**

**[0439]** BALB/c nude mice inoculated with human NCI-H460 human NSCLC were treated with ISIS 455291. The effect of the treatment on tumor growth and tolerability in the mice was evaluated.

***Treatment***

**[0440]** The study was conducted at Pharmaron Inc (Beijing, P.R. China). The BALB/c nude mice were obtained from Beijing HFK Bio-Technology Co., Ltd. NCI-H460 human NSCLC cells were maintained in vitro as a monolayer culture in RPMI-1640 medium supplemented with 10% heat-inactivated fetal calf serum, 100 U/mL penicillin, 100 µg/mL streptomycin, and 2 mM L-glutamine. The cells were maintained at 37°C in an atmosphere of 5% $CO_2$ in air. The tumor cells were routinely sub-cultured twice weekly with trypsin-EDTA treatment. Cells growing in an exponential growth phase were harvested and counted for tumor inoculation.

**[0441]** Two groups of eight randomly assigned 6-8 week-old female BALB/c nude mice each were inoculated subcutaneously with 2 x $10^6$ NCI-H460 tumor cells for tumor development. Antisense oligonucleotide treatment started at day 6 after tumor inoculation when the mean tumor size reached approximately 100 $mm^3$. One of the groups was injected intraperitoneally twice a week for 3 weeks with 50 mg/kg of ISIS 455291. The other group of mice was injected intraperitoneally twice a week for 3 weeks with PBS, and served as the control group.

**[0442]** All procedures related to animal handling, care, and treatment, were performed according to the guidelines approved by the Institutional Animal Care and Use Committee (IACUC). At the time of routine monitoring, the animals were checked for any effects of tumor growth on normal behavior, such as mobility, food consumption, body weight changes and any other abnormal effect.

***Effect on tumor growth***

**[0443]** Tumor size was measured twice weekly in two dimensions using a caliper, and tumor volumes were calculated using the formula: $V = 0.5 \times a \times b^2$, where *a* and *b* are the long and short diameters of the tumor, respectively. The tumor size was utilized for calculations of the T-C and $T_V/C_V$ values. T-C was calculated with T as the median time (in days) required for the tumors in the treatment groups to reach a pre-determined size (1,500 $mm^3$), and C as the median time (in days) for the tumors in the control group to reach the same size. The $T_V/C_V$ value (expressed as percentage) is an indication of the anti-tumor effectiveness of the ISIS oligonucleotides, where $T_V$ and $C_V$ were the mean volume of the treated and control groups, respectively, on a given day (day 20).

**[0444]** The results are presented in Tables 75 and 76. The data indicates that inhibition of STAT3 significantly impeded tumor growth.

**Table 75**

| Effect of antisense inhibition of STAT3 on tumor growth in the NCI-H460 xenograft model | | |
|---|---|---|
| Days | PBS | ISIS 455291 |
| 6 | 104 | 104 |
| 8 | 303 | 180 |
| 11 | 746 | 408 |
| 13 | 1,175 | 620 |
| 15 | 1,642 | 819 |
| 18 | 2,277 | 1,320 |
| 20 | 2,859 | 1,812 |
| 22 | - | 2,330 |

**Table 76**

| Effect of antisense inhibition of STAT3 on tumor growth inhibition in the NCI-H460 xenograft model | | | |
|---|---|---|---|
| Treatment | Tumor Size ($mm^3$) at day 20 | $T_V/C_V$ (%) | T-C at 800 $mm^3$ |
| PBS | 1,210 | - | - |
| ISIS 455291 | 1,812 | 63 | 4 |

***Body weight measurements***

**[0445]** To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body weights were measured on a regular basis during the treatment period. The data is presented in Table 77 and indicate that treatment with ISIS 455291 does not affect the overall body weight of the mice.

**Table 77**

| Body weigth measurement of mice in the NCI-H460 xenograft model | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day 6 | Day 8 | Day 11 | Day 13 | Day 15 | Day 18 | Day 20 | Day 22 |
| PBS | 20 | 20 | 20 | 20 | 20 | 20 | 21 | - |
| ISIS 455291 | 20 | 20 | 20 | 20 | 20 | 19 | 20 | 20 |

**Example 52: Effect of antisense inhibition of human STAT3 in a human glioblastoma orthotopic mouse model**

**[0446]** NU/J mice orthotopically implanted with human glioblastoma cells were treated with ISIS 455291, a 5-10-5 MOE gapmer having a sequence of CAGCAGATCAAGTCCAGGGA (SEQ ID NO: 1590. The effect of the treatment on tumor growth and tolerability in the mice was evaluated.

***Treatment***

**[0447]** Thirty NU/J mice were stereotactically implanted in the right frontal lobe with 5 x $10^5$ U-87 MG-luc2 cells. On day 15 after tumor cell implantation, 15 of these mice were dosed intracranially with a bolus injection at the site of tumor implantation with 100 µg of ISIS 455291, which was dissolved in 2 µL of PBS. The remaining 15 mice were dosed intracranially with a bolus injection at the site of tumor implantation with 2 µL of PBS. The second group of mice served as the control group.

***Analysis***

**[0448]** On day 18 after tumor transplantation, five mice from each group were euthanized by $CO_2$ inhalation and brain samples were collected for RNA analysis. RNA was extracted from tumor tissue for real-time PCR analysis of human STAT3 mRNA levels using primer probe set RTS199, described hereinabove. Treatment with ISIS 455291 resulted in 27% reduction of human STAT3 mRNA in the tumor tissue in comparison to the PBS control.

**[0449]** The remaining mice in each group were monitored regularly up to 2 weeks for survival analysis. The median survival for the PBS control group was 30.5 days. The medial survival for the ISIS oligonucleotide-treated mice was 35 days. The P value was 0.2088.

**Example 53: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in PC9 cells**

**[0450]** ISIS 455703 and ISIS 455291, from the studies described above, were further tested at different doses in PC9 cells, a non small cell lung carcinoma cell line. Cells were plated at a density of 3,000 cells per well. Cells were incubated with 0.02µM, 0.1 µM, 0.5 µM, 2.5 µM, and 10.0 µM concentrations of antisense oligonucleotide, as specified in Table 78. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human

primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0451]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 78. As illustrated in Table 78, ISIS 455703 and ISIS 455291were able to penetrate the cell membrane.

**Table 78**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by PC9 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 455703 | 6 | 5 | 17 | 50 | 49 | 9.0 |
| 455291 | 0 | 0 | 42 | 67 | 75 | 1.2 |

**Example 54: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in C42B cells**

**[0452]** ISIS 455291, from the studies described above, was further tested at different doses in C42B cells, a prostate cancer cell line. Cells were plated at a density of 3,000 cells per well. Cells were incubated with 0.02μM, 0.1 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 79. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0453]** As illustrated in Table 79, ISIS 455291 was able to penetrate the cell membrane.

**Table 79**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by C42B cells | | | | | |
|---|---|---|---|---|---|
| ISIS No | 0.02 | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM |
| 455291 | 0 | 0 | 17 | 10 | 41 |

**Example 55: Dose-dependent antisense inhibition of STAT3 following free uptake of antisense oligonucleotide in Colo201 cells**

**[0454]** ISIS 455291, from the studies described above, was further tested at different doses in Colo201 cells, a colorectal cancer cell line. Cells were plated at a density of 3,000 cells per well. Cells were incubated with 0.02μM, 0.1 μM, 0.5 μM, 2.5 μM, and 10.0 μM concentrations of antisense oligonucleotide, as specified in Table 80. After approximately 24 hours, RNA was isolated from the cells and STAT3 mRNA levels were

measured by quantitative real-time PCR. Human STAT3 primer probe set RTS2033 (forward sequence GAGGCCCGCCCAACA, designated herein as SEQ ID NO: 1520; reverse sequence TTCTGCTAATGACGTTATCCAGTTTT, designated herein as SEQ ID NO: 1521; probe sequence CTGCCTAGATCGGC, designated herein as SEQ ID NO: 1522) was used to measure mRNA levels. STAT3 mRNA levels were adjusted according to content of beta-actin, a housekeeping gene, as measured by human primer probe set HTS5002 (forward sequence CGGACTATGACTTAGTTGCGTTACA, designated herein as SEQ ID NO: 1529; reverse sequence GCCATGCCAATCTCATCTTGT, designated herein as SEQ ID NO: 1530; probe sequence CCTTTCTTGACAAAACCTAACTTGCGCAGA, designated herein as SEQ ID NO: 1531). Results are presented as percent inhibition of STAT3, relative to untreated control cells.

**[0455]** The half maximal inhibitory concentration ($IC_{50}$) of each oligonucleotide is also presented in Table 80. As illustrated in Table 29, ISIS 455291 was able to penetrate the cell membrane.

**Table 80**

| Dose-dependent antisense inhibition of STAT3 mRNA levels by free-uptake of ISIS oligonucleotide by Colo201 cells | | | | | | |
|---|---|---|---|---|---|---|
| ISIS No | 0.02 μM | 0.1 μM | 0.5 μM | 2.5 μM | 10.0 μM | $IC_{50}$ (μM) |
| 455291 | 21 | 18 | 34 | 52 | 81 | 1.2 |

# REFERENCES CITED IN THE DESCRIPTION

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**Patent documents cited in the description**


- US20050196781A **[0009]**
- WO2005083124A **[0009]**
- WO2008101157A **[0176]**
- US20050130923A **[0176]**
- WO2007134181A **[0176]**
- US7399845B **[0178]** **[0178]**
- WO2009006478A **[0178]**
- WO2008150729A **[0178]**
- US20040171570A **[0178]** **[0178]**
- US7427672B **[0178]**
- WO2008154401A **[0178]**
- US6670461B **[0178]**
- US7053207B **[0178]**
- US6268490B **[0178]**
- US6770748B **[0178]**
- US6794499B **[0178]**
- US7034133B **[0178]**
- US6525191B **[0178]**
- WO2004106356A **[0178]**
- WO9414226PCT **[0178]**

- WO2005021570A [0178]
- WO2007134181PCT [0178]
- US20070287831A [0178]
- US20080039618A [0178]
- US12129154B [0178]
- US60989574B [0178]
- US61026995B [0178]
- US61026998B [0178]
- US61056564B [0178]
- US61086231B [0178]
- US61097787B [0178]
- US61099844B [0178]
- US2008064591W [0178]
- US2008066154W [0178]
- US2008068922W [0178]
- DK9800393W [0178]
- WO9914226A [0178] [0189] [0190]
- WO9839352A [0189]
- WO03004602A [0211]


**Non-patent literature cited in the description**


- **DARNELL, JR., J.E. et al.**Science, 1994, vol. 264, 1415-1421 [0005]
- **YANG, C.-H. et al.**Proc. Natl. Acad. Sci. USA, 1998, vol. 95, 5568-5572 [0005]
- **JAIN, N. et al.**Oncogene, 1998, vol. 17, 3157-3167 [0005]
- **ZHONG, Z. et al.**Proc. Natl. Acad. Sci. USA, 1994, vol. 91, 4806-4810 [0006]
- **FUKADA, T. et al.**Immunity, 1996, vol. 5, 449-460 [0006]
- **GOUGH, D.J. et al.**Science, 2009, vol. 324, 1713-1716 [0007]
- **WOOLF et al.**Proc. Natl. Acad. Sci. USA, 1992, vol. 89, 7305-7309 [0133]
- **GAUTSCHI et al.**J. Natl. Cancer Inst., 2001, vol. 93, 463-471 [0134]
- **MAHERDOLNICK**Nuc. Acid. Res., 1988, vol. 16, 3341-3358 [0135]
- **ALTSCHUL et al.**J. Mol. Biol., 1990, vol. 215, 403-410 [0160]
- **ZHANGMADDEN**Genome Res., 1997, vol. 7, 649-656 [0160]
- **SMITHWATERMAN**Adv. Appl. Math., 1981, vol. 2, 482-489 [0160]
- **CHATTOPADHYAYA et al.**J. Org. Chem., 2009, vol. 74, 118-134 [0178]
- **SINGH et al.**Chem. Commun., 1998, vol. 4, 455-456 [0178]
- **KOSHKIN et al.**Tetrahedron, 1998, vol. 54, 3607-3630 [0178] [0189]
- **WAHLESTEDT et al.**Proc. Natl. Acad. Sci. U. S. A., 2000, vol. 97, 5633-5638 [0178]
- **KUMAR et al.**Bioorg. Med. Chem. Lett., 1998, vol. 8, 2219-2222 [0178] [0190]
- **SINGH et al.**J. Org. Chem., 1998, vol. 63, 10035-10039 [0178] [0190]
- **SRIVASTAVA et al.**J. Am. Chem. Soc., 2007, vol. 129, 268362-8379 [0178]
- **ELAYADI et al.**Curr. Opinion Invens. Drugs, 2001, vol. 2, 558-561 [0178]
- **BRAASCH et al.**Chem. Biol., 2001, vol. 8, 1-7 [0178]
- **ORUM et al.**Curr. Opinion Mol. Ther., 2001, vol. 3, 239-243 [0178]
- **FRIEDEN et al.**Nucleic Acids Research, 2003, vol. 21, 6365-6372 [0181]
- **FREIER et al.**Nucleic Acids Research, 1997, vol. 25, 224429-4443 [0192]
- **ALBAEK et al.**J. Org. Chem., 2006, vol. 71, 7731-7740 [0192]
- **SRIVASTAVA et al.**J. Am. Chem. Soc., 2007, vol. 129, 268362-8379 [0192]

- **BAKER et al.**J. Biol. Chem., 1997, vol. 272, 11944-12000 [0195]
- **MARTIN, P.**Helv. Chim. Acta, 1995, vol. 78, 486-504 [0195]
- **ALTMANN et al.**Chimia, 1996, vol. 50, 168-176 [0195]
- **ALTMANN et al.**Biochem. Soc. Trans., 1996, vol. 24, 630-637 [0195]
- **ALTMANN et al.**Nucleosides Nucleotides, 1997, vol. 16, 917-926 [0195]
- **LEUMANN, CJ.**Bioorg. & Med. Chem., 2002, vol. 10, 841-854 [0196]
- **LEUMANN, J. C**Bioorganic & Medicinal Chemistry, 2002, vol. 10, 841-854 [0202]
- **JONES, L.J. et al.**Analytical Biochemistry, 1998, vol. 265, 368-374 [0226]
- **MOSER A.R. et al.**Science, 1990, vol. 247, 322-324 [0321]

Patentkrav

1. Enkeltstrenget forbindelse, der omfatter et modificeret enkeltstrenget oligonukleotid, der består af 16 koblede nukleosider med en nukleobasesekvens, der består af SEQ ID NO: 245, eller et farmaceutisk acceptabelt salt deraf, hvor det modificerede oligonukleotid omfatter:
en 5'-vinge, der består af 3 koblede nukleosider;
en 3'-vinge, der består af 3 koblede nukleosider;
et mellemrum mellem 5'-vingen og 3'-vingen, der består af 10 koblede 2'-deoxynukleosider;
hvor hvert nukleosid i hver af 5'-vingen og 3'-vingen omfatter et ufrit ethylnukleosid;
hvor hver internukleosidbinding er en phosphorothioatbinding; og
hvor hver cytosin er en 5-methylcytosin.

2. Forbindelse ifølge krav 1 eller et farmaceutisk acceptabelt salt deraf, hvor oligonukleotidet er kovalent bundet til en eller flere konjugatgrupper.

3. Forbindelse ifølge krav 2 eller et farmaceutisk acceptabelt salt deraf, hvor den ene eller de flere konjugatgrupper indbefatter carbohydrater.

4. Farmaceutisk sammensætning, der omfatter forbindelsen ifølge et hvilket som helst af kravene 1 til 3 eller et farmaceutisk acceptabelt salt deraf og et farmaceutisk acceptabelt fortyndingsmiddel eller bæremateriale.

5. Enkeltstrenget forbindelse, der omfatter et modificeret enkeltstrenget oligonukleotid ifølge et hvilket som helst af kravene 1 til 3 eller et farmaceutisk acceptabelt salt deraf eller den farmaceutiske forbindelse ifølge krav 4 til anvendelse til behandling af en hyperproliferativ sygdom hos et dyr.

6. Forbindelse eller sammensætning ifølge krav 5, hvor dyret

er et menneske.

7. Forbindelse eller sammensætning ifølge krav 5 eller 6, hvor den hyperproliferative sygdom er cancer.