US 20110263682A1

(19) **United States**

(12) **Patent Application Publication**

De Kimpe et al.

(10) **Pub. No.: US 2011/0263682 A1**

(43) **Pub. Date: Oct. 27, 2011**

(54) **METHODS AND MEANS FOR EFFICIENT SKIPPING OF AT LEAST ONE OF THE FOLLOWING EXONS OF THE HUMAN DUCHENNE MUSCULAR DYSTROPHY GENE: 43, 46, 50-53**

(75) Inventors: **Josephus Johannes De Kimpe**, Utrecht (NL); **Gerardus Johannes Platenburg**, Voorschoten (NL); **Judith Christina Theodora Van Deutekom**, Dordrecht (NL); **Annemieke Aartsma-Rus**, Hoofddorp (NL); **Garrit-Jan Boudewijn Van Ommen**, Amsterdam (NL)

(73) Assignees: **Academisch Ziekenhuis Leiden**, Leiden (NL); **Prosensa Holding BV**, Leiden (NL); **Prosensa Technologies B.V.**, Leiden (NL); **Prosensa B.V.**, Leiden (NL)

(21) Appl. No.: **13/094,571**

(22) Filed: **Apr. 26, 2011**

Related U.S. Application Data

(63) Continuation of application No. PCT/NL2009/050113, filed on Mar. 11, 2009.

(30) **Foreign Application Priority Data**

Oct. 26, 2007 (EP) 07119351.0
Oct. 27, 2008 (NL) PCT/NL2008/050673

Publication Classification

(51) **Int. Cl.**

A61K 31/7088	(2006.01)
C12N 5/071	(2010.01)
C12N 15/85	(2006.01)
C07H 21/02	(2006.01)
A61P 21/00	(2006.01)

(52) **U.S. Cl.** ..... **514/44 A**; 536/24.5; 435/320.1; 435/375

(57) **ABSTRACT**

The invention relates a method wherein a molecule is used for inducing and/or promoting skipping of at least one of exon 43, exon 46, exons 50-53 of the DMD pre-mRNA in a patient, preferably in an isolated cell of a patient, the method comprising providing said cell and/or said patient with a molecule. The invention also relates to said molecule as such.

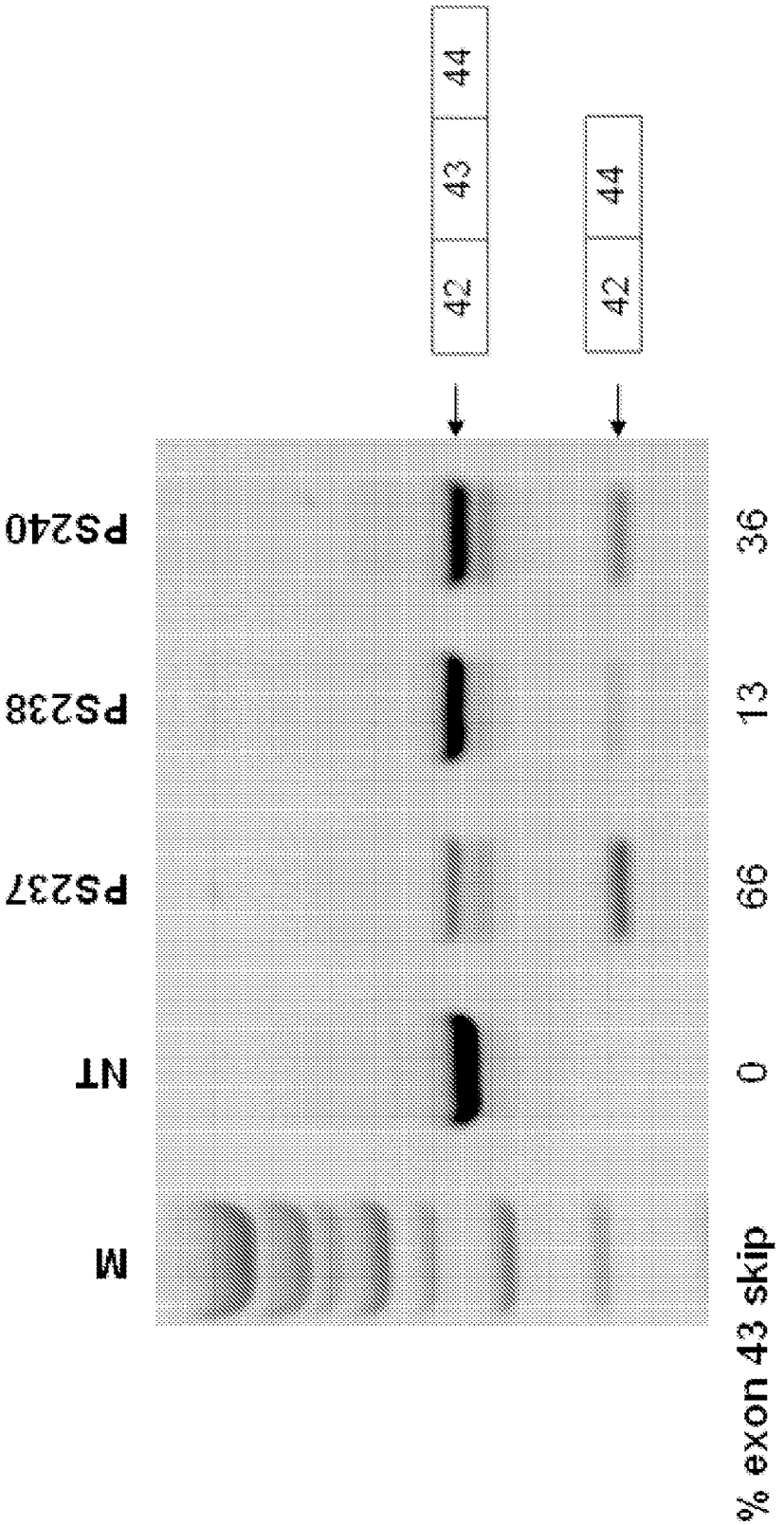
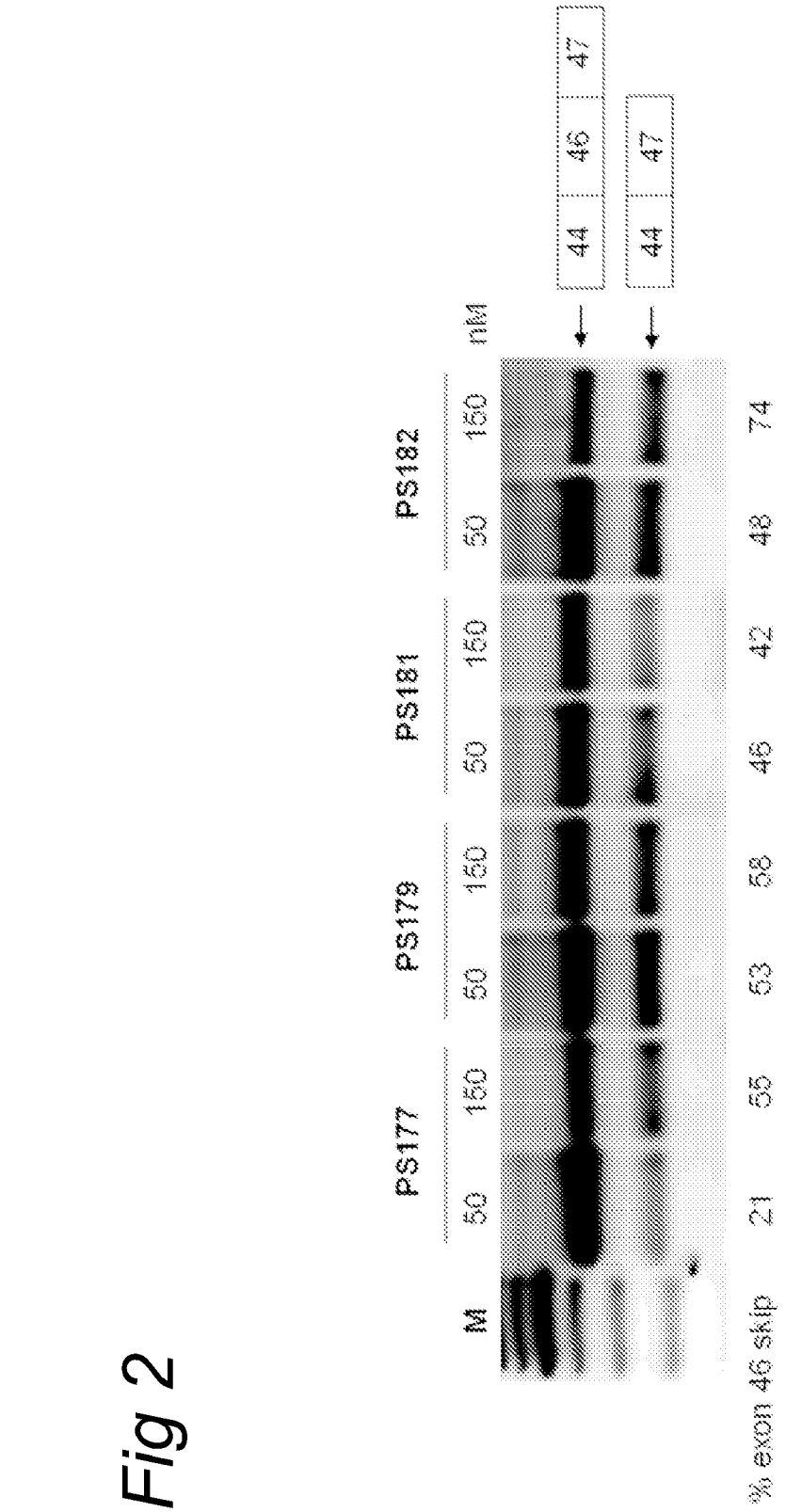


Fig 1

Fig 2


M
PS177
PS179
PS181
PS182
nM
50
150
50
150
50
150
50
150
44
46
47
44
47
% exon 46 skip
21
55
53
58
46
42
48
74

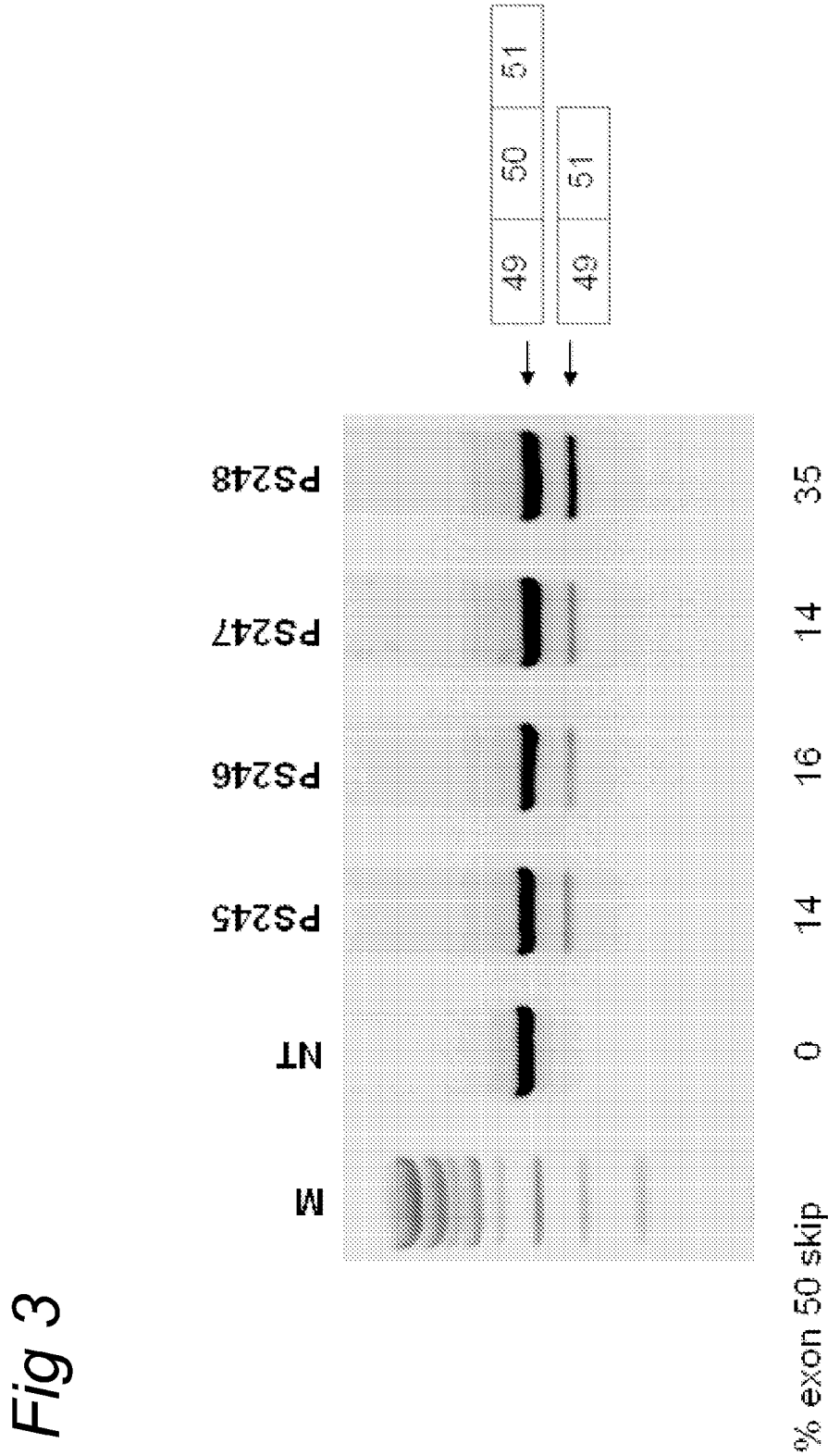
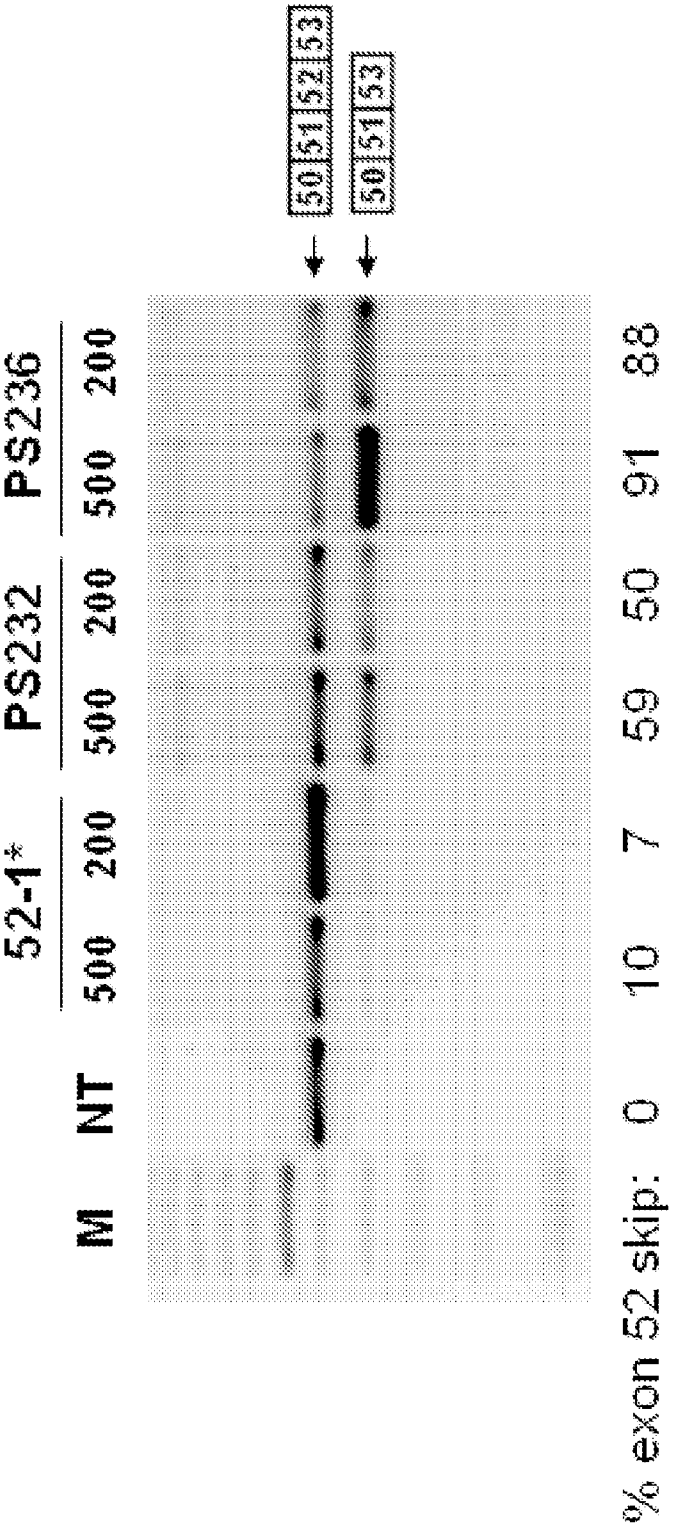

49
50
51
49
51
M
NT
PS245
PS246
PS247
PS248
0
14
16
14
35
% exon 50 skip

Fig 3

Fig 4


M
NT
52-1*
500
200
PS232
500
200
PS236
500
200
50 51 52 53
50 51 53
% exon 52 skip: 0 10 7 59 50 91 88

METHODS AND MEANS FOR EFFICIENT SKIPPING OF AT LEAST ONE OF THE FOLLOWING EXONS OF THE HUMAN DUCHENNE MUSCULAR DYSTROPHY GENE: 43, 46, 50-53

[0001] This U.S. patent application is a continuation of PCT/NL2009/050113, filed on Mar. 11, 2009 which claims priority to PCT/NL2008/050673, filed on Oct. 27, 2008, which claims priority to European application no. 07119351.0, filed on Oct. 26, 2007, which claims the benefit of U.S. provisional patent application No. 61/000,670, filed on Oct. 26, 2007, the entirety of which is incorporated herein by reference. The invention relates to the field of genetics, more specifically human genetics. The invention in particular relates to modulation of splicing of the human Duchenne Muscular Dystrophy pre-mRNA.

BACKGROUND OF THE INVENTION

Field

[0002] Myopathies are disorders that result in functional impairment of muscles. Muscular dystrophy (MD) refers to genetic diseases that are characterized by progressive weakness and degeneration of skeletal muscles. Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are the most common childhood forms of muscular dystrophy. They are recessive disorders and because the gene responsible for DMD and BMD resides on the X-chromosome, mutations mainly affect males with an incidence of about 1 in 3500 boys.

[0003] DMD and BMD are caused by genetic defects in the DMD gene encoding dystrophin, a muscle protein that is required for interactions between the cytoskeleton and the extracellular matrix to maintain muscle fiber stability during contraction. DMD is a severe, lethal neuromuscular disorder resulting in a dependency on wheelchair support before the age of 12 and DMD patients often die before the age of thirty due to respiratory- or heart failure. In contrast, BMD patients often remain ambulatory until later in life, and have near normal life expectancies. DMD mutations in the DMD gene are characterized by frame shifting insertions or deletions or nonsense point mutations, resulting in the absence of functional dystrophin. BMD mutations in general keep the reading frame intact, allowing synthesis of a partly functional dystrophin.

[0004] During the last decade, specific modification of splicing in order to restore the disrupted reading frame of the dystrophin transcript has emerged as a promising therapy for Duchenne muscular dystrophy (DMD) (van Ommen, van Deutekom, Aartsma-Rus, Curr Opin Mol. Ther. 2008; 10(2): 140-9, Yokota, Duddy, Partidge, Acta Myol. 2007; 26(3):179-84, van Deutekom et al., N Engl J. Med. 2007; 357(26):2677-86).

[0005] Using antisense oligonucleotides (AONs) interfering with splicing signals the skipping of specific exons can be induced in the DMD pre-mRNA, thus restoring the open reading frame and converting the severe DMD into a milder BMD phenotype (van Deutekom et al. Hum Mol. Genet. 2001; 10: 1547-54; Aartsma-Rus et al., Hum Mol Genet. 2003; 12(8):907-14.). In vivo proof-of-concept was first obtained in the mdx mouse model, which is dystrophin-deficient due to a nonsense mutation in exon 23. Intramuscular and intravenous injections of AONs targeting the mutated exon 23 restored dystrophin expression for at least three months (Lu et al. Nat. Med. 2003; 8: 1009-14; Lu et al., Proc Natl Acad Sci USA. 2005; 102(1):198-203). This was accompanied by restoration of dystrophin-associated proteins at the fiber membrane as well as functional improvement of the treated muscle. In vivo skipping of human exons has also been achieved in the hDMD mouse model, which contains a complete copy of the human DMD gene integrated in chromosome 5 of the mouse (Bremmer-Bout et al. Molecular Therapy. 2004; 10: 232-40; 't Hoen et al. J Biol. Chem. 2008; 283: 5899-907).

[0006] Recently, a first-in-man study was successfully completed where an AON inducing the skipping of exon 51 was injected into a small area of the tibialis anterior muscle of four DMD patients. Novel dystrophin expression was observed in the majority of muscle fibers in all four patients treated, and the AON was safe and well tolerated (van Deutekom et al. N Engl J. Med. 2007; 357: 2677-86).

DESCRIPTION OF THE INVENTION

Method

[0007] In a first aspect, the present invention provides a method for inducing, and/or promoting skipping of at least one of exons 43, 46, 50-53 of the DMD pre-mRNA in a patient, preferably in an isolated cell of a patient, the method comprising providing said cell and/or said patient with a molecule that binds to a continuous stretch of at least 8 nucleotides within said exon. It is to be understood that said method encompasses an in vitro, in vivo or ex vivo method.

[0008] Accordingly, a method is provided for inducing and/or promoting skipping of at least one of exons 43, 46, 50-53 of DMD pre-mRNA in a patient, preferably in an isolated cell of said patient, the method comprising providing said cell and/or said patient with a molecule that binds to a continuous stretch of at least 8 nucleotides within said exon.

[0009] As defined herein a DMD pre-mRNA preferably means the pre-mRNA of a DMD gene of a DMD or BMD patient.

[0010] A patient is preferably intended to mean a patient having DMD or BMD as later defined herein or a patient susceptible to develop DMD or BMD due to his or her genetic background. In the case of a DMD patient, an oligonucleotide used will preferably correct one mutation as present in the DMD gene of said patient and therefore will preferably create a DMD protein that will look like a BMD protein: said protein will preferably be a functional dystrophin as later defined herein. In the case of a BMD patient, an oligonucleotide as used will preferably correct one mutation as present in the BMD gene of said patient and therefore will preferably create a dystrophin which will be more functional than the dystrophin which was originally present in said BMD patient.

[0011] Exon skipping refers to the induction in a cell of a mature mRNA that does not contain a particular exon that is normally present therein. Exon skipping is performed by providing a cell expressing the pre-mRNA of said mRNA with a molecule capable of interfering with essential sequences such as for example the splice donor of splice acceptor sequence that required for splicing of said exon, or a molecule that is capable of interfering with an exon inclusion signal that is required for recognition of a stretch of nucleotides as an exon to be included in the mRNA. The term

pre-mRNA refers to a non-processed or partly processed precursor mRNA that is synthesized from a DNA template in the cell nucleus by transcription.

[0012] Within the context of the invention, inducing and/or promoting skipping of an exon as indicated herein means that at least 1%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more of the DMD mRNA in one or more (muscle) cells of a treated patient will not contain said exon. This is preferably assessed by PCR as described in the examples.

[0013] Preferably, a method of the invention by inducing and/or promoting skipping of at least one of the following exons 43, 46, 50-53 of the DMD pre-mRNA in one or more (muscle) cells of a patient, provides said patient with a functional dystrophin protein and/or decreases the production of an aberrant dystrophin protein in said patient and/or increases the production of a functional dystrophin is said patient.

[0014] Providing a patient with a functional dystrophin protein and/or decreasing the production of an aberrant dystrophin protein in said patient is typically applied in a DMD patient. Increasing the production of a functional dystrophin is typically applied in a BMD patient.

[0015] Therefore a preferred method is a method, wherein a patient or one or more cells of said patient is provided with a functional dystrophin protein and/or wherein the production of an aberrant dystrophin protein in said patient is decreased and/or wherein the production of a functional dystrophin is increased in said patient, wherein the level of said aberrant or functional dystrophin is assessed by comparison to the level of said dystrophin in said patient at the onset of the method.

[0016] Decreasing the production of an aberrant dystrophin may be assessed at the mRNA level and preferably means that 99%, 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10%, 5% or less of the initial amount of aberrant dystrophin mRNA, is still detectable by RT PCR. An aberrant dystrophin mRNA or protein is also referred to herein as a non-functional dystrophin mRNA or protein. A non functional dystrophin protein is preferably a dystrophin protein which is not able to bind actin and/or members of the DGC protein complex. A non-functional dystrophin protein or dystrophin mRNA does typically not have, or does not encode a dystrophin protein with an intact C-terminus of the protein.

[0017] Increasing the production of a functional dystrophin in said patient or in a cell of said patient may be assessed at the mRNA level (by RT-PCR analysis) and preferably means that a detectable amount of a functional dystrophin mRNA is detectable by RT PCR. In another embodiment, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more of the detectable dystrophin mRNA is a functional dystrophin mRNA.

[0018] Increasing the production of a functional dystrophin in said patient or in a cell of said patient may be assessed at the protein level (by immuno fluorescence and western blot analyses) and preferably means that a detectable amount of a functional dystrophin protein is detectable by immunofluorescence or western blot analysis. In another embodiment, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more of the detectable dystrophin protein is a functional dystrophin protein.

[0019] As defined herein, a functional dystrophin is preferably a wild type dystrophin corresponding to a protein having the amino acid sequence as identified in SEQ ID NO: 1. A functional dystrophin is preferably a dystrophin, which has an actin binding domain in its N terminal part (first 240 amino acids at the N terminus), a cystein-rich domain (amino acid 3361 till 3685) and a C terminal domain (last 325 amino acids at the C terminus) each of these domains being present in a wild type dystrophin as known to the skilled person. The amino acids indicated herein correspond to amino acids of the wild type dystrophin being represented by SEQ ID NO:1. In other words, a functional dystrophin is a dystrophin which exhibits at least to some extent an activity of a wild type dystrophin. "At least to some extent" preferably means at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 100% of a corresponding activity of a wild type functional dystrophin. In this context, an activity of a functional dystrophin is preferably binding to actin and to the dystrophin-associated glycoprotein complex (DGC) (Aartsma-Rus A et al, (2006), Entries in the leiden Duchenne Muscular Dystrophy mutation database: an overview of mutation types and paradoxical cases that confirm the reading-frame rule, Muscle Nerve, 34: 135-144). Binding of dystrophin to actin and to the DGC complex may be visualized by either co-immunoprecipitation using total protein extracts or immuno fluorescence analysis of cross-sections, from a muscle biopsy, as known to the skilled person.

[0020] Individuals or patients suffering from Duchenne muscular dystrophy typically have a mutation in the gene encoding dystrophin that prevent synthesis of the complete protein, i.e of a premature stop prevents the synthesis of the C-terminus. In Becker muscular dystrophy the DMD gene also comprises a mutation compared tot the wild type gene but the mutation does typically not induce a premature stop and the C-terminus is typically synthesized. As a result a functional dystrophin protein is synthesized that has at least the same activity in kind as the wild type protein, not although not necessarily the same amount of activity. The genome of a BMD individual typically encodes a dystrophin protein comprising the N terminal part (first 240 amino acids at the N terminus), a cystein-rich domain (amino acid 3361 till 3685) and a C terminal domain (last 325 amino acids at the C terminus) but its central rod shaped domain may be shorter than the one of a wild type dystrophin (Aartsma-Rus A et al, (2006), Entries in the leiden Duchenne Muscular Dystrophy mutation database: an overview of mutation types and paradoxical cases that confirm the reading-frame rule, Muscle Nerve, 34: 135-144). Exon skipping for the treatment of DMD is typically directed to overcome a premature stop in the pre-mRNA by skipping an exon in the rod-shaped domain to correct the reading frame and allow synthesis of remainder of the dystrophin protein including the C-terminus, albeit that the protein is somewhat smaller as a result of a smaller rod domain. In a preferred embodiment, an individual having DMD and being treated by a method as defined herein will be provided a dystrophin which exhibits at least to some extent an activity of a wild type dystrophin. More preferably, if said individual is a Duchenne patient or is suspected to be a Duchenne patient, a functional dystrophin is a dystrophin of an individual having BMD: typically said dystrophin is able to interact with both actin and the DGC, but its central rod shaped domain may be shorter than the one of a wild type dystrophin (Aartsma-Rus A et al, (2006), Entries in the leiden Duchenne Muscular Dystrophy mutation database: an overview of mutation types and paradoxical cases that confirm the reading-frame rule, Muscle Nerve, 34: 135-144). The central rod-shaped domain of wild type dystrophin comprises 24 spectrin-like repeats (Aartsma-Rus A et al, (2006), Entries in the leiden Duchenne Muscular Dystrophy mutation database: an overview of mutation types and paradoxical cases that

confirm the reading-frame rule, Muscle Nerve, 34: 135-144). For example, a central rod-shaped domain of a dystrophin as provided herein may comprise 5 to 23, 10 to 22 or 12 to 18 spectrin-like repeats as long as it can bind to actin and to DGC.

[0021] A method of the invention may alleviate one or more characteristics of a myogenic or muscle cell of a patient or alleviate one or more symptoms of a DMD patient having a deletion including but not limited to exons 44, 44-46, 44-47, 44-48, 44-49, 44-51, 44-53 (correctable by exon 43 skipping), 19-45, 21-45, 43-45, 45, 47-54, 47-56 (correctable by exon 46 skipping), 51, 51-53, 51-55, 51-57 (correctable by exon 50 skipping), 13-50, 19-50, 29-50, 43-50, 45-50, 47-50, 48-50, 49-50, 50, 52 (correctable by exon 51 skipping), exons 8-51, 51, 53, 53-55, 53-57, 53-59, 53-60, (correctable by exon 52 skipping) and exons 10-52, 42-52, 43-52, 45-52, 47-52, 48-52, 49-52, 50-52, 52 (correctable by exon 53 skipping) in the DMD gene, occurring in a total of 68% of all DMD patients with a deletion (Aartsma-Rus et al., Hum. Mut. 2009).

[0022] Alternatively, a method of the invention may improve one or more characteristics of a muscle cell of a patient or alleviate one or more symptoms of a DMD patient having small mutations in, or single exon duplications of exon 43, 46, 50-53 in the DMD gene, occurring in a total of 36% of all DMD patients with a deletion (Aartsma-Rus et al, Hum. Mut. 2009)

[0023] Furthermore, for some patients the simultaneous skipping of one of more exons in addition to exon 43, exon 46 and/or exon 50-53 is required to restore the open reading frame, including patients with specific deletions, small (point) mutations, or double or multiple exon duplications, such as (but not limited to) a deletion of exons 44-50 requiring the co-skipping of exons 43 and 51, with a deletion of exons 46-50 requiring the co-skipping of exons 45 and 51, with a deletion of exons 44-52 requiring the co-skipping of exons 43 and 53, with a deletion of exons 46-52 requiring the co-skipping of exons 45 and 53, with a deletion of exons 51-54 requiring the co-skipping of exons 50 and 55, with a deletion of exons 53-54 requiring the co-skipping of exons 52 and 55, with a deletion of exons 53-56 requiring the co-skipping of exons 52 and 57, with a nonsense mutation in exon 43 or exon 44 requiring the co-skipping of exon 43 and 44, with a nonsense mutation in exon 45 or exon 46 requiring the co-skipping of exon 45 and 46, with a nonsense mutation in exon 50 or exon 51 requiring the co-skipping of exon 50 and 51, with a nonsense mutation in exon 51 or exon 52 requiring the co-skipping of exon 51 and 52, with a nonsense mutation in exon 52 or exon 53 requiring the co-skipping of exon 52 and 53, or with a double or multiple exon duplication involving exons 43, 46, 50, 51, 52, and/or 53.

[0024] In a preferred method, the skipping of exon 43 is induced, or the skipping of exon 46 is induced, or the skipping of exon 50 is induced or the skipping of exon 51 is induced or the skipping of exon 52 is induced or the skipping of exon 53 is induced. An induction of the skipping of two of these exons is also encompassed by a method of the invention. For example, preferably skipping of exons 50 and 51, or 52 and 53, or 43 and 51, or 43 and 53, or 51 and 52. Depending on the type and the identity (the specific exons involved) of mutation identified in a patient, the skilled person will know which combination of exons needs to be skipped in said patient.

[0025] In a preferred method, one or more symptom(s) of a DMD or a BMD patient is/are alleviated and/or one or more characteristic(s) of one or more muscle cells from a DMD or a BMD patient is/are improved. Such symptoms or characteristics may be assessed at the cellular, tissue level or on the patient self.

[0026] An alleviation of one or more characteristics may be assessed by any of the following assays on a myogenic cell or muscle cell from a patient: reduced calcium uptake by muscle cells, decreased collagen synthesis, altered morphology, altered lipid biosynthesis, decreased oxidative stress, and/or improved muscle fiber function, integrity, and/or survival. These parameters are usually assessed using immunofluorescence and/or histochemical analyses of cross sections of muscle biopsies.

[0027] The improvement of muscle fiber function, integrity and/or survival may be assessed using at least one of the following assays: a detectable decrease of creatine kinase in blood, a detectable decrease of necrosis of muscle fibers in a biopsy cross-section of a muscle suspected to be dystrophic, and/or a detectable increase of the homogeneity of the diameter of muscle fibers in a biopsy cross-section of a muscle suspected to be dystrophic. Each of these assays is known to the skilled person.

[0028] Creatine kinase may be detected in blood as described in Hodgetts et al (Hodgetts S., et al, (2006), Neuromuscular Disorders, 16: 591-602.2006). A detectable decrease in creatine kinase may mean a decrease of 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more compared to the concentration of creatine kinase in a same DMD or BMD patient before treatment.

[0029] A detectable decrease of necrosis of muscle fibers is preferably assessed in a muscle biopsy, more preferably as described in Hodgetts et al (Hodgetts S., et al, (2006), Neuromuscular Disorders, 16: 591-602.2006) using biopsy cross-sections. A detectable decrease of necrosis may be a decrease of 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more of the area wherein necrosis has been identified using biopsy cross-sections. The decrease is measured by comparison to the necrosis as assessed in a same DMD or BMD patient before treatment.

[0030] A detectable increase of the homogeneity of the diameter of a muscle fiber is preferably assessed in a muscle biopsy cross-section, more preferably as described in Hodgetts et al (Hodgetts S., et al, (2006), Neuromuscular Disorders, 16: 591-602.2006). The increase is measured by comparison to the homogeneity of the diameter of a muscle fiber in a same DMD or BMD patient before treatment

[0031] An alleviation of one or more symptoms may be assessed by any of the following assays on the patient self: prolongation of time to loss of walking, improvement of muscle strength, improvement of the ability to lift weight, improvement of the time taken to rise from the floor, improvement in the nine-meter walking time, improvement in the time taken for four-stairs climbing, improvement of the leg function grade, improvement of the pulmonary function, improvement of cardiac function, improvement of the quality of life. Each of these assays is known to the skilled person. As an example, the publication of Manzur at al (Manzur A Y et al, (2008), Glucocorticoid corticosteroids for Duchenne muscular dystrophy (review), Wiley publishers, The Cochrane collaboration.) gives an extensive explanation of each of these assays. For each of these assays, as soon as a detectable improvement or prolongation of a parameter measured in an assay has been found, it will preferably mean that one or more symptoms of Duchenne Muscular Dystrophy or Becker Mus-

cular Dystrophy has been alleviated in an individual using a method of the invention. Detectable improvement or prolongation is preferably a statistically significant improvement or prolongation as described in Hodgetts et al (Hodgetts S., et al, (2006), Neuromuscular Disorders, 16: 591-602.2006). Alternatively, the alleviation of one or more symptom(s) of Duchenne Muscular Dystrophy or Becker Muscular Dystrophy may be assessed by measuring an improvement of a muscle fiber function, integrity and/or survival as later defined herein.

[0032] A treatment in a method according to the invention may have a duration of at least one week, at least one month, at least several months, at least one year, at least 2, 3, 4, 5, 6 years or more.

[0033] Each molecule or oligonucleotide or equivalent thereof as defined herein for use according to the invention may be suitable for direct administration to a cell, tissue and/or an organ in vivo of individuals affected by or at risk of developing DMD or BMD, and may be administered directly in vivo, ex vivo or in vitro. The frequency of administration of a molecule or an oligonucleotide or a composition of the invention may depend on several parameters such as the age of the patient, the mutation of the patient, the number of molecules (dose), the formulation of said molecule. The frequency may be ranged between at least once in a two weeks, or three weeks or four weeks or five weeks or a longer time period.

[0034] A molecule or oligonucleotide or equivalent thereof can be delivered as is to a cell. When administering said molecule, oligonucleotide or equivalent thereof to an individual, it is preferred that it is dissolved in a solution that is compatible with the delivery method. For intravenous, subcutaneous, intramuscular, intrathecal and/or intraventricular administration it is preferred that the solution is a physiological salt solution. Particularly preferred for a method of the invention is the use of an excipient that will further enhance delivery of said molecule, oligonucleotide or functional equivalent thereof as defined herein, to a cell and into a cell, preferably a muscle cell. Preferred excipient are defined in the section entitled "pharmaceutical composition".

[0035] In a preferred method of the invention, an additional molecule is used which is able to induce and/or promote skipping of another exon of the DMD pre-mRNA of a patient. Preferably, the second exon is selected from: exon 6, 7, 11, 17, 19, 21, 43, 44, 45, 50, 51, 52, 53, 55, 57, 59, 62, 63, 65, 66, 69, or 75 of the DMD pre-mRNA of a patient. Molecules which can be used are depicted in any one of Table 1 to 7. This way, inclusion of two or more exons of a DMD pre-mRNA in mRNA produced from this pre-mRNA is prevented. This embodiment is further referred to as double- or multi-exon skipping (Aartsma-Rus A, Janson A A, Kaman W E, et al. Antisense-induced multiexon skipping for Duchenne muscular dystrophy makes more sense. Am J Hum Genet. 2004; 74(1):83-92, Aartsma-Rus A, Kaman W E, Weij R, den Dunnen J T, van Ommen G J, van Deutekom J C. Exploring the frontiers of therapeutic exon skipping for Duchenne muscular dystrophy by double targeting within one or multiple exons. Mol Ther 2006; 14(3):401-7). In most cases double-exon skipping results in the exclusion of only the two targeted exons from the DMD pre-mRNA. However, in other cases it was found that the targeted exons and the entire region in between said exons in said pre-mRNA were not present in the produced mRNA even when other exons (intervening exons) were present in such region. This multi-skipping was notably so for the combination of oligonucleotides derived from the DMD gene, wherein one oligonucleotide for exon 45 and one oligonucleotide for exon 51 was added to a cell transcribing the DMD gene. Such a set-up resulted in mRNA being produced that did not contain exons 45 to 51. Apparently, the structure of the pre-mRNA in the presence of the mentioned oligonucleotides was such that the splicing machinery was stimulated to connect exons 44 and 52 to each other.

[0036] It is possible to specifically promote the skipping of also the intervening exons by providing a linkage between the two complementary oligonucleotides. Hence, in one embodiment stretches of nucleotides complementary to at least two dystrophin exons are separated by a linking moiety. The at least two stretches of nucleotides are thus linked in this embodiment so as to form a single molecule.

[0037] In case, more than one compounds or molecules are used in a method of the invention, said compounds can be administered to an individual in any order. In one embodiment, said compounds are administered simultaneously (meaning that said compounds are administered within 10 hours, preferably within one hour). This is however not necessary. In another embodiment, said compounds are administered sequentially.

Molecule

[0038] In a second aspect, there is provided a molecule for use in a method as described in the previous section entitled "Method". A molecule as defined herein is preferably an oligonucleotide or antisense oligonucleotide (AON).

[0039] It was found by the present investigators that any of exon 43, 46, 50-53 is specifically skipped at a high frequency using a molecule that preferably binds to a continuous stretch of at least 8 nucleotides within said exon. Although this effect can be associated with a higher binding affinity of said molecule, compared to a molecule that binds to a continuous stretch of less than 8 nucleotides, there could be other intracellular parameters involved that favor thermodynamic, kinetic, or structural characteristics of the hybrid duplex. In a preferred embodiment, a molecule that binds to a continuous stretch of at least 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 nucleotides within said exon is used.

[0040] In a preferred embodiment, a molecule or an oligonucleotide of the invention which comprises a sequence that is complementary to a part of any of exon 43, 46, 50-53 of DMD pre-mRNA is such that the complementary part is at least 50% of the length of the oligonucleotide of the invention, more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80%, even more preferably at least 90% or even more preferably at least 95%, or even more preferably 98% and most preferably up to 100%. "A part of said exon" preferably means a stretch of at least 8 nucleotides. In a most preferred embodiment, an oligonucleotide of the invention consists of a sequence that is complementary to part of said exon DMD pre-mRNA as defined herein. For example, an oligonucleotide may comprise a sequence that is complementary to part of said exon DMD pre-mRNA as defined herein and additional flanking sequences. In a more preferred embodiment, the length of said complementary part of said oligonucleotide is of at least 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 nucleotides. Preferably,

additional flanking sequences are used to modify the binding of a protein to said molecule or oligonucleotide, or to modify a thermodynamic property of the oligonucleotide, more preferably to modify target RNA binding affinity.

[0041] A preferred molecule to be used in a method of the invention binds or is complementary to a continuous stretch of at least 8 nucleotides within one of the following nucleotide sequences selected from:

(SEQ ID NO: 2)
5'-AGAUAGUCUACAACAAAGCUCAGGUCGGAUUGACAUUAUUCAUAG

CAAGAAGACAGCAGCAUUGCAAAGUGCAACGCCUGUGG-3'
for skipping of exon 43;

(SEQ ID NO: 3)
5'-UUAUGGUUGGAGGAAGCAGAUAACAUUGCUAGUAUCCCACUUGAA

CCUGGAAAAGAGCAGCAACUAAAAGAAAAGC-3'
for skipping of exon 46;

(SEQ ID NO: 4)
5'-GGCGGTAAACCGUUUACUUCAAGAGCUGAGGGCAAAGCAGCCUGA

CCUAGC UCCUGGACUGACCACUAUUGG-3'
for skipping of exon 50;

(SEQ ID NO: 5)
5'-CUCCUACUCAGACUGUUACUCUGGUGACACAACCUGUGGUUACUA

AGGAAACUGCCAUC UCCAAACUAGAAAUGCCAUCUUCCUUGAUGUUG

GAGGUAC-3'
for skipping of exon 51;

(SEQ ID NO: 6)
5'-AUGCAGGAUUUGGAACAGAGGCGUCCCCAGUUGGAAGAACUCAUU

ACCGCUGCCCAAAAUUUGAAAAACAAGACCAGCAAUCAAGAGGCU-3'
for skipping of exon 52,
and

(SEQ ID NO: 7)
5'-AAAUGUUAAAGGAUUCAACACAAUGGCUGGAAGCUAAGGAAGAAG

CUGAGCAGGUCUUAGGACAGGCCAGAG-3'
for skipping of exon 53.

[0042] Of the numerous molecules that theoretically can be prepared to bind to the continuous nucleotide stretches as defined by SEQ ID NO 2-7 within one of said exons, the invention provides distinct molecules that can be used in a method for efficiently skipping of at least one of exon 43, exon 46 and/or exon 50-53. Although the skipping effect can be addressed to the relatively high density of putative SR protein binding sites within said stretches, there could be other parameters involved that favor uptake of the molecule or other, intracellular parameters such as thermodynamic, kinetic, or structural characteristics of the hybrid duplex.

[0043] It was found that a molecule that binds to a continuous stretch comprised within or consisting of any of SEQ ID NO 2-7 results in highly efficient skipping of exon 43, exon 46 and/or exon 50-53 respectively in a cell and/or in a patient provided with this molecule. Therefore, in a preferred embodiment, a method is provided wherein a molecule binds to a continuous stretch of at least 8, 10, 12, 15, 18, 20, 25, 30, 35, 40, 45, 50 nucleotides within SEQ ID NO 2-7.

[0044] In a preferred embodiment for inducing and/or promoting the skipping of any of exon 43, exon 46 and/or exon 50-53, the invention provides a molecule comprising or consisting of an antisense nucleotide sequence selected from the antisense nucleotide sequences depicted in any of Tables 1 to 6. A molecule of the invention preferably comprises or consist of the antisense nucleotide sequence of SEQ ID NO 16, SEQ ID NO 65, SEQ ID NO 70, SEQ ID NO 91, SEQ ID NO 110, SEQ ID NO 117, SEQ ID NO 127, SEQ ID NO 165, SEQ ID NO 166, SEQ ID NO 167, SEQ ID NO 246, SEQ ID NO 299, SEQ ID NO:357.

[0045] A preferred molecule of the invention comprises a nucleotide-based or nucleotide or an antisense oligonucleotide sequence of between 8 and 50 nucleotides or bases, more preferred between 10 and 50 nucleotides, more preferred between 20 and 40 nucleotides, more preferred between 20 and 30 nucleotides, such as 20 nucleotides, 21 nucleotides, 22 nucleotides, 23 nucleotides, 24 nucleotides, 25 nucleotides, 26 nucleotides, 27 nucleotides, 28 nucleotides, 29 nucleotides, 30 nucleotides, 31 nucleotides, 32 nucleotides, 33 nucleotides, 34 nucleotides, 35 nucleotides, 36 nucleotides, 37 nucleotides, 38 nucleotides, 39 nucleotides, 40 nucleotides, 41 nucleotides, 42 nucleotides, 43 nucleotides, 44 nucleotides, 45 nucleotides, 46 nucleotides, 47 nucleotides, 48 nucleotides, 49 nucleotides or 50 nucleotides.

[0046] A most preferred molecule of the invention comprises a nucleotide-based sequence of 25 nucleotides.

[0047] Furthermore, none of the indicated sequences is derived from conserved parts of splice-junction sites. Therefore, said molecule is not likely to mediate differential splicing of other exons from the DMD pre-mRNA or exons from other genes.

[0048] In one embodiment, a molecule of the invention is a compound molecule that binds to the specified sequence, or a protein such as an RNA-binding protein or a non-natural zinc-finger protein that has been modified to be able to bind to the corresponding nucleotide sequence on a DMD pre-RNA molecule. Methods for screening compound molecules that bind specific nucleotide sequences are, for example, disclosed in PCT/NL01/00697 and U.S. Pat. No. 6,875,736, which are herein incorporated by reference. Methods for designing RNA-binding Zinc-finger proteins that bind specific nucleotide sequences are disclosed by Friesen and Darby, Nature Structural Biology 5: 543-546 (1998) which is herein incorporated by reference.

[0049] A preferred molecule of the invention binds to at least part of the sequence of SEQ ID NO 2: 5'-AGAUAGUCUACAACAAAGCUCAGGUCGGAUUGACAUUAUUCAU AGCAAGAAGACAGCAGCAUUGCAAAGUGCAACGCCUGUGG-3' which is present in exon 43 of the DMD gene. More preferably, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 8 to SEQ ID NO 69.

[0050] In an even more preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 16 and/or SEQ ID NO 65.

[0051] In a most preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 65. It was found that this molecule is very efficient in modulating splicing of exon 43 of the DMD pre-mRNA in a muscle cell and/or in a patient.

[0052] Another preferred molecule of the invention binds to at least part of the sequence of SEQ ID NO 3: 5'-UUAUGGUUGGAGGAAGCAGAUAACAUUGCUAGUAUCCCACUUG AACCUGGAAAAGAGCAGCAACUAAAAGAAAAGC-3' which is present in exon 46 of

the DMD gene. More preferably, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 70 to SEQ ID NO 122. In an even more preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 70, SEQ ID NO 91, SEQ ID NO 110, and/or SEQ ID NO 117.

[0053] In a most preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 117. It was found that this molecule is very efficient in modulating splicing of exon 46 of the DMD pre-mRNA in a muscle cell or in a patient.

[0054] Another preferred molecule of the invention binds to at least part of the sequence of SEQ ID NO 4: 5'-GGCGGTAAACCGUUUACUUCAAGAGCU GAGGGCAAAGCAGCCUG ACCUAGCUCCUGGACUGACCACUAUUGG-3' which is present in exon 50 of the DMD gene. More preferably, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 123 to SEQ ID NO 167 and/or SEQ ID NO 529 to SEQ ID NO 535.

[0055] In an even more preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 127, or SEQ ID NO 165, or SEQ ID NO 166 and/or SEQ ID NO 167.

[0056] In a most preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 127. It was found that this molecule is very efficient in modulating splicing of exon 50 of the DMD pre-mRNA in a muscle cell and/or in a patient.

[0057] Another preferred molecule of the invention binds to at least part of the sequence of SEQ ID NO 5: 5'-CUCCUACUCAGACUGUUACUCUGGUGACACAACCUGUGGUUACU AAGGAAACUGCCAUC UCCAAACUAGAAAUGCCAUCUUCCUUGAUG UUGGAGGUAC-3' which is present in exon 51 of the DMD gene. More preferably, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 168 to SEQ ID NO 241.

[0058] Another preferred molecule of the invention binds to at least part of the sequence of SEQ ID NO 6: 5'-AUGCAGGAUUUGGAACAGAGGCGUCCCCAGUUGGAAGAACUCAU UACCGCUGCCCAAAAUUUGAAAAACAAGACCAGCAAUCAAGAGGCU-3' which is present in exon 52 of the DMD gene. More preferably, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 242 to SEQ ID NO 310. In an even more preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 246 and/or SEQ ID NO 299. In a most preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 299. It was found that this molecule is very efficient in modulating splicing of exon 52 of the DMD pre-mRNA in a muscle cell and/or in a patient.

[0059] Another preferred molecule of the invention binds to at least part of the sequence of SEQ ID NO 7: 5'-AAAUGUUAAAGGAUUCAACACAAUGGCUGGAAGCUAAGGAAGAA GCUGAGCAGGUCUUAGGACAGGCCAGAG-3' which is present in exon 53 of the DMD gene. More preferably, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 311 to SEQ ID NO 358.

[0060] In a most preferred embodiment, the invention provides a molecule comprising or consisting of the antisense nucleotide sequence of SEQ ID NO 357. It was found that this molecule is very efficient in modulating splicing of exon 53 of the DMD pre-mRNA in a muscle cell and/or in a patient.

[0061] A nucleotide sequence of a molecule of the invention may contain RNA residues, or one or more DNA residues, and/or one or more nucleotide analogues or equivalents, as will be further detailed herein below.

[0062] It is preferred that a molecule of the invention comprises one or more residues that are modified to increase nuclease resistance, and/or to increase the affinity of the antisense nucleotide for the target sequence. Therefore, in a preferred embodiment, the antisense nucleotide sequence comprises at least one nucleotide analogue or equivalent, wherein a nucleotide analogue or equivalent is defined as a residue having a modified base, and/or a modified backbone, and/or a non-natural internucleoside linkage, or a combination of these modifications.

[0063] In a preferred embodiment, the nucleotide analogue or equivalent comprises a modified backbone. Examples of such backbones are provided by morpholino backbones, carbamate backbones, siloxane backbones, sulfide, sulfoxide and sulfone backbones, formacetyl and thioformacetyl backbones, methyleneformacetyl backbones, riboacetyl backbones, alkene containing backbones, sulfamate, sulfonate and sulfonamide backbones, methyleneimino and methylenehydrazino backbones, and amide backbones. Phosphorodiamidate morpholino oligomers are modified backbone oligonucleotides that have previously been investigated as antisense agents. Morpholino oligonucleotides have an uncharged backbone in which the deoxyribose sugar of DNA is replaced by a six membered ring and the phosphodiester linkage is replaced by a phosphorodiamidate linkage. Morpholino oligonucleotides are resistant to enzymatic degradation and appear to function as antisense agents by arresting translation or interfering with pre-mRNA splicing rather than by activating RNase H. Morpholino oligonucleotides have been successfully delivered to tissue culture cells by methods that physically disrupt the cell membrane, and one study comparing several of these methods found that scrape loading was the most efficient method of delivery; however, because the morpholino backbone is uncharged, cationic lipids are not effective mediators of morpholino oligonucleotide uptake in cells. A recent report demonstrated triplex formation by a morpholino oligonucleotide and, because of the non-ionic backbone, these studies showed that the morpholino oligonucleotide was capable of triplex formation in the absence of magnesium.

[0064] It is further preferred that that the linkage between the residues in a backbone do not include a phosphorus atom, such as a linkage that is formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages.

[0065] A preferred nucleotide analogue or equivalent comprises a Peptide Nucleic Acid (PNA), having a modified polyamide backbone (Nielsen, et al. (1991) Science 254, 1497-1500). PNA-based molecules are true mimics of DNA molecules in terms of base-pair recognition. The backbone of the PNA is composed of N-(2-aminoethyl)-glycine units linked by peptide bonds, wherein the nucleobases are linked to the backbone by methylene carbonyl bonds. An alternative

backbone comprises a one-carbon extended pyrrolidine PNA monomer (Govindaraju and Kumar (2005) Chem. Commun, 495-497). Since the backbone of a PNA molecule contains no charged phosphate groups, PNA-RNA hybrids are usually more stable than RNA-RNA or RNA-DNA hybrids, respectively (Egholm et al (1993) Nature 365, 566-568).

[0066] A further preferred backbone comprises a morpholino nucleotide analog or equivalent, in which the ribose or deoxyribose sugar is replaced by a 6-membered morpholino ring. A most preferred nucleotide analog or equivalent comprises a phosphorodiamidate morpholino oligomer (PMO), in which the ribose or deoxyribose sugar is replaced by a 6-membered morpholino ring, and the anionic phosphodiester linkage between adjacent morpholino rings is replaced by a non-ionic phosphorodiamidate linkage.

[0067] In yet a further embodiment, a nucleotide analogue or equivalent of the invention comprises a substitution of one of the non-bridging oxygens in the phosphodiester linkage. This modification slightly destabilizes base-pairing but adds significant resistance to nuclease degradation. A preferred nucleotide analogue or equivalent comprises phosphorothioate, chiral phosphorothioate, phosphorodithioate, phosphotriester, aminoalkylphosphotriester, H-phosphonate, methyl and other alkyl phosphonate including 3'-alkylene phosphonate, 5'-alkylene phosphonate and chiral phosphonate, phosphinate, phosphoramidate including 3'-amino phosphoramidate and aminoalkylphosphoramidate, thionophosphoramidate, thionoalkylphosphonate, thionoalkylphosphotriester, selenophosphate or boranophosphate.

[0068] A further preferred nucleotide analogue or equivalent of the invention comprises one or more sugar moieties that are mono- or disubstituted at the 2', 3' and/or 5' position such as a —OH; —F; substituted or unsubstituted, linear or branched lower (C1-C10) alkyl, alkenyl, alkynyl, alkaryl, allyl, aryl, or aralkyl, that may be interrupted by one or more heteroatoms; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; O-, S- or N-alkynyl; O-, S-, or N-allyl; O-alkyl-O-alkyl, -methoxy, -aminopropoxy; -aminoxy; methoxyethoxy; -dimethylaminooxyethoxy; and -dimethylaminoethoxyethoxy. The sugar moiety can be a pyranose or derivative thereof, or a deoxypyranose or derivative thereof, preferably a ribose or a derivative thereof, or a deoxyribose or a derivative thereof. Such preferred derivatized sugar moieties comprise Locked Nucleic Acid (LNA), in which the 2'-carbon atom is linked to the 3' or 4' carbon atom of the sugar ring thereby forming a bicyclic sugar moiety. A preferred LNA comprises 2'-O,4'-C-ethylene-bridged nucleic acid (Morita et al. 2001. Nucleic Acid Res Supplement No. 1: 241-242). These substitutions render the nucleotide analogue or equivalent RNase H and nuclease resistant and increase the affinity for the target RNA.

[0069] It is understood by a skilled person that it is not necessary for all positions in an antisense oligonucleotide to be modified uniformly. In addition, more than one of the aforementioned analogues or equivalents may be incorporated in a single antisense oligonucleotide or even at a single position within an antisense oligonucleotide. In certain embodiments, an antisense oligonucleotide of the invention has at least two different types of analogues or equivalents.

[0070] A preferred antisense oligonucleotide according to the invention comprises a 2'-O alkyl phosphorothioate antisense oligonucleotide, such as 2'-O-methyl modified ribose (RNA), 2'-O-ethyl modified ribose, 2'-O-propyl modified ribose, and/or substituted derivatives of these modifications such as halogenated derivatives.

[0071] A most preferred antisense oligonucleotide according to the invention comprises of 2'-O-methyl phosphorothioate ribose.

[0072] A functional equivalent of a molecule of the invention may be defined as an oligonucleotide as defined herein wherein an activity of said functional equivalent is retained to at least some extent. Preferably, an activity of said functional equivalent is inducing exon 43, 46, 50, 51, 52, or 53 skipping and providing a functional dystrophin protein. Said activity of said functional equivalent is therefore preferably assessed by detection of exon 43, 46, 50, 51, 52, or 53 skipping and by quantifying the amount of functional dystrophin protein. A functional dystrophin is herein preferably defined as being a dystrophin able to bind actin and members of the DGC protein complex. The assessment of said activity of an oligonucleotide is preferably done by RT-PCR or by immunofluorescence or Western blot analyses. Said activity is preferably retained to at least some extent when it represents at least 50%, or at least 60%, or at least 70% or at least 80% or at least 90% or at least 95% or more of corresponding activity of said oligonucleotide the functional equivalent derives from. Throughout this application, when the word oligonucleotide is used it may be replaced by a functional equivalent thereof as defined herein.

[0073] It will be understood by a skilled person that distinct antisense oligonucleotides can be combined for efficiently skipping any of exon 43, exon 46, exon 50, exon 51, exon 52 and/or exon 53 of the human DMD pre-mRNA. It is encompassed by the present invention to use one, two, three, four, five or more oligonucleotides for skipping one of said exons (i.e. exon, 43, 46, 50, 51, 52, or 53). It is also encompassed to use at least two oligonucleotides for skipping at least two, of said exons. Preferably two of said exons are skipped. More preferably, these two exons are:
43 and 51, or
43 and 53, or
50 and 51, or
51 and 52, or
52 and 53.

[0074] The skilled person will know which combination of exons is preferred to be skipped depending on the type, the number and the location of the mutation present in a DMD or BMD patient.

[0075] An antisense oligonucleotide can be linked to a moiety that enhances uptake of the antisense oligonucleotide in cells, preferably muscle cells. Examples of such moieties are cholesterols, carbohydrates, vitamins, biotin, lipids, phospholipids, cell-penetrating peptides including but not limited to antennapedia, TAT, transportan and positively charged amino acids such as oligoarginine, poly-arginine, oligolysine or polylysine, antigen-binding domains such as provided by an antibody, a Fab fragment of an antibody, or a single chain antigen binding domain such as a cameloid single domain antigen-binding domain.

[0076] A preferred antisense oligonucleotide comprises a peptide-linked PMO.

[0077] A preferred antisense oligonucleotide comprising one or more nucleotide analogs or equivalents of the invention modulates splicing in one or more muscle cells, including heart muscle cells, upon systemic delivery. In this respect, systemic delivery of an antisense oligonucleotide comprising a specific nucleotide analog or equivalent might result in targeting a subset of muscle cells, while an antisense oligonucleotide comprising a distinct nucleotide analog or equiva-

lent might result in targeting of a different subset of muscle cells. Therefore, in one embodiment it is preferred to use a combination of antisense oligonucleotides comprising different nucleotide analogs or equivalents for inducing skipping of exon 43, 46, 50, 51, 52, or 53 of the human DMD pre-mRNA.

[0078] A cell can be provided with a molecule capable of interfering with essential sequences that result in highly efficient skipping of exon 43, exon 46, exon 50, exon 51, exon 52 or exon 53 of the human DMD pre-mRNA by plasmid-derived antisense oligonucleotide expression or viral expression provided by adenovirus- or adeno-associated virus-based vectors. In a preferred embodiment, there is provided a viral-based expression vector comprising an expression cassette that drives expression of a molecule as identified herein. Expression is preferably driven by a polymerase III promoter, such as a U1, a U6, or a U7 RNA promoter. A muscle or myogenic cell can be provided with a plasmid for antisense oligonucleotide expression by providing the plasmid in an aqueous solution. Alternatively, a plasmid can be provided by transfection using known transfection agentia such as, for example, LipofectAMINE™ 2000 (Invitrogen) or polyethyleneimine (PEI; ExGen500 (MBI Fermentas)), or derivatives thereof.

[0079] One preferred antisense oligonucleotide expression system is an adenovirus associated virus (AAV)-based vector. Single chain and double chain AAV-based vectors have been developed that can be used for prolonged expression of small antisense nucleotide sequences for highly efficient skipping of exon 43, 46, 50, 51, 52 or 53 of the DMD pre-mRNA.

[0080] A preferred AAV-based vector comprises an expression cassette that is driven by a polymerase III-promoter (Pol III). A preferred Pol III promoter is, for example, a U1, a U6, or a U7 RNA promoter.

[0081] The invention therefore also provides a viral-based vector, comprising a Pol III-promoter driven expression cassette for expression of one or more antisense sequences of the invention for inducing skipping of exon 43, exon 46, exon 50, exon 51, exon 52 or exon 53 of the human DMD pre-mRNA.

Pharmaceutical Composition

[0082] If required, a molecule or a vector expressing an antisense oligonucleotide of the invention can be incorporated into a pharmaceutically active mixture or composition by adding a pharmaceutically acceptable carrier.

[0083] Therefore, in a further aspect, the invention provides a composition, preferably a pharmaceutical composition comprising a molecule comprising an antisense oligonucleotide according to the invention, and/or a viral-based vector expressing the antisense sequence(s) according to the invention and a pharmaceutically acceptable carrier.

[0084] A preferred pharmaceutical composition comprises a molecule as defined herein and/or a vector as defined herein, and a pharmaceutical acceptable carrier or excipient, optionally combined with a molecule and/or a vector as defined herein which is able to induce skipping of exon 6, 7, 11, 17, 19, 21, 43, 44, 45, 50, 51, 52, 53, 55, 57, 59, 62, 63, 65, 66, 69, or 75 of the DMD pre-mRNA. Preferred molecules able to induce skipping of any of these exon are identified in any one of Tables 1 to 7.

[0085] Preferred excipients include excipients capable of forming complexes, vesicles and/or liposomes that deliver such a molecule as defined herein, preferably an oligonucleotide complexed or trapped in a vesicle or liposome through a cell membrane. Many of these excipients are known in the art. Suitable excipients comprise polyethylenimine and derivatives, or similar cationic polymers, including polypropyleneimine or polyethylenimine copolymers (PECs) and derivatives, ExGen 500, synthetic amphiphils (SAINT-18), Lipofectin™, DOTAP and/or viral capsid proteins that are capable of self assembly into particles that can deliver such molecule, preferably an oligonucleotide as defined herein to a cell, preferably a muscle cell. Such excipients have been shown to efficiently deliver (oligonucleotide such as antisense) nucleic acids to a wide variety of cultured cells, including muscle cells. Their high transfection potential is combined with an excepted low to moderate toxicity in terms of overall cell survival. The ease of structural modification can be used to allow further modifications and the analysis of their further (in vivo) nucleic acid transfer characteristics and toxicity.

[0086] Lipofectin represents an example of a liposomal transfection agent. It consists of two lipid components, a cationic lipid N-[1-(2,3 dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA) (cp. DOTAP which is the methylsulfate salt) and a neutral lipid dioleoylphosphatidylethanolamine (DOPE). The neutral component mediates the intracellular release. Another group of delivery systems are polymeric nanoparticles.

[0087] Polycations such like diethylaminoethylaminoethyl (DEAE)-dextran, which are well known as DNA transfection reagent can be combined with butylcyanoacrylate (PBCA) and hexylcyanoacrylate (PHCA) to formulate cationic nanoparticles that can deliver a molecule or a compound as defined herein, preferably an oligonucleotide across cell membranes into cells.

[0088] In addition to these common nanoparticle materials, the cationic peptide protamine offers an alternative approach to formulate a compound as defined herein, preferably an oligonucleotide as colloids. This colloidal nanoparticle system can form so called proticles, which can be prepared by a simple self-assembly process to package and mediate intracellular release of a compound as defined herein, preferably an oligonucleotide. The skilled person may select and adapt any of the above or other commercially available alternative excipients and delivery systems to package and deliver a compound as defined herein, preferably an oligonucleotide for use in the current invention to deliver said compound for the treatment of Duchenne Muscular Dystrophy or Becker Muscular Dystrophy in humans.

[0089] In addition, a compound as defined herein, preferably an oligonucleotide could be covalently or non-covalently linked to a targeting ligand specifically designed to facilitate the uptake in to the cell, cytoplasm and/or its nucleus. Such ligand could comprise (i) a compound (including but not limited to peptide(-like) structures) recognising cell, tissue or organ specific elements facilitating cellular uptake and/or (ii) a chemical compound able to facilitate the uptake in to cells and/or the intracellular release of an a compound as defined herein, preferably an oligonucleotide from vesicles, e.g. endosomes or lysosomes.

[0090] Therefore, in a preferred embodiment, a compound as defined herein, preferably an oligonucleotide are formulated in a medicament which is provided with at least an excipient and/or a targeting ligand for delivery and/or a delivery device of said compound to a cell and/or enhancing its intracellular delivery. Accordingly, the invention also encompasses a pharmaceutically acceptable composition comprising a compound as defined herein, preferably an oligonucle-

otide and further comprising at least one excipient and/or a targeting ligand for delivery and/or a delivery device of said compound to a cell and/or enhancing its intracellular delivery.

[0091] It is to be understood that a molecule or compound or oligonucleotide may not be formulated in one single composition or preparation. Depending on their identity, the skilled person will know which type of formulation is the most appropriate for each compound.

[0092] In a preferred embodiment, an in vitro concentration of a molecule or an oligonucleotide as defined herein, which is ranged between 0.1 nM and 1 □M is used. More preferably, the concentration used is ranged between 0.3 to 400 nM, even more preferably between 1 to 200 nM. A molecule or an oligonucleotide as defined herein may be used at a dose which is ranged between 0.1 and 20 mg/kg, preferably 0.5 and 10 mg/kg. If several molecules or oligonucleotides are used, these concentrations may refer to the total concentration of oligonucleotides or the concentration of each oligonucleotide added. The ranges of concentration of oligonucleotide(s) as given above are preferred concentrations for in vitro or ex vivo uses. The skilled person will understand that depending on the oligonucleotide(s) used, the target cell to be treated, the gene target and its expression levels, the medium used and the transfection and incubation conditions, the concentration of oligonucleotide(s) used may further vary and may need to be optimised any further.

[0093] More preferably, a compound preferably an oligonucleotide to be used in the invention to prevent, treat DMD or BMD are synthetically produced and administered directly to a cell, a tissue, an organ and/or patients in formulated form in a pharmaceutically acceptable composition or preparation. The delivery of a pharmaceutical composition to the subject is preferably carried out by one or more parenteral injections, e.g. intravenous and/or subcutaneous and/or intramuscular and/or intrathecal and/or intraventricular administrations, preferably injections, at one or at multiple sites in the human body.

[0094] A preferred oligonucleotide as defined herein optionally comprising one or more nucleotide analogs or equivalents of the invention modulates splicing in one or more muscle cells, including heart muscle cells, upon systemic delivery. In this respect, systemic delivery of an oligonucleotide comprising a specific nucleotide analog or equivalent might result in targeting a subset of muscle cells, while an oligonucleotide comprising a distinct nucleotide analog or equivalent might result in targeting of a different subset of muscle cells.

[0095] In this respect, systemic delivery of an oligonucleotide comprising a specific nucleotide analog or equivalent might result in targeting a subset of muscle cells, while an oligonucleotide comprising a distinct nucleotide analog or equivalent might result in targeting a different subset of muscle cells. Therefore, in this embodiment, it is preferred to use a combination of oligonucleotides comprising different nucleotide analogs or equivalents for modulating splicing of the DMD mRNA in at least one type of muscle cells.

[0096] In a preferred embodiment, there is provided a molecule or a viral-based vector for use as a medicament, preferably for modulating splicing of the DMD pre-mRNA, more preferably for promoting or inducing skipping of any of exon 43, 46, 50-53 as identified herein.

Use

[0097] In yet a further aspect, the invention provides the use of an antisense oligonucleotide or molecule according to the invention, and/or a viral-based vector that expresses one or more antisense sequences according to the invention and/or a pharmaceutical composition, for modulating splicing of the DMD pre-mRNA. The splicing is preferably modulated in a human myogenic cell or muscle cell in vitro. More preferred is that splicing is modulated in a human muscle cell in vivo. Accordingly, the invention further relates to the use of the molecule as defined herein and/or the vector as defined herein and/or or the pharmaceutical composition as defined herein for modulating splicing of the DMD pre-mRNA or for the preparation of a medicament for the treatment of a DMD or BMD patient.

[0098] In this document and in its claims, the verb "to comprise" and its conjugations is used in its non-limiting sense to mean that items following the word are included, but items not specifically mentioned are not excluded. In addition the verb "to consist" may be replaced by "to consist essentially of" meaning that a molecule or a viral-based vector or a composition as defined herein may comprise additional component(s) than the ones specifically identified, said additional component(s) not altering the unique characteristic of the invention. In addition, reference to an element by the indefinite article "a" or "an" does not exclude the possibility that more than one of the element is present, unless the context clearly requires that there be one and only one of the elements. The indefinite article "a" or "an" thus usually means "at least one". Each embodiment as identified herein may be combined together unless otherwise indicated. All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

[0099] The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

EXAMPLES

Examples 1-4

Materials and Methods

[0100] AON design was based on (partly) overlapping open secondary structures of the target exon RNA as predicted by the m-fold program, on (partly) overlapping putative SR-protein binding sites as predicted by the ESE-finder software. AONs were synthesized by Prosensa Therapeutics B.V. (Leiden, Netherlands), and contain 2'-O-methyl RNA and full-length phosphorothioate (PS) backbones.

Tissue Culturing, Transfection and RT-PCR Analysis

[0101] Myotube cultures derived from a healthy individual ("human control") (examples 1, 3, and 4; exon 43, 50, 52 skipping) or a DMD patient carrying an exon 45 deletion (example 2; exon 46 skipping) were processed as described previously (Aartsma-Rus et al., Neuromuscul. Disord. 2002; 12: S71-77 and Hum Mol Genet. 2003; 12(8): 907-14). For the screening of AONs, myotube cultures were transfected with 50 nM and 150 nM (example 2), 200 nM and 500 nM (example 4) or 500 nM only (examples 1 and 3) of each AON. Transfection reagent UNIFectylin (Prosensa Therapeutics BV, Netherlands) was used, with 2 □l UNIFectylin per □g AON. Exon skipping efficiencies were determined by nested RT-PCR analysis using primers in the exons flanking the targeted exons (43, 46, 50, 51, 52, or 53). PCR fragments were isolated from agarose gels for sequence verification. For

quantification, the PCR products were analyzed using the DNA 1000 LabChips Kit on the Agilent 2100 bioanalyzer (Agilent Technologies, USA).

Results

DMD Exon 43 Skipping.

[0102] A series of AONs targeting sequences within exon 43 were designed and transfected in healthy control myotube cultures. Subsequent RT-PCR and sequence analysis of isolated RNA demonstrated that almost all AONs targeting a continuous nucleotide stretch within exon 43 herein defined as SEQ ID NO 2, was indeed capable of inducing exon 43 skipping. PS237 (SEQ ID NO: 65) reproducibly induced highest levels of exon 43 skipping (up to 66%) at 500 nM, as shown in FIG. **1**. For comparison, also PS238 and PS240 are shown, inducing exon 43 skipping levels up to 13% and 36% respectively (FIG. **1**). The precise skipping of exon 43 was confirmed by sequence analysis of the novel smaller transcript fragments. No exon 43 skipping was observed in non-treated cells (NT).

DMD Exon 46 Skipping

[0103] A series of AONs targeting sequences within exon 46 were designed and transfected in myotube cultures derived from a DMD patient carrying an exon 45 deletion in the DMD gene. For patients with such mutation antisense-induced exon 46 skipping would induce the synthesis of a novel, BMD-like dystrophin protein that may indeed alleviate one or more symptoms of the disease. Subsequent RT-PCR and sequence analysis of isolated RNA demonstrated that almost all AONs targeting a continuous nucleotide stretch within exon 46 herein defined as SEQ ID NO 3, was indeed capable of inducing exon 46 skipping, even at relatively low AON concentrations of 50 nM. PS182 (SEQ ID NO: 117) reproducibly induced highest levels of exon 46 skipping (up to 50% at 50 nM and 74% at 150 nM), as shown in FIG. **2**. For comparison, also PS177, PS179, and PS181 are shown, inducing exon 46 skipping levels up to 55%, 58% and 42% respectively at 150 nM (FIG. **2**). The precise skipping of exon 46 was confirmed by sequence analysis of the novel smaller transcript fragments. No exon 46 skipping was observed in non-treated cells (NT).

DMD Exon 50 Skipping

[0104] A series of AONs targeting sequences within exon 50 were designed and transfected in healthy control myotube cultures. Subsequent RT-PCR and sequence analysis of isolated RNA demonstrated that almost all AONs targeting a continuous nucleotide stretch within exon 50 herein defined as SEQ ID NO 4, was indeed capable of inducing exon 50 skipping. PS248 (SEQ ID NO: 127) reproducibly induced highest levels of exon 50 skipping (up to 35% at 500 nM), as shown in FIG. **3**. For comparison, also PS245, PS246, and PS247 are shown, inducing exon 50 skipping levels up to 14-16% at 500 nM (FIG. **3**). The precise skipping of exon 50 was confirmed by sequence analysis of the novel smaller transcript fragments. No exon 50 skipping was observed in non-treated cells (NT).

DMD Exon 51 Skipping

[0105] A series of AONs targeting sequences within exon 51 were designed and transfected in healthy control myotube cultures. Subsequent RT-PCR and sequence analysis of isolated RNA demonstrated that almost all AONs targeting a continuous nucleotide stretch within exon 51 herein defined as SEQ ID NO 5, was indeed capable of inducing exon 51 skipping. The AON with SEQ ID NO 180 reproducibly induced highest levels of exon 51 skipping (not shown).

DMD Exon 52 Skipping

[0106] A series of AONs targeting sequences within exon 52 were designed and transfected in healthy control myotube cultures. Subsequent RT-PCR and sequence analysis of isolated RNA demonstrated that almost all AONs targeting a continuous nucleotide stretch within exon 52 herein defined as SEQ ID NO 6, was indeed capable of inducing exon 52 skipping. PS236 (SEQ ID NO: 299) reproducibly induced highest levels of exon 52 skipping (up to 88% at 200 nM and 91% at 500 nM), as shown in FIG. **4**. For comparison, also PS232 and AON 52-1 (previously published by Aartsma-Rus et al. *Oligonucleotides* 2005) are shown, inducing exon 52 skipping at levels up to 59% and 10% respectively when applied at 500 nM (FIG. **4**). The precise skipping of exon 52 was confirmed by sequence analysis of the novel smaller transcript fragments. No exon 52 skipping was observed in non-treated cells (NT).

DMD Exon 53 Skipping

[0107] A series of AONs targeting sequences within exon 53 were designed and transfected in healthy control myotube cultures. Subsequent RT-PCR and sequence analysis of isolated RNA demonstrated that almost all AONs targeting a continuous nucleotide stretch within exon 53 herein defined as SEQ ID NO 7, was indeed capable of inducing exon 53 skipping. The AON with SEQ ID NO 328 reproducibly induced highest levels of exon 53 skipping (not shown).

Sequence Listing:

[0108]

DMD gene amino acid sequence
SEQ ID NO: 1:
MLWWEEVEDCYEREDVQKKTFTKWVNAQFSKFGKQHIENLFSDLQDGR

RLLDLLEGLTGQKLPKEKGSTRVHALNNVNKALRVLQNNNVDLVNIGS

TDIVDGNHKLTLGLIWNIILHWQVKNVMKNIMAGLQQTNSEKILLSWV

RQSTRNYPQVNVINFTTSWSDGLALNALIHSHRPDLFDWSVVCQQSAT

QRLEHAFNIARYQLGIEKLLDPEDVDTTYPDKKSILMYITSLFQVLPQ

QVSIEAIQEVEMLPRPPKVTKEEHFQLHHQMHYSQQITVSLAQGYERT

SSPKPRFKSYAYTQAAYVTTSDPTRSPFPSQHLEAPEDKSFGSSLMES

EVNLDRYQTALEEVLSWLLSAEDTLQAQGEISNDVEVVKDQFHTHEGY

MMDLTAHQGRVGNILQLGSKLIGTGKLSEDEETEVQEQMNLLNSRWEC

LRVASMEKQSNLHRVLMDLQNQKLKELNDWLTKTEERTRKMEEEPLGP

DLEDLKRQVQQHKVLQCDLEQEQVRVNSLTHMVVVVDESSGDHATAAL

EEQLKVLGQRVVANICRWTEDRWVLLQDILLKWQRLTEEQCLFSAWLS

EKEDAVNKIHTTGFKDQNEMLSSLQKLAVLKADLEKKKQSMGKLYSLK

QDLLSTLKNKSVTQKTEAWLDNFARCWDNLVQKLEKSTAQISQAVTTT

-continued

QPSLTQTTVMETVTTVTTREQILVKHAQEELPPPPPQKKRQITVDSEI

RKRLDVDITELHSWITRSEAVLQSPEFAIFRKEGNFSDLKEKVNAIER

EKAEKFRKLQDASRSAQALVEQMVNEGVNADSIKQASEQLNSRWIEFC

QLLSERLNWLEYQNNIIAFYNQLQQLEOMTTTAENWLKIQPTTPSEPT

AIKSQLKICKDEVNRLSGLQPQIERLKIQSIALKEKGQGPMFLDADFV

AFTNHFKQVFSDVQAREKELQTIFDTLPPMRYQETMSAIRTWVQQSET

KLSIPQLSVTDYEIMEQRLGELQALQSSLQEQQSGLYYLSTTVKEMSK

KAPSEISRKYQSEFEEIEGRWKKLSSQLVEHCQKLEEQMNKLRKIQNH

IQTLKKWMAEVDVFLKEEWPALGDSEILKKQLKQCRLLVSDIQTIQPS

LNSVNEGGQKIKNEAEPEFASRLETELKELNTQWDHMCQQVYARKEAL

KGGLEKTVSLQKDLSEMHEWMTQAEEEYLERDFEYKTPQELQKAVEEM

KRAKEEAQQKEAKVKLLTESVNSVIAQAPPVAQEALKKELETLTTNYQ

WLCTRLNGKCKTLEEVWACWHELLSYLEKANKWLNEVEFKLKTTENIP

GGAEEISEVLDSLENLMRHSEDNPNQIRILAQTLTDGGVMDELINEEL

ETFNSRWRELHEEAVRRQKLLEQSIQSAQETEKSLHLIQESLTFIDKQ

LAAYIADKVDAAQMPQEAQKIQSDLTSHEISLEEMKKHNQGKEAAQRV

LSQIDVAQKKLQDVSMKFRLFQKPANFEQRLQESKMILDEVKMHLPAL

ETKSVEQEVVQSQLNHCVNLYKSLSEVKSEVEMVIKTGRQIVQKKQTE

NPKELDERVTALKLHYNELGAKVTERKQQLEKCLKLSRKMRKEMNVLT

EWLAATDMELTKRSAVEGMPSNLDSEVAWGKATQKEIEKOKVHLKSIT

EVGEALKTVLGKKETLVEDKLSLLNSNWIAVTSRAEEWLNLLLEYOKH

METFDQNVDHITKWIIQADTLLDESEKKKPQQKEDVLKRLKAELNDIR

PKVDSTRDQAANLMANRGDHCRKLVEPQISELNHRFAAISHRIKTGKA

SIPLKELEQFNSDIQKLLEPLEAEIQQGVNLKEEDFNKDMNEDNCGTV

KELLQRGDNLQQRITDERKREEIKIKQQLLQTKHNALKDLRSQRRKKA

LEISHQWYQYKRQADDLLKCLDDIEKKLASLPEPRDERKIKEIDRELQ

KKKEELNAVRRQAEGLSEDGAAMAVEPTQIQLSKRWREIESKFAQFRR

LNFAQIHTVREETMMVMTEDMPLEISYVPSTYLTEITHVSQALLEVEQ

LLNAPDLCAKDFEDLFKQEESLKNIKDSLQQSSGRIDIIHSKKTAALQ

SATPVERVKLQEALSQLDFQWEKVNKMYKDRQGRFDRSVEKWRRFHYD

IKIFNQWLTEAEQFLRKTQIPENWEHAKYKWYLKELQDGIGQRQTWRT

LNATGEEIIQQSSKTDASILQEKLGSLNLRWQEVCKQLSDRKKRLEEQ

KNILSEFQRDLNEFVLWLEEADNIASIPLEPGKEQOLKEKLEQVKLLV

EELPLRQCILKQLNETGGPVLVSAPISPEEQDKLENKLKQTNLQWIKV

SRALPEKQGEIEAQIKDLGQLEKKLEDLEEQLNHLLLWLSPIRNQLEI

YNQPNQEGPFDVQETEIAVQAKQPDVEEILSKGQHLYKEKPATQPVKR

KLEDLSSEWKAVNRLLQELRAKQPDLAPGLTTKIGASPTQTVTLVTQP

WTKETAISKLEMPSSLMLEVPALADFNRAWTELTDWLSLLDQVIKSQR

-continued

VMVGDLEDINEMIIKQKATMQDLEQRRPQLEELITAAQNLKNKTSNQE

ARTIITDRIERIQNQWDEVQEHLQNRRQQLNEMLKDSTQWLEAKEEAE

QVLGQARAKLESWKEGPYTVDAIQKKITETKQLAKDLRQWQTNVDVAN

DLALKLLRDYSADDTRKVHMITENINASWRSIHKRVSEREAALEETHR

LLQQFPLDLEKFLAWLTEAETTANVLQDATRKERLLEDSKGVKELMKQ

WQDLQGEIEAHTDVYHNLDENSQKILRSLEGSDDAVLLQRRLDNMNFK

WSELRKKSLNIRSHLEASSDQWKRLHLSLQELLVWLQLKDDELSRQAP

IGGDFPAVQKQNDVHRAFKRELKTKEPVIMSTLETVRIFLTEQPLEGL

EKLYQEPRELPPEERAQNVTRLLRKQAEEVNTEWEKLNLHSADWQRKI

DETLERLQELQEATDELDLKLRQAEVIKGSWQPVGDLLIDSLQDHLEK

VKALRGEIAPLKENVSHVNDLARQLTTLGIQLSPYNLSTLEDLNTRWK

LLQVAVEDRVRQLHEAHRDFGPASQHFLSTSVQGPWERAISPNKVPYY

INHETQTTCWDHPKMTELYQSLADLNNVRFSAYRTAMKLRRLQKALCL

DLLSLSAACDALDQHNLKQNDQPMDILQIINCLTTIYDRLEQEHNNLV

NVPLCVDMCLNWLLNVYDTGRTGRIRVLSFKTGIISLCKAHLEDKYRY

LFKQVASSTGFCDQRRLGLLLHDSIQIPRQLGEVASFGGSNIEPSVRS

CFQFANNKPEIEAALFLDWMRLEPQSMVWLPVLHRVAAAETAKHQAKC

NICKECPIIGFRYRSLKHFNYDICQSCFFSGRVAKGHKMHYPMVEYCT

PTTSGEDVRDFAKVLKNKFRTKRYFAKHPRMGYLPVQTVLEGDNMETP

VTLINFWPVDSAPASSPQLSHDDTHSRIEHYASRLAEMENSNGSYLND

SISPNESIDDEHLLIQHYCQSLNQDSPLSQPRSPAQILISLESEERGE

LERILADLEEENRNLQAEYDRLKQQHEHKGLSPLPSPPEMMPTSPQSP

RDAELIAEAKLLRQHKGRLEARMQILEDHNKQLESQLHRLRQLLEQPQ

AEAKVNGTTVSSPSTSLQRSDSSQPMLLRVVGSQTSDSMGEEDLLSPP

QDTSTGLEEVMEQLNNSFPSSRGRNTPGKPMREDTM

SEQ ID NO 2 (exon 43):
AGAUAGUCUACAACAAAGCUCAGGUCGGAUUGACAUUAUUCAUAGCAA

GAAGACAGCAGCAUUGCAAAGUGCAACGCCUGUGG

SEQ ID NO 3 (exon 46):
UUAUGGUUGGAGGAAGCAGAUAACAUUGCUAGUAUCCCACUUGAACCU

GGAAAAGAGCAGCAACUAAAAGAAAAGC

SEQ ID NO 4 (exon 50):
'GGCGGTAAACCGUUUACUUCAAGAGCUGAGGGCAAAGCAGCCUG AC

CUAGCUCCUGGACUGACCACUAUUGG

SEQ ID NO 5 (exon 51):
CUCCUACUCAGACUGUUACUCUGGUGACACAACCUGUGGUUACUAAGG

AAACUGCCAUCUCCAAACUAGAAAUGCCAUCUUCCUUGAUGUUGGAGG

UAC

SEQ ID NO 6 (exon 52):
AUGCAGGAUUUGGAACAGAGGCGUCCCCAGUUGGAAGAACUCAUUACC

GCUGCCCAAAAUUUGAAAAA CAAGACCAGCAAUCAAGAGGCU

-continued

SEQ ID NO 7 (exon 53):
AAAUGUUAAAGGAUUCAACACAAUGGCUGGAAGCUAAGGAAGAAGCUG

AGCAGGUCUUAGGACAGGCCAGAG

TABLE 1

oligonucleotides for skipping DMD Gene Exon 43	
SEQ ID NO 8	CCACAGGCGUUGCACUUUGCAAUGC
SEQ ID NO 9	CACAGGCGUUGCACUUUGCAAUGCU
SEQ ID NO 10	ACAGGCGUUGCACUUUGCAAUGCUG
SEQ ID NO 11	CAGGCGUUGCACUUUGCAAUGCUGC
SEQ ID NO 12	AGGCGUUGCACUUUGCAAUGCUGCU
SEQ ID NO 13	GGCGUUGCACUUUGCAAUGCUGCUG
SEQ ID NO 14	GCGUUGCACUUUGCAAUGCUGCUGU
SEQ ID NO 15	CGUUGCACUUUGCAAUGCUGCUGUC
SEQ ID NO 16 PS240	CGUUGCACUUUGCAAUGCUGCUG
SEQ ID NO 17	GUUGCACUUUGCAAUGCUGCUGUCU
SEQ ID NO 18	UUGCACUUUGCAAUGCUGCUGUCUU
SEQ ID NO 19	UGCACUUUGCAAUGCUGCUGUCUUC
SEQ ID NO 20	GCACUUUGCAAUGCUGCUGUCUUCU
SEQ ID NO 21	CACUUUGCAAUGCUGCUGUCUUCUU
SEQ ID NO 22	ACUUUGCAAUGCUGCUGUCUUCUUG
SEQ ID NO 23	CUUUGCAAUGCUGCUGUCUUCUUGC
SEQ ID NO 24	UUUGCAAUGCUGCUGUCUUCUUGCU
SEQ ID NO 25	UUGCAAUGCUGCUGUCUUCUUGCUA
SEQ ID NO 26	UGCAAUGCUGCUGUCUUCUUGCUAU
SEQ ID NO 27	GCAAUGCUGCUGUCUUCUUGCUAUG
SEQ ID NO 28	CAAUGCUGCUGUCUUCUUGCUAUGA
SEQ ID NO 29	AAUGCUGCUGUCUUCUUGCUAUGAA
SEQ ID NO 30	AUGCUGCUGUCUUCUUGCUAUGAAU
SEQ ID NO 31	UGCUGCUGUCUUCUUGCUAUGAAUA
SEQ ID NO 32	GCUGCUGUCUUCUUGCUAUGAAUAA
SEQ ID NO 33	CUGCUGUCUUCUUGCUAUGAAUAAU
SEQ ID NO 34	UGCUGUCUUCUUGCUAUGAAUAAUG
SEQ ID NO 35	GCUGUCUUCUUGCUAUGAAUAAUGU
SEQ ID NO 36	CUGUCUUCUUGCUAUGAAUAAUGUC
SEQ ID NO 37	UGUCUUCUUGCUAUGAAUAAUGUCA
SEQ ID NO 38	GUCUUCUUGCUAUGAAUAAUGUCAA
SEQ ID NO 39	UCUUCUUGCUAUGAAUAAUGUCAAU
SEQ ID NO 40	CUUCUUGCUAUGAAUAAUGUCAAUC

TABLE 1-continued

oligonucleotides for skipping DMD Gene Exon 43	
SEQ ID NO 41	UUCUUGCUAUGAAUAAUGUCAAUCC
SEQ ID NO 42	UCUUGCUAUGAAUAAUGUCAAUCCG
SEQ ID NO 43	CUUGCUAUGAAUAAUGUCAAUCCGA
SEQ ID NO 44	UUGCUAUGAAUAAUGUCAAUCCGAC
SEQ ID NO 45	UGCUAUGAAUAAUGUCAAUCCGACC
SEQ ID NO 46	GCUAUGAAUAAUGUCAAUCCGACCU
SEQ ID NO 47	CUAUGAAUAAUGUCAAUCCGACCUG
SEQ ID NO 48	UAUGAAUAAUGUCAAUCCGACCUGA
SEQ ID NO 49	AUGAAUAAUGUCAAUCCGACCUGAG
SEQ ID NO 50	UGAAUAAUGUCAAUCCGACCUGAGC
SEQ ID NO 51	GAAUAAUGUCAAUCCGACCUGAGCU
SEQ ID NO 52	AAUAAUGUCAAUCCGACCUGAGCUU
SEQ ID NO 53	AUAAUGUCAAUCCGACCUGAGCUUU
SEQ ID NO 54	UAAUGUCAAUCCGACCUGAGCUUUG
SEQ ID NO 55	AAUGUCAAUCCGACCUGAGCUUUGU
SEQ ID NO 56	AUGUCAAUCCGACCUGAGCUUUGUU
SEQ ID NO 57	UGUCAAUCCGACCUGAGCUUUGUUG
SEQ ID NO 58	GUCAAUCCGACCUGAGCUUUGUUGU
SEQ ID NO 59	UCAAUCCGACCUGAGCUUUGUUGUA
SEQ ID NO 60	CAAUCCGACCUGAGCUUUGUUGUAG
SEQ ID NO 61	AAUCCGACCUGAGCUUUGUUGUAGA
SEQ ID NO 62	AUCCGACCUGAGCUUUGUUGUAGAC
SEQ ID NO 63	UCCGACCUGAGCUUUGUUGUAGACU
SEQ ID NO 64	CCGACCUGAGCUUUGUUGUAGACUA
SEQ ID NO 65 PS237	CGACCUGAGCUUUGUUGUAG
SEQ ID NO 66 PS238	CGACCUGAGCUUUGUUGUAGACUAU
SEQ ID NO 67	GACCUGAGCUUUGUUGUAGACUAUC
SEQ ID NO 68	ACCUGAGCUUUGUUGUAGACUAUCA
SEQ ID NO 69	CCUGA GCUUU GUUGU AGACU AUC

TABLE 2

oligonucleotides for skipping DMD Gene Exon 46	
SEQ ID NO 70 PS179	GCUUUUCUUUUAGUUGCUGCUCUUU
SEQ ID NO 71	CUUUUCUUUUAGUUGCUGCUCUUUU
SEQ ID NO 72	UUUUCUUUUAGUUGCUGCUCUUUUC

TABLE 2-continued

oligonucleotides for skipping DMD Gene Exon 46	
SEQ ID NO 73	UUUCUUUUAGUUGCUGCUCUUUUCC
SEQ ID NO 74	UUCUUUUAGUUGCUGCUCUUUUCCA
SEQ ID NO 75	UCUUUUAGUUGCUGCUCUUUUCCAG
SEQ ID NO 76	CUUUUAGUUGCUGCUCUUUUCCAGG
SEQ ID NO 77	UUUUAGUUGCUGCUCUUUUCCAGGU
SEQ ID NO 78	UUUAGUUGCUGCUCUUUUCCAGGUU
SEQ ID NO 79	UUAGUUGCUGCUCUUUUCCAGGUUC
SEQ ID NO 80	UAGUUGCUGCUCUUUUCCAGGUUCA
SEQ ID NO 81	AGUUGCUGCUCUUUUCCAGGUUCAA
SEQ ID NO 82	GUUGCUGCUCUUUUCCAGGUUCAAG
SEQ ID NO 83	UUGCUGCUCUUUUCCAGGUUCAAGU
SEQ ID NO 84	UGCUGCUCUUUUCCAGGUUCAAGUG
SEQ ID NO 85	GCUGCUCUUUUCCAGGUUCAAGUGG
SEQ ID NO 86	CUGCUCUUUUCCAGGUUCAAGUGGG
SEQ ID NO 87	UGCUCUUUUCCAGGUUCAAGUGGGA
SEQ ID NO 88	GCUCUUUUCCAGGUUCAAGUGGGAC
SEQ ID NO 89	CUCUUUUCCAGGUUCAAGUGGGAUA
SEQ ID NO 90	UCUUUUCCAGGUUCAAGUGGGAUAC
SEQ ID NO 91 PS177	UCUUUUCCAGGUUCAAGUGG
SEQ ID NO 92	CUUUUCCAGGUUCAAGUGGGAUACU
SEQ ID NO 93	UUUUCCAGGUUCAAGUGGGAUACUA
SEQ ID NO 94	UUUCCAGGUUCAAGUGGGAUACUAG
SEQ ID NO 95	UUCCAGGUUCAAGUGGGAUACUAGC
SEQ ID NO 96	UCCAGGUUCAAGUGGGAUACUAGCA
SEQ ID NO 97	CCAGGUUCAAGUGGGAUACUAGCAA
SEQ ID NO 98	CAGGUUCAAGUGGGAUACUAGCAAU
SEQ ID NO 99	AGGUUCAAGUGGGAUACUAGCAAUG
SEQ ID NO 100	GGUUCAAGUGGGAUACUAGCAAUGU
SEQ ID NO 101	GUUCAAGUGGGAUACUAGCAAUGUU
SEQ ID NO 102	UUCAAGUGGGAUACUAGCAAUGUUA
SEQ ID NO 103	UCAAGUGGGAUACUAGCAAUGUUAU
SEQ ID NO 104	CAAGUGGGAUACUAGCAAUGUUAUC
SEQ ID NO 105	AAGUGGGAUACUAGCAAUGUUAUCU
SEQ ID NO 106	AGUGGGAUACUAGCAAUGUUAUCUG
SEQ ID NO 107	GUGGGAUACUAGCAAUGUUAUCUGC
SEQ ID NO 108	UGGGAUACUAGCAAUGUUAUCUGCU

TABLE 2-continued

oligonucleotides for skipping DMD Gene Exon 46	
SEQ ID NO 109	GGGAUACUAGCAAUGUUAUCUGCUU
SEQ ID NO 110 PS181	GGAUACUAGCAAUGUUAUCUGCUUC
SEQ ID NO 111	GAUACUAGCAAUGUUAUCUGCUUCC
SEQ ID NO 112	AUACUAGCAAUGUUAUCUGCUUCCU
SEQ ID NO 113	UACUAGCAAUGUUAUCUGCUUCCUC
SEQ ID NO 114	ACUAGCAAUGUUAUCUGCUUCCUCC
SEQ ID NO 115	CUAGCAAUGUUAUCUGCUUCCUCCA
SEQ ID NO 116	UAGCAAUGUUAUCUGCUUCCUCCAA
SEQ ID NO 117 PS182	AGCAAUGUUAUCUGCUUCCUCCAAC
SEQ ID NO 118	GCAAUGUUAUCUGCUUCCUCCAACC
SEQ ID NO 119	CAAUGUUAUCUGCUUCCUCCAACCA
SEQ ID NO 120	AAUGUUAUCUGCUUCCUCCAACCAU
SEQ ID NO 121	AUGUUAUCUGCUUCCUCCAACCAUA
SEQ ID NO 122	UGUUAUCUGCUUCCUCCAACCAUAA

TABLE 3

oligonucleotides for skipping DMD Gene Exon 50	
SEQ ID NO 123	CCAAUAGUGGUCAGUCCAGGAGCUA
SEQ ID NO 124	CAAUAGUGGUCAGUCCAGGAGCUAG
SEQ ID NO 125	AAUAGUGGUCAGUCCAGGAGCUAGG
SEQ ID NO 126	AUAGUGGUCAGUCCAGGAGCUAGGU
SEQ ID NO 127 PS248	AUAGUGGUCAGUCCAGGAGCU
SEQ ID NO 128	UAGUGGUCAGUCCAGGAGCUAGGUC
SEQ ID NO 129	AGUGGUCAGUCCAGGAGCUAGGUCA
SEQ ID NO 130	GUGGUCAGUCCAGGAGCUAGGUCAG
SEQ ID NO 131	UGGUCAGUCCAGGAGCUAGGUCAGG
SEQ ID NO 132	GGUCAGUCCAGGAGCUAGGUCAGGC
SEQ ID NO 133	GUCAGUCCAGGAGCUAGGUCAGGCU
SEQ ID NO 134	UCAGUCCAGGAGCUAGGUCAGGCUG
SEQ ID NO 135	CAGUCCAGGAGCUAGGUCAGGCUGC
SEQ ID NO 136	AGUCCAGGAGCUAGGUCAGGCUGCU
SEQ ID NO 137	GUCCAGGAGCUAGGUCAGGCUGCUU
SEQ ID NO 138	UCCAGGAGCUAGGUCAGGCUGCUUU
SEQ ID NO 139	CCAGGAGCUAGGUCAGGCUGCUUUG
SEQ ID NO 140	CAGGAGCUAGGUCAGGCUGCUUUGC

TABLE 3-continued

oligonucleotides for skipping DMD Gene Exon 50	
SEQ ID NO 141	AGGAGCUAGGUCAGGCUGCUUUGCC
SEQ ID NO 142	GGAGCUAGGUCAGGCUGCUUUGCCC
SEQ ID NO 143	GAGCUAGGUCAGGCUGCUUUGCCCU
SEQ ID NO 144	AGCUAGGUCAGGCUGCUUUGCCCUC
SEQ ID NO 145	GCUAGGUCAGGCUGCUUUGCCCUCA
SEQ ID NO 530	CUCAGCUCUUGAAGUAAACGGUUUA
SEQ ID NO 532	CAGCUCUUGAAGUAAACGGUUUACC
SEQ ID NO 534	GCUCUUGAAGUAAACGGUUUACCGC
SEQ ID NO 146	CUAGGUCAGGCUGCUUUGCCCUCAG
SEQ ID NO 147	UAGGUCAGGCUGCUUUGCCCUCAGC
SEQ ID NO 148	AGGUCAGGCUGCUUUGCCCUCAGCU
SEQ ID NO 149	GGUCAGGCUGCUUUGCCCUCAGCUC
SEQ ID NO 150	GUCAGGCUGCUUUGCCCUCAGCUCU
SEQ ID NO 151	UCAGGCUGCUUUGCCCUCAGCUCUU
SEQ ID NO 152	CAGGCUGCUUUGCCCUCAGCUCUUG
SEQ ID NO 153	AGGCUGCUUUGCCCUCAGCUCUUGA
SEQ ID NO 154	GGCUGCUUUGCCCUCAGCUCUUGAA
SEQ ID NO 155	GCUGCUUUGCCCUCAGCUCUUGAAG
SEQ ID NO 156	CUGCUUUGCCCUCAGCUCUUGAAGU
SEQ ID NO 157	UGCUUUGCCCUCAGCUCUUGAAGUA
SEQ ID NO 158	GCUUUGCCCUCAGCUCUUGAAGUAA
SEQ ID NO 159	CUUUGCCCUCAGCUCUUGAAGUAAA
SEQ ID NO 160	UUUGCCCUCAGCUCUUGAAGUAAAC
SEQ ID NO 161	UUGCCCUCAGCUCUUGAAGUAAACG
SEQ ID NO 162	UGCCCUCAGCUCUUGAAGUAAACGG
SEQ ID NO 163	GCCCUCAGCUCUUGAAGUAAACGGU
SEQ ID NO 164	CCCUCAGCUCUUGAAGUAAACGGUU
SEQ ID NO 165 PS246	CCUCAGCUCUUGAAGUAAAC
SEQ ID NO 166 PS247	CCUCAGCUCUUGAAGUAAACG
SEQ ID NO 167 PS245	CUCAGCUCUUGAAGUAAACG
SEQ ID NO 529	CCUCAGCUCUUGAAGUAAACGGUUU
SEQ ID NO 531	UCAGCUCUUGAAGUAAACGGUUUAC
SEQ ID NO 533	AGCUCUUGAAGUAAACGGUUUACCG
SEQ ID NO 535	CUCUUGAAGUAAACGGUUUACCGCC

TABLE 4

oligonucleotides for skipping DMD Gene Exon 51	
SEQ ID NO 168	GUACCUCCAACAUCAAGGAAGAUGG
SEQ ID NO 169	UACCUCCAACAUCAAGGAAGAUGGC
SEQ ID NO 170	ACCUCCAACAUCAAGGAAGAUGGCA
SEQ ID NO 171	CCUCCAACAUCAAGGAAGAUGGCAU
SEQ ID NO 172	CUCCAACAUCAAGGAAGAUGGCAUU
SEQ ID NO 173	UCCAACAUCAAGGAAGAUGGCAUUU
SEQ ID NO 174	CCAACAUCAAGGAAGAUGGCAUUUC
SEQ ID NO 175	CAACAUCAAGGAAGAUGGCAUUUCU
SEQ ID NO 176	AACAUCAAGGAAGAUGGCAUUUCUA
SEQ ID NO 177	ACAUCAAGGAAGAUGGCAUUUCUAG
SEQ ID NO 178	CAUCAAGGAAGAUGGCAUUUCUAGU
SEQ ID NO 179	AUCAAGGAAGAUGGCAUUUCUAGUU
SEQ ID NO 180	UCAAGGAAGAUGGCAUUUCUAGUUU
SEQ ID NO 181	CAAGGAAGAUGGCAUUUCUAGUUUG
SEQ ID NO 182	AAGGAAGAUGGCAUUUCUAGUUUGG
SEQ ID NO 183	AGGAAGAUGGCAUUUCUAGUUUGGA
SEQ ID NO 184	GGAAGAUGGCAUUUCUAGUUUGGAG
SEQ ID NO 185	GAAGAUGGCAUUUCUAGUUUGGAGA
SEQ ID NO 186	AAGAUGGCAUUUCUAGUUUGGAGAU
SEQ ID NO 187	AGAUGGCAUUUCUAGUUUGGAGAUG
SEQ ID NO 188	GAUGGCAUUUCUAGUUUGGAGAUGG
SEQ ID NO 189	AUGGCAUUUCUAGUUUGGAGAUGGC
SEQ ID NO 190	UGGCAUUUCUAGUUUGGAGAUGGCA
SEQ ID NO 191	GGCAUUUCUAGUUUGGAGAUGGCAG
SEQ ID NO 192	GCAUUUCUAGUUUGGAGAUGGCAGU
SEQ ID NO 193	CAUUUCUAGUUUGGAGAUGGCAGUU
SEQ ID NO 194	AUUUCUAGUUUGGAGAUGGCAGUUU
SEQ ID NO 195	UUUCUAGUUUGGAGAUGGCAGUUUC
SEQ ID NO 196	UUCUAGUUUGGAGAUGGCAGUUUCC
SEQ ID NO 197	UCUAGUUUGGAGAUGGCAGUUUCCU
SEQ ID NO 198	CUAGUUUGGAGAUGGCAGUUUCCUU
SEQ ID NO 199	UAGUUUGGAGAUGGCAGUUUCCUUA
SEQ ID NO 200	AGUUUGGAGAUGGCAGUUUCCUUAG
SEQ ID NO 201	GUUUGGAGAUGGCAGUUUCCUUAGU
SEQ ID NO 202	UUUGGAGAUGGCAGUUUCCUUAGUA
SEQ ID NO 203	UUGGAGAUGGCAGUUUCCUUAGUAA
SEQ ID NO 204	UGGAGAUGGCAGUUUCCUUAGUAAC

TABLE 4-continued

oligonucleotides for skipping DMD Gene Exon 51	
SEQ ID NO 205	GAGAUGGCAGUUUCCUUAGUAACCA
SEQ ID NO 206	AGAUGGCAGUUUCCUUAGUAACCAC
SEQ ID NO 207	GAUGGCAGUUUCCUUAGUAACCACA
SEQ ID NO 208	AUGGCAGUUUCCUUAGUAACCACAG
SEQ ID NO 209	UGGCAGUUUCCUUAGUAACCACAGG
SEQ ID NO 210	GGCAGUUUCCUUAGUAACCACAGGU
SEQ ID NO 211	GCAGUUUCCUUAGUAACCACAGGUU
SEQ ID NO 212	CAGUUUCCUUAGUAACCACAGGUUG
SEQ ID NO 213	AGUUUCCUUAGUAACCACAGGUUGU
SEQ ID NO 214	GUUUCCUUAGUAACCACAGGUUGUG
SEQ ID NO 215	UUUCCUUAGUAACCACAGGUUGUGU
SEQ ID NO 216	UUCCUUAGUAACCACAGGUUGUGUC
SEQ ID NO 217	UCCUUAGUAACCACAGGUUGUGUCA
SEQ ID NO 218	CCUUAGUAACCACAGGUUGUGUCAC
SEQ ID NO 219	CUUAGUAACCACAGGUUGUGUCACC
SEQ ID NO 220	UUAGUAACCACAGGUUGUGUCACCA
SEQ ID NO 221	UAGUAACCACAGGUUGUGUCACCAG
SEQ ID NO 222	AGUAACCACAGGUUGUGUCACCAGA
SEQ ID NO 223	GUAACCACAGGUUGUGUCACCAGAG
SEQ ID NO 224	UAACCACAGGUUGUGUCACCAGAGU
SEQ ID NO 225	AACCACAGGUUGUGUCACCAGAGUA
SEQ ID NO 226	ACCACAGGUUGUGUCACCAGAGUAA
SEQ ID NO 227	CCACAGGUUGUGUCACCAGAGUAAC
SEQ ID NO 228	CACAGGUUGUGUCACCAGAGUAACA
SEQ ID NO 229	ACAGGUUGUGUCACCAGAGUAACAG
SEQ ID NO 230	CAGGUUGUGUCACCAGAGUAACAGU
SEQ ID NO 231	AGGUUGUGUCACCAGAGUAACAGUC
SEQ ID NO 232	GGUUGUGUCACCAGAGUAACAGUCU
SEQ ID NO 233	GUUGUGUCACCAGAGUAACAGUCUG
SEQ ID NO 234	UUGUGUCACCAGAGUAACAGUCUGA
SEQ ID NO 235	UGUGUCACCAGAGUAACAGUCUGAG
SEQ ID NO 236	GUGUCACCAGAGUAACAGUCUGAGU
SEQ ID NO 237	UGUCACCAGAGUAACAGUCUGAGUA
SEQ ID NO 238	GUCACCAGAGUAACAGUCUGAGUAG
SEQ ID NO 239	UCACCAGAGUAACAGUCUGAGUAGG
SEQ ID NO 240	CACCAGAGUAACAGUCUGAGUAGGA
SEQ ID NO 241	ACCAGAGUAACAGUCUGAGUAGGAG

TABLE 5

oligonucleotides for skipping DMD Gene Exon 52	
SEQ ID NO 242	AGCCUCUUGAUUGCUGGUCUUGUUU
SEQ ID NO 243	GCCUCUUGAUUGCUGGUCUUGUUUU
SEQ ID NO 244	CCUCUUGAUUGCUGGUCUUGUUUUU
SEQ ID NO 245	CCUCUUGAUUGCUGGUCUUG
SEQ ID NO 246 PS232	CUCUUGAUUGCUGGUCUUGUUUUUC
SEQ ID NO 247	UCUUGAUUGCUGGUCUUGUUUUUCA
SEQ ID NO 248	CUUGAUUGCUGGUCUUGUUUUUCAA
SEQ ID NO 249	UUGAUUGCUGGUCUUGUUUUUCAAA
SEQ ID NO 250	UGAUUGCUGGUCUUGUUUUUCAAAU
SEQ ID NO 251	GAUUGCUGGUCUUGUUUUUCAAAUU
SEQ ID NO 252	GAUUGCUGGUCUUGUUUUUC
SEQ ID NO 253	AUUGCUGGUCUUGUUUUUCAAAUUU
SEQ ID NO 254	UUGCUGGUCUUGUUUUUCAAAUUUU
SEQ ID NO 255	UGCUGGUCUUGUUUUUCAAAUUUUG
SEQ ID NO 256	GCUGGUCUUGUUUUUCAAAUUUUGG
SEQ ID NO 257	CUGGUCUUGUUUUUCAAAUUUUGGG
SEQ ID NO 258	UGGUCUUGUUUUUCAAAUUUUGGGC
SEQ ID NO 259	GGUCUUGUUUUUCAAAUUUUGGGCA
SEQ ID NO 260	GUCUUGUUUUUCAAAUUUUGGGCAG
SEQ ID NO 261	UCUUGUUUUUCAAAUUUUGGGCAGC
SEQ ID NO 262	CUUGUUUUUCAAAUUUUGGGCAGCG
SEQ ID NO 263	UUGUUUUUCAAAUUUUGGGCAGCGG
SEQ ID NO 264	UGUUUUUCAAAUUUUGGGCAGCGGU
SEQ ID NO 265	GUUUUUCAAAUUUUGGGCAGCGGUA
SEQ ID NO 266	UUUUUCAAAUUUUGGGCAGCGGUAA
SEQ ID NO 267	UUUUCAAAUUUUGGGCAGCGGUAAU
SEQ ID NO 268	UUUCAAAUUUUGGGCAGCGGUAAUG
SEQ ID NO 269	UUCAAAUUUUGGGCAGCGGUAAUGA
SEQ ID NO 270	UCAAAUUUUGGGCAGCGGUAAUGAG
SEQ ID NO 271	CAAAUUUUGGGCAGCGGUAAUGAGU
SEQ ID NO 272	AAAUUUUGGGCAGCGGUAAUGAGUU
SEQ ID NO 273	AAUUUUGGGCAGCGGUAAUGAGUUC
SEQ ID NO 274	AUUUUGGGCAGCGGUAAUGAGUUCU
SEQ ID NO 275	UUUUGGGCAGCGGUAAUGAGUUCU
SEQ ID NO 276	UUUGGGCAGCGGUAAUGAGUUCUUC
SEQ ID NO 277	UUGGGCAGCGGUAAUGAGUUCUUCC
SEQ ID NO 278	UGGGCAGCGGUAAUGAGUUCUUCCA

TABLE 5-continued

oligonucleotides for skipping DMD Gene Exon 52

SEQ ID NO 279	GGGCAGCGGUAAUGAGUUCUUCCAA
SEQ ID NO 280	GGCAGCGGUAAUGAGUUCUUCCAAC
SEQ ID NO 281	GCAGCGGUAAUGAGUUCUUCCAACU
SEQ ID NO 282	CAGCGGUAAUGAGUUCUUCCAACUG
SEQ ID NO 283	AGCGGUAAUGAGUUCUUCCAACUGG
SEQ ID NO 284	GCGGUAAUGAGUUCUUCCAACUGGG
SEQ ID NO 285	CGGUAAUGAGUUCUUCCAACUGGGG
SEQ ID NO 286	GGUAAUGAGUUCUUCCAACUGGGGA
SEQ ID NO 287	GGUAAUGAGUUCUUCCAACUGG
SEQ ID NO 288	GUAAUGAGUUCUUCCAACUGGGGAC
SEQ ID NO 289	UAAUGAGUUCUUCCAACUGGGGACG
SEQ ID NO 290	AAUGAGUUCUUCCAACUGGGGACGC
SEQ ID NO 291	AUGAGUUCUUCCAACUGGGGACGCC
SEQ ID NO 292	UGAGUUCUUCCAACUGGGGACGCCU
SEQ ID NO 293	GAGUUCUUCCAACUGGGGACGCCUC
SEQ ID NO 294	AGUUCUUCCAACUGGGGACGCCUCU
SEQ ID NO 295	GUUCUUCCAACUGGGGACGCCUCUG
SEQ ID NO 296	UUCUUCCAACUGGGGACGCCUCUGU
SEQ ID NO 297	UCUUCCAACUGGGGACGCCUCUGUU
SEQ ID NO 298	CUUCCAACUGGGGACGCCUCUGUUC
SEQ ID NO 299 PS236	UUCCAACUGGGGACGCCUCUGUUCC
SEQ ID NO 300	UCCAACUGGGGACGCCUCUGUUCCA
SEQ ID NO 301	CCAACUGGGGACGCCUCUGUUCCAA
SEQ ID NO 302	CAACUGGGGACGCCUCUGUUCCAAA
SEQ ID NO 303	AACUGGGGACGCCUCUGUUCCAAAU
SEQ ID NO 304	ACUGGGGACGCCUCUGUUCCAAAUC
SEQ ID NO 305	CUGGGGACGCCUCUGUUCCAAAUCC
SEQ ID NO 306	UGGGGACGCCUCUGUUCCAAAUCCU
SEQ ID NO 307	GGGGACGCCUCUGUUCCAAAUCCUG
SEQ ID NO 308	GGGACGCCUCUGUUCCAAAUCCUGC
SEQ ID NO 309	GGACGCCUCUGUUCCAAAUCCUGCA
SEQ ID NO 310	GACGCCUCUGUUCCAAAUCCUGCAU

TABLE 6

oligonucleotides for skipping DMD Gene Exon 53

SEQ ID NO 311	CUCUGGCCUGUCCUAAGACCUGCUC
SEQ ID NO 312	UCUGGCCUGUCCUAAGACCUGCUCA
SEQ ID NO 313	CUGGCCUGUCCUAAGACCUGCUCAG
SEQ ID NO 314	UGGCCUGUCCUAAGACCUGCUCAGC
SEQ ID NO 315	GGCCUGUCCUAAGACCUGCUCAGCU
SEQ ID NO 316	GCCUGUCCUAAGACCUGCUCAGCUU
SEQ ID NO 317	CCUGUCCUAAGACCUGCUCAGCUUC
SEQ ID NO 318	CUGUCCUAAGACCUGCUCAGCUUCU
SEQ ID NO 319	UGUCCUAAGACCUGCUCAGCUUCUU
SEQ ID NO 320	GUCCUAAGACCUGCUCAGCUUCUUC
SEQ ID NO 321	UCCUAAGACCUGCUCAGCUUCUUCC
SEQ ID NO 322	CCUAAGACCUGCUCAGCUUCUUCCU
SEQ ID NO 323	CUAAGACCUGCUCAGCUUCUUCCUU
SEQ ID NO 324	UAAGACCUGCUCAGCUUCUUCCUUA
SEQ ID NO 325	AAGACCUGCUCAGCUUCUUCCUUAG
SEQ ID NO 326	AGACCUGCUCAGCUUCUUCCUUAGC
SEQ ID NO 327	GACCUGCUCAGCUUCUUCCUUAGCU
SEQ ID NO 328	ACCUGCUCAGCUUCUUCCUUAGCUU
SEQ ID NO 329	CCUGCUCAGCUUCUUCCUUAGCUUC
SEQ ID NO 330	CUGCUCAGCUUCUUCCUUAGCUUCC
SEQ ID NO 331	UGCUCAGCUUCUUCCUUAGCUUCCA
SEQ ID NO 332	GCUCAGCUUCUUCCUUAGCUUCCAG
SEQ ID NO 333	CUCAGCUUCUUCCUUAGCUUCCAGC
SEQ ID NO 334	UCAGCUUCUUCCUUAGCUUCCAGCC
SEQ ID NO 335	CAGCUUCUUCCUUAGCUUCCAGCCA
SEQ ID NO 336	AGCUUCUUCCUUAGCUUCCAGCCAU
SEQ ID NO 337	GCUUCUUCCUUAGCUUCCAGCCAUU
SEQ ID NO 338	CUUCUUCCUUAGCUUCCAGCCAUUG
SEQ ID NO 339	UUCUUCCUUAGCUUCCAGCCAUUGU
SEQ ID NO 340	UCUUCCUUAGCUUCCAGCCAUUGUG
SEQ ID NO 341	CUUCCUUAGCUUCCAGCCAUUGUGU
SEQ ID NO 342	UUCCUUAGCUUCCAGCCAUUGUGUU
SEQ ID NO 343	UCCUUAGCUUCCAGCCAUUGUGUUG
SEQ ID NO 344	CCUUAGCUUCCAGCCAUUGUGUUGA
SEQ ID NO 345	CUUAGCUUCCAGCCAUUGUGUUGAA
SEQ ID NO 346	UUAGCUUCCAGCCAUUGUGUUGAAU
SEQ ID NO 347	UAGCUUCCAGCCAUUGUGUUGAAUC

TABLE 6-continued

oligonucleotides for skipping DMD Gene Exon 53	
SEQ ID NO 348	AGCUUCCAGCCAUUGUGUUGAAUCC
SEQ ID NO 349	GCUUCCAGCCAUUGUGUUGAAUCCU
SEQ ID NO 350	CUUCCAGCCAUUGUGUUGAAUCCUU
SEQ ID NO 351	UUCCAGCCAUUGUGUUGAAUCCUUU
SEQ ID NO 352	UCCAGCCAUUGUGUUGAAUCCUUUA
SEQ ID NO 353	CCAGCCAUUGUGUUGAAUCCUUUAA
SEQ ID NO 354	CAGCCAUUGUGUUGAAUCCUUUAAC
SEQ ID NO 355	AGCCAUUGUGUUGAAUCCUUUAACA
SEQ ID NO 356	GCCAUUGUGUUGAAUCCUUUAACAU
SEQ ID NO 357	CCAUUGUGUUGAAUCCUUUAACAUU
SEQ ID NO 358	CAUUGUGUUGAAUCCUUUAACAUUU

TABLE 7

oligonucleotides for skipping other exons of the DMD gene as identified	
DMD Gene Exon 6	
SEQ ID NO 359	CAUUUUUGACCUACAUGUGG
SEQ ID NO 360	UUUGACCUACAUGUGGAAAG
SEQ ID NO 361	UACAUUUUUGACCUACAUGUGGAAA G
SEQ ID NO 362	GGUCUCCUUACCUAUGA
SEQ ID NO 363	UCUUACCUAUGACUAUGGAUGAGA
SEQ ID NO 364	AUUUUUGACCUACAUGGGAAAG
SEQ ID NO 365	UACGAGUUGAUUGUCGGACCCAG
SEQ ID NO 366	GUGGUCUCCUUACCUAUGACUGUGG
SEQ ID NO 367	UGUCUCAGUAAUCUUCUUACCUAU
DMD Gene Exon 7	
SEQ ID NO 368	UGCAUGUUCCAGUCGUUGUGUGG
SEQ ID NO 369	CACUAUUCCAGUCAAAUAGGUCUGG
SEQ ID NO 370	AUUUACCAACCUUCAGGAUCGAGUA
SEQ ID NO 371	GGCCUAAAACACAUACACAUA
DMD Gene Exon 11	
SEQ ID NO 372	CCCUGAGGCAUUCCCAUCUUGAAU
SEQ ID NO 373	AGGACUUACUUGCUUUGUUU
SEQ ID NO 374	CUUGAAUUUAGGAGAUUCAUCUG
SEQ ID NO 375	CAUCUUCUGAUAAUUUUCCUGUU

TABLE 7-continued

oligonucleotides for skipping other exons of the DMD gene as identified	
DMD Gene Exon 17	
SEQ ID NO 376	CCAUUACAGUUGUCUGUGUU
SEQ ID NO 377	UGACAGCCUGUGAAAUCUGUGAG
SEQ ID NO 378	UAAUCUGCCUCUUCUUUUGG
DMD Gene Exon 19	
SEQ ID NO 379	CAGCAGUAGUUGUCAUCUGC
SEQ ID NO 380	GCCUGAGCUGAUCUGCUGGCAUCUUGC
SEQ ID NO 381	GCCUGAGCUGAUCUGCUGGCAUCUUGCAGUU
SEQ ID NO 382	UCUGCUGGCAUCUUGC
DMD Gene Exon 21	
SEQ ID NO 383	GCCGGUUGACUUCAUCCUGUGC
SEQ ID NO 384	GUCUGCAUCCAGGAACAUGGGUC
SEQ ID NO 385	UACUUACUGUCUGUAGCUCUUUCU
SEQ ID NO 386	CUGCAUCCAGGAACAUGGGUCC
SEQ ID NO 387	GUUGAAGAUCUGAUAGCCGGUUGA
DMD Gene Exon 44	
SEQ ID NO 388	UCAGCUUCUGUUAGCCACUG
SEQ ID NO 389	UUCAGCUUCUGUUAGCCACU
SEQ ID NO 390	UUCAGCUUCUGUUAGCCACUG
SEQ ID NO 391	UCAGCUUCUGUUAGCCACUGA
SEQ ID NO 392	UUCAGCUUCUGUUAGCCACUGA
SEQ ID NO 393	UCAGCUUCUGUUAGCCACUGA
SEQ ID NO 394	UUCAGCUUCUGUUAGCCACUGA
SEQ ID NO 395	UCAGCUUCUGUUAGCCACUGAU
SEQ ID NO 396	UUCAGCUUCUGUUAGCCACUGAU
SEQ ID NO 397	UCAGCUUCUGUUAGCCACUGAUU
SEQ ID NO 398	UUCAGCUUCUGUUAGCCACUGAUU
SEQ ID NO 399	UCAGCUUCUGUUAGCCACUGAUUA
SEQ ID NO 400	UUCAGCUUCUGUUAGCCACUGAUA
SEQ ID NO 401	UCAGCUUCUGUUAGCCACUGAUUAA
SEQ ID NO 402	UUCAGCUUCUGUUAGCCACUGAUUAA
SEQ ID NO 403	UCAGCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 404	UUCAGCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 405	CAGCUUCUGUUAGCCACUG
SEQ ID NO 406	CAGCUUCUGUUAGCCACUGAU
SEQ ID NO 407	AGCUUCUGUUAGCCACUGAUU

TABLE 7-continued

oligonucleotides for skipping other exons of the DMD gene as identified	
SEQ ID NO 408	CAGCUUCUGUUAGCCACUGAUU
SEQ ID NO 409	AGCUUCUGUUAGCCACUGAUUA
SEQ ID NO 410	CAGCUUCUGUUAGCCACUGAUUA
SEQ ID NO 411	AGCUUCUGUUAGCCACUGAUUAA
SEQ ID NO 412	CAGCUUCUGUUAGCCACUGAUUAA
SEQ ID NO 413	AGCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 414	CAGCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 415	AGCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 416	AGCUUCUGUUAGCCACUGAU
SEQ ID NO 417	GCUUCUGUUAGCCACUGAUU
SEQ ID NO 418	AGCUUCUGUUAGCCACUGAUU
SEQ ID NO 419	GCUUCUGUUAGCCACUGAUUA
SEQ ID NO 420	AGCUUCUGUUAGCCACUGAUUA
SEQ ID NO 421	GCUUCUGUUAGCCACUGAUUAA
SEQ ID NO 422	AGCUUCUGUUAGCCACUGAUUAA
SEQ ID NO 423	GCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 424	AGCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 425	GCUUCUGUUAGCCACUGAUUAAA
SEQ ID NO 426	CCAUUUGUAUUUAGCAUGUUCCC
SEQ ID NO 427	AGAUACCAUUUGUAUUUAGC
SEQ ID NO 428	GCCAUUUCUCAACAGAUCU
SEQ ID NO 429	GCCAUUUCUCAACAGAUCUGUCA
SEQ ID NO 430	AUUCUCAGGAAUUUGUGUCUUUC
SEQ ID NO 431	UCUCAGGAAUUUGUGUCUUUC
SEQ ID NO 432	GUUCAGCUUCUGUUAGCC
SEQ ID NO 433	CUGAUUAAAUAUCUUUAUAU C
SEQ ID NO 434	GCCGCCAUUUCUCAACAG
SEQ ID NO 435	GUAUUUAGCAUGUUCCCA
SEQ ID NO 436	CAGGAAUUUGUGUCUUUC
DMD Gene Exon 45	
SEQ ID NO 437	UUUGCCGCUGCCCAAUGCCAUCCUG
SEQ ID NO 438	AUUCAAUGUUCUGACAACAGUUUGC
SEQ ID NO 439	CCAGUUGCAUUCAAUGUUCUGACAA
SEQ ID NO 440	CAGUUGCAUUCAAUGUUCUGAC
SEQ ID NO 441	AGUUGCAUUCAAUGUUCUGA
SEQ ID NO 442	GAUUGCUGAAUUAUUUCUUCC
SEQ ID NO 443	GAUUGCUGAAUUAUUUCUUCCCCAG

TABLE 7-continued

oligonucleotides for skipping other exons of the DMD gene as identified	
SEQ ID NO 444	AUUGCUGAAUUAUUUCUUCCCCAGU
SEQ ID NO 445	UUGCUGAAUUAUUUCUUCCCCAGUU
SEQ ID NO 446	UGCUGAAUUAUUUCUUCCCCAGUUG
SEQ ID NO 447	GCUGAAUUAUUUCUUCCCCAGUUGC
SEQ ID NO 448	CUGAAUUAUUUCUUCCCCAGUUGCA
SEQ ID NO 449	UGAAUUAUUUCUUCCCCAGUUGCAU
SEQ ID NO 450	GAAUUAUUUCUUCCCCAGUUGCAUU
SEQ ID NO 451	AAUUAUUUCUUCCCCAGUUGCAUUC
SEQ ID NO 452	AUUAUUUCUUCCCCAGUUGCAUUCA
SEQ ID NO 453	UUAUUUCUUCCCCAGUUGCAUUCAA
SEQ ID NO 454	UAUUUCUUCCCCAGUUGCAUUCAAU
SEQ ID NO 455	AUUUCUUCCCCAGUUGCAUUCAAUG
SEQ ID NO 456	UUUCUUCCCCAGUUGCAUUCAAUGU
SEQ ID NO 457	UUCUUCCCCAGUUGCAUUCAAUGUU
SEQ ID NO 458	UCUUCCCCAGUUGCAUUCAAUGUUC
SEQ ID NO 459	CUUCCCCAGUUGCAUUCAAUGUUCU
SEQ ID NO 460	UUCCCCAGUUGCAUUCAAUGUUCUG
SEQ ID NO 461	UCCCCAGUUGCAUUCAAUGUUCUGA
SEQ ID NO 462	CCCCAGUUGCAUUCAAUGUUCUGAC
SEQ ID NO 463	CCCAGUUGCAUUCAAUGUUCUGACA
SEQ ID NO 464	CCAGUUGCAUUCAAUGUUCUGACAA
SEQ ID NO 465	CAGUUGCAUUCAAUGUUCUGACAAC
SEQ ID NO 466	AGUUGCAUUCAAUGUUCUGACAACA
SEQ ID NO 467	UCC UGU AGA AUA CUG GCA UC
SEQ ID NO 468	UGCAGACCUCCUGCCACCGCAGAUUCA
SEQ ID NO 469	UUGCAGACCUCCUGCCACCGCAGAUUCAGGCUUC
SEQ ID NO 470	GUUGCAUUCAAUGUUCUGACAACAG
SEQ ID NO 471	UUGCAUUCAAUGUUCUGACAACAGU
SEQ ID NO 472	UGCAUUCAAUGUUCUGACAACAGUU
SEQ ID NO 473	GCAUUCAAUGUUCUGACAACAGUUU
SEQ ID NO 474	CAUUCAAUGUUCUGACAACAGUUUG
SEQ ID NO 475	AUUCAAUGUUCUGACAACAGUUUGC
SEQ ID NO 476	UCAAUGUUCUGACAACAGUUUGCCG
SEQ ID NO 477	CAAUGUUCUGACAACAGUUUGCCGC
SEQ ID NO 478	AAUGUUCUGACAACAGUUUGCCGCU
SEQ ID NO 479	AUGUUCUGACAACAGUUUGCCGCUG

TABLE 7-continued

oligonucleotides for skipping other exons of the DMD gene as identified	
SEQ ID NO 480	UGUUCUGACAACAGUUUGCCGCUGC
SEQ ID NO 481	GUUCUGACAACAGUUUGCCGCUGCC
SEQ ID NO 482	UUCUGACAACAGUUUGCCGCUGCCC
SEQ ID NO 483	UCUGACAACAGUUUGCCGCUGCCCA
SEQ ID NO 484	CUGACAACAGUUUGCCGCUGCCCAA
SEQ ID NO 485	UGACAACAGUUUGCCGCUGCCCAAU
SEQ ID NO 486	GACAACAGUUUGCCGCUGCCCAAUG
SEQ ID NO 487	ACAACAGUUUGCCGCUGCCCAAUGC
SEQ ID NO 488	CAACAGUUUGCCGCUGCCCAAUGCC
SEQ ID NO 489	AACAGUUUGCCGCUGCCCAAUGCCA
SEQ ID NO 490	ACAGUUUGCCGCUGCCCAAUGCCAU
SEQ ID NO 491	CAGUUUGCCGCUGCCCAAUGCCAUC
SEQ ID NO 492	AGUUUGCCGCUGCCCAAUGCCAUCC
SEQ ID NO 493	GUUUGCCGCUGCCCAAUGCCAUCCU
SEQ ID NO 494	UUUGCCGCUGCCCAAUGCCAUCCUG
SEQ ID NO 495	UUGCCGCUGCCCAAUGCCAUCCUGG
SEQ ID NO 496	UGCCGCUGCCCAAUGCCAUCCUGGA
SEQ ID NO 497	GCCGCUGCCCAAUGCCAUCCUGGAG
SEQ ID NO 498	CCGCUGCCCAAUGCCAUCCUGGAGU
SEQ ID NO 499	CGCUGCCCAAUGCCAUCCUGGAGUU
SEQ ID NO 500	UGUUUUUGAGGAUUGCUGAA
SEQ ID NO 501	UGUUCUGACAACAGUUUGCCGCUGCCCAAUGCCA UCCUGG
DMD Gene Exon 55	
SEQ ID NO 502	CUGUUGCAGUAAUCUAUGAG
SEQ ID NO 503	UGCAGUAAUCUAUGAGUUUC
SEQ ID NO 504	GAGUCUUCUAGGAGCCUU
SEQ ID NO 505	UGCCAUUGUUUCAUCAGCUCUUU
SEQ ID NO 506	UCCUGUAGGACAUUGGCAGU
SEQ ID NO 507	CUUGGAGUCUUCUAGGAGCC
DMD Gene Exon 57	
SEQ ID NO 508	UAGGUGCCUGCCGGCUU
SEQ ID NO 509	UUCAGCUGUAGCCACACC
SEQ ID NO 510	CUGAACUGCUGGAAAGUCGCC
SEQ ID NO 511	CUGGCUUCCAAAUGGGACCUGAAAAAGAAC

TABLE 7-continued

oligonucleotides for skipping other exons of the DMD gene as identified	
DMD Gene Exon 59	
SEQ ID NO 512	CAAUUUUUCCCACUCAGUAUU
SEQ ID NO 513	UUGAAGUUCCUGGAGUCUU
SEQ ID NO 514	UCCUCAGGAGGCAGCUCUAAAU
DMD Gene Exon 62	
SEQ ID NO 515	UGGCUCUCUCCCAGGG
SEQ ID NO 516	GAGAUGGCUCUCUCCCAGGGACCCUGG
SEQ ID NO 517	GGGCACUUUGUUUGGCG
DMD Gene Exon 63	
SEQ ID NO 518	GGUCCCAGCAAGUUGUUUG
SEQ ID NO 519	UGGGAUGGUCCCAGCAAGUUGUUUG
SEQ ID NO 520	GUAGAGCUCUGUCAUUUUGGG
DMD Gene Exon 65	
SEQ ID NO 521	GCUCAAGAGAUCCACUGCAAAAAAC
SEQ ID NO 522	GCCAUACGUACGUAUCAUAAACAUUC
SEQ ID NO 523	UCUGCAGGAUAUCCAUGGGCUGGUC
DMD Gene Exon 66	
SEQ ID NO 524	GAUCCUCCCUGUUCGUCCCCUAUUAUG
DMD Gene Exon 69	
SEQ ID NO 525	UGCUUUAGACUCCUGUACCUGAUA
DMD Gene Exon 75	
SEQ ID NO 526	GGCGGCCUUUGUGUUGAC
SEQ ID NO 527	GGACAGGCCUUUAUGUUCGUGCUGC
SEQ ID NO 528	CCUUUAUGUUCGUGCUGCU

FIGURE LEGENDS

[0109] FIG. **1**. In human control myotubes, a series of AONs (PS237, PS238, and PS240; SEQ ID NO 65, 66, 16 respectively) targeting exon 43 was tested at 500 nM. PS237 (SEQ ID NO 65) reproducibly induced highest levels of exon 43 skipping. (M: DNA size marker; NT: non-treated cells)

[0110] FIG. **2**. In myotubes from a DMD patient with an exon 45 deletion, a series of AONs (PS177, PS179, PS181, and PS182; SEQ ID NO 91, 70, 110, and 117 respectively) targeting exon 46 was tested at two different concentrations (50 and 150 nM). PS182 (SEQ ID NO 117) reproducibly induced highest levels of exon 46 skipping. (M: DNA size marker)

[0111] FIG. **3**. In human control myotubes, a series of AONs (PS245, PS246, PS247, and PS248; SEQ ID NO 167, 165, 166, and 127 respectively) targeting exon 50 was tested

at 500 nM. PS248 (SEQ ID NO 127) reproducibly induced highest levels of exon 50 skipping. (M: DNA size marker; NT: non-treated cells).

[0112] FIG. **4**. In human control myotubes, two novel AONs (PS232 and PS236; SEQ ID NO 246 and 299 respectively) targeting exon 52 were tested at two different concentrations (200 and 500 nM) and directly compared to a previously described AON (52-1). PS236 (SEQ ID NO 299) reproducibly induced highest levels of exon 52 skipping. (M: DNA size marker; NT: non-treated cells).

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 535

<210> SEQ ID NO 1
<211> LENGTH: 3685
<212> TYPE: PRT
<213> ORGANISM: homo sapiens

<400> SEQUENCE: 1

```
Met Leu Trp Trp Glu Glu Val Glu Asp Cys Tyr Glu Arg Glu Asp Val
1               5                  10                  15

Gln Lys Lys Thr Phe Thr Lys Trp Val Asn Ala Gln Phe Ser Lys Phe
            20                  25                  30

Gly Lys Gln His Ile Glu Asn Leu Phe Ser Asp Leu Gln Asp Gly Arg
        35                  40                  45

Arg Leu Leu Asp Leu Leu Glu Gly Leu Thr Gly Gln Lys Leu Pro Lys
    50                  55                  60

Glu Lys Gly Ser Thr Arg Val His Ala Leu Asn Asn Val Asn Lys Ala
65                  70                  75                  80

Leu Arg Val Leu Gln Asn Asn Asn Val Asp Leu Val Asn Ile Gly Ser
                85                  90                  95

Thr Asp Ile Val Asp Gly Asn His Lys Leu Thr Leu Gly Leu Ile Trp
            100                 105                 110

Asn Ile Ile Leu His Trp Gln Val Lys Asn Val Met Lys Asn Ile Met
        115                 120                 125

Ala Gly Leu Gln Gln Thr Asn Ser Glu Lys Ile Leu Leu Ser Trp Val
    130                 135                 140

Arg Gln Ser Thr Arg Asn Tyr Pro Gln Val Asn Val Ile Asn Phe Thr
145                 150                 155                 160

Thr Ser Trp Ser Asp Gly Leu Ala Leu Asn Ala Leu Ile His Ser His
                165                 170                 175

Arg Pro Asp Leu Phe Asp Trp Asn Ser Val Val Cys Gln Gln Ser Ala
            180                 185                 190

Thr Gln Arg Leu Glu His Ala Phe Asn Ile Ala Arg Tyr Gln Leu Gly
        195                 200                 205

Ile Glu Lys Leu Leu Asp Pro Glu Asp Val Asp Thr Thr Tyr Pro Asp
    210                 215                 220

Lys Lys Ser Ile Leu Met Tyr Ile Thr Ser Leu Phe Gln Val Leu Pro
225                 230                 235                 240

Gln Gln Val Ser Ile Glu Ala Ile Gln Glu Val Glu Met Leu Pro Arg
                245                 250                 255

Pro Pro Lys Val Thr Lys Glu Glu His Phe Gln Leu His His Gln Met
            260                 265                 270

His Tyr Ser Gln Gln Ile Thr Val Ser Leu Ala Gln Gly Tyr Glu Arg
        275                 280                 285

Thr Ser Ser Pro Lys Pro Arg Phe Lys Ser Tyr Ala Tyr Thr Gln Ala
    290                 295                 300
```

-continued

```
Ala Tyr Val Thr Thr Ser Asp Pro Thr Arg Ser Pro Phe Pro Ser Gln
305                 310                 315                 320

His Leu Glu Ala Pro Glu Asp Lys Ser Phe Gly Ser Ser Leu Met Glu
                325                 330                 335

Ser Glu Val Asn Leu Asp Arg Tyr Gln Thr Ala Leu Glu Glu Val Leu
            340                 345                 350

Ser Trp Leu Leu Ser Ala Glu Asp Thr Leu Gln Ala Gln Gly Glu Ile
        355                 360                 365

Ser Asn Asp Val Glu Val Val Lys Asp Gln Phe His Thr His Glu Gly
    370                 375                 380

Tyr Met Met Asp Leu Thr Ala His Gln Gly Arg Val Gly Asn Ile Leu
385                 390                 395                 400

Gln Leu Gly Ser Lys Leu Ile Gly Thr Gly Lys Leu Ser Glu Asp Glu
                405                 410                 415

Glu Thr Glu Val Gln Glu Gln Met Asn Leu Leu Asn Ser Arg Trp Glu
            420                 425                 430

Cys Leu Arg Val Ala Ser Met Glu Lys Gln Ser Asn Leu His Arg Val
        435                 440                 445

Leu Met Asp Leu Gln Asn Gln Lys Leu Lys Glu Leu Asn Asp Trp Leu
    450                 455                 460

Thr Lys Thr Glu Glu Arg Thr Arg Lys Met Glu Glu Glu Pro Leu Gly
465                 470                 475                 480

Pro Asp Leu Glu Asp Leu Lys Arg Gln Val Gln Gln His Lys Val Leu
                485                 490                 495

Gln Glu Asp Leu Glu Gln Glu Gln Val Arg Val Asn Ser Leu Thr His
            500                 505                 510

Met Val Val Val Val Asp Glu Ser Ser Gly Asp His Ala Thr Ala Ala
        515                 520                 525

Leu Glu Glu Gln Leu Lys Val Leu Gly Asp Arg Trp Ala Asn Ile Cys
    530                 535                 540

Arg Trp Thr Glu Asp Arg Trp Val Leu Leu Gln Asp Ile Leu Leu Lys
545                 550                 555                 560

Trp Gln Arg Leu Thr Glu Glu Gln Cys Leu Phe Ser Ala Trp Leu Ser
                565                 570                 575

Glu Lys Glu Asp Ala Val Asn Lys Ile His Thr Thr Gly Phe Lys Asp
            580                 585                 590

Gln Asn Glu Met Leu Ser Ser Leu Gln Lys Leu Ala Val Leu Lys Ala
        595                 600                 605

Asp Leu Glu Lys Lys Lys Gln Ser Met Gly Lys Leu Tyr Ser Leu Lys
    610                 615                 620

Gln Asp Leu Leu Ser Thr Leu Lys Asn Lys Ser Val Thr Gln Lys Thr
625                 630                 635                 640

Glu Ala Trp Leu Asp Asn Phe Ala Arg Cys Trp Asp Asn Leu Val Gln
                645                 650                 655

Lys Leu Glu Lys Ser Thr Ala Gln Ile Ser Gln Ala Val Thr Thr Thr
            660                 665                 670

Gln Pro Ser Leu Thr Gln Thr Thr Val Met Glu Thr Val Thr Thr Val
        675                 680                 685

Thr Thr Arg Glu Gln Ile Leu Val Lys His Ala Gln Glu Glu Leu Pro
    690                 695                 700

Pro Pro Pro Pro Gln Lys Lys Arg Gln Ile Thr Val Asp Ser Glu Ile
```

-continued

```
705                 710                 715                 720

Arg Lys Arg Leu Asp Val Asp Ile Thr Glu Leu His Ser Trp Ile Thr
                725                 730                 735

Arg Ser Glu Ala Val Leu Gln Ser Pro Glu Phe Ala Ile Phe Arg Lys
            740                 745                 750

Glu Gly Asn Phe Ser Asp Leu Lys Glu Lys Val Asn Ala Ile Glu Arg
        755                 760                 765

Glu Lys Ala Glu Lys Phe Arg Lys Leu Gln Asp Ala Ser Arg Ser Ala
    770                 775                 780

Gln Ala Leu Val Glu Gln Met Val Asn Glu Gly Val Asn Ala Asp Ser
785                 790                 795                 800

Ile Lys Gln Ala Ser Glu Gln Leu Asn Ser Arg Trp Ile Glu Phe Cys
                805                 810                 815

Gln Leu Leu Ser Glu Arg Leu Asn Trp Leu Glu Tyr Gln Asn Asn Ile
            820                 825                 830

Ile Ala Phe Tyr Asn Gln Leu Gln Gln Leu Glu Gln Met Thr Thr Thr
        835                 840                 845

Ala Glu Asn Trp Leu Lys Ile Gln Pro Thr Thr Pro Ser Glu Pro Thr
    850                 855                 860

Ala Ile Lys Ser Gln Leu Lys Ile Cys Lys Asp Glu Val Asn Arg Leu
865                 870                 875                 880

Ser Gly Leu Gln Pro Gln Ile Glu Arg Leu Lys Ile Gln Ser Ile Ala
                885                 890                 895

Leu Lys Glu Lys Gly Gln Gly Pro Met Phe Leu Asp Ala Asp Phe Val
            900                 905                 910

Ala Phe Thr Asn His Phe Lys Gln Val Phe Ser Asp Val Gln Ala Arg
        915                 920                 925

Glu Lys Glu Leu Gln Thr Ile Phe Asp Thr Leu Pro Pro Met Arg Tyr
    930                 935                 940

Gln Glu Thr Met Ser Ala Ile Arg Thr Trp Val Gln Gln Ser Glu Thr
945                 950                 955                 960

Lys Leu Ser Ile Pro Gln Leu Ser Val Thr Asp Tyr Glu Ile Met Glu
                965                 970                 975

Gln Arg Leu Gly Glu Leu Gln Ala Leu Gln Ser Ser Leu Gln Glu Gln
            980                 985                 990

Gln Ser Gly Leu Tyr Tyr Leu Ser  Thr Thr Val Lys Glu  Met Ser Lys
        995                 1000                1005

Lys Ala  Pro Ser Glu Ile Ser  Arg Lys Tyr Gln Ser  Glu Phe Glu
    1010                1015                1020

Glu Ile  Glu Gly Arg Trp Lys  Lys Leu Ser Ser Gln  Leu Val Glu
    1025                1030                1035

His Cys  Gln Lys Leu Glu Glu  Gln Met Asn Lys Leu  Arg Lys Ile
    1040                1045                1050

Gln Asn  His Ile Gln Thr Leu  Lys Lys Trp Met Ala  Glu Val Asp
    1055                1060                1065

Val Phe  Leu Lys Glu Glu Trp  Pro Ala Leu Gly Asp  Ser Glu Ile
    1070                1075                1080

Leu Lys  Lys Gln Leu Lys Gln  Cys Arg Leu Leu Val  Ser Asp Ile
    1085                1090                1095

Gln Thr  Ile Gln Pro Ser Leu  Asn Ser Val Asn Glu  Gly Gly Gln
    1100                1105                1110
```

-continued

```
Lys Ile  Lys Asn Glu Ala Glu  Pro Glu Phe Ala Ser  Arg Leu Glu
    1115                1120                1125

Thr Glu  Leu Lys Glu Leu Asn  Thr Gln Trp Asp His  Met Cys Gln
    1130                1135                1140

Gln Val  Tyr Ala Arg Lys Glu  Ala Leu Lys Gly Gly  Leu Glu Lys
    1145                1150                1155

Thr Val  Ser Leu Gln Lys Asp  Leu Ser Glu Met His  Glu Trp Met
    1160                1165                1170

Thr Gln  Ala Glu Glu Glu Tyr  Leu Glu Arg Asp Phe  Glu Tyr Lys
    1175                1180                1185

Thr Pro  Asp Glu Leu Gln Lys  Ala Val Glu Glu Met  Lys Arg Ala
    1190                1195                1200

Lys Glu  Glu Ala Gln Gln Lys  Glu Ala Lys Val Lys  Leu Leu Thr
    1205                1210                1215

Glu Ser  Val Asn Ser Val Ile  Ala Gln Ala Pro Pro  Val Ala Gln
    1220                1225                1230

Glu Ala  Leu Lys Lys Glu Leu  Glu Thr Leu Thr Thr  Asn Tyr Gln
    1235                1240                1245

Trp Leu  Cys Thr Arg Leu Asn  Gly Lys Cys Lys Thr  Leu Glu Glu
    1250                1255                1260

Val Trp  Ala Cys Trp His Glu  Leu Leu Ser Tyr Leu  Glu Lys Ala
    1265                1270                1275

Asn Lys  Trp Leu Asn Glu Val  Glu Phe Lys Leu Lys  Thr Thr Glu
    1280                1285                1290

Asn Ile  Pro Gly Gly Ala Glu  Glu Ile Ser Glu Val  Leu Asp Ser
    1295                1300                1305

Leu Glu  Asn Leu Met Arg His  Ser Glu Asp Asn Pro  Asn Gln Ile
    1310                1315                1320

Arg Ile  Leu Ala Gln Thr Leu  Thr Asp Gly Gly Val  Met Asp Glu
    1325                1330                1335

Leu Ile  Asn Glu Glu Leu Glu  Thr Phe Asn Ser Arg  Trp Arg Glu
    1340                1345                1350

Leu His  Glu Glu Ala Val Arg  Arg Gln Lys Leu Leu  Glu Gln Ser
    1355                1360                1365

Ile Gln  Ser Ala Gln Glu Thr  Glu Lys Ser Leu His  Leu Ile Gln
    1370                1375                1380

Glu Ser  Leu Thr Phe Ile Asp  Lys Gln Leu Ala Ala  Tyr Ile Ala
    1385                1390                1395

Asp Lys  Val Asp Ala Ala Gln  Met Pro Gln Glu Ala  Gln Lys Ile
    1400                1405                1410

Gln Ser  Asp Leu Thr Ser His  Glu Ile Ser Leu Glu  Glu Met Lys
    1415                1420                1425

Lys His  Asn Gln Gly Lys Glu  Ala Ala Gln Arg Val  Leu Ser Gln
    1430                1435                1440

Ile Asp  Val Ala Gln Lys Lys  Leu Gln Asp Val Ser  Met Lys Phe
    1445                1450                1455

Arg Leu  Phe Gln Lys Pro Ala  Asn Phe Glu Gln Arg  Leu Gln Glu
    1460                1465                1470

Ser Lys  Met Ile Leu Asp Glu  Val Lys Met His Leu  Pro Ala Leu
    1475                1480                1485
```

-continued

```
Glu Thr  Lys Ser Val Glu Gln  Glu Val Val Gln Ser  Gln Leu Asn
    1490                1495                1500

His Cys  Val Asn Leu Tyr Lys  Ser Leu Ser Glu Val  Lys Ser Glu
    1505                1510                1515

Val Glu  Met Val Ile Lys Thr  Gly Arg Gln Ile Val  Gln Lys Lys
    1520                1525                1530

Gln Thr  Glu Asn Pro Lys Glu  Leu Asp Glu Arg Val  Thr Ala Leu
    1535                1540                1545

Lys Leu  His Tyr Asn Glu Leu  Gly Ala Lys Val Thr  Glu Arg Lys
    1550                1555                1560

Gln Gln  Leu Glu Lys Cys Leu  Lys Leu Ser Arg Lys  Met Arg Lys
    1565                1570                1575

Glu Met  Asn Val Leu Thr Glu  Trp Leu Ala Ala Thr  Asp Met Glu
    1580                1585                1590

Leu Thr  Lys Arg Ser Ala Val  Glu Gly Met Pro Ser  Asn Leu Asp
    1595                1600                1605

Ser Glu  Val Ala Trp Gly Lys  Ala Thr Gln Lys Glu  Ile Glu Lys
    1610                1615                1620

Gln Lys  Val His Leu Lys Ser  Ile Thr Glu Val Gly  Glu Ala Leu
    1625                1630                1635

Lys Thr  Val Leu Gly Lys Lys  Glu Thr Leu Val Glu  Asp Lys Leu
    1640                1645                1650

Ser Leu  Leu Asn Ser Asn Trp  Ile Ala Val Thr Ser  Arg Ala Glu
    1655                1660                1665

Glu Trp  Leu Asn Leu Leu Leu  Glu Tyr Gln Lys His  Met Glu Thr
    1670                1675                1680

Phe Asp  Gln Asn Val Asp His  Ile Thr Lys Trp Ile  Ile Gln Ala
    1685                1690                1695

Asp Thr  Leu Leu Asp Glu Ser  Glu Lys Lys Lys Pro  Gln Gln Lys
    1700                1705                1710

Glu Asp  Val Leu Lys Arg Leu  Lys Ala Glu Leu Asn  Asp Ile Arg
    1715                1720                1725

Pro Lys  Val Asp Ser Thr Arg  Asp Gln Ala Ala Asn  Leu Met Ala
    1730                1735                1740

Asn Arg  Gly Asp His Cys Arg  Lys Leu Val Glu Pro  Gln Ile Ser
    1745                1750                1755

Glu Leu  Asn His Arg Phe Ala  Ala Ile Ser His Arg  Ile Lys Thr
    1760                1765                1770

Gly Lys  Ala Ser Ile Pro Leu  Lys Glu Leu Glu Gln  Phe Asn Ser
    1775                1780                1785

Asp Ile  Gln Lys Leu Leu Glu  Pro Leu Glu Ala Glu  Ile Gln Gln
    1790                1795                1800

Gly Val  Asn Leu Lys Glu Glu  Asp Phe Asn Lys Asp  Met Asn Glu
    1805                1810                1815

Asp Asn  Glu Gly Thr Val Lys  Glu Leu Leu Gln Arg  Gly Asp Asn
    1820                1825                1830

Leu Gln  Gln Arg Ile Thr Asp  Glu Arg Lys Arg Glu  Glu Ile Lys
    1835                1840                1845

Ile Lys  Gln Gln Leu Leu Gln  Thr Lys His Asn Ala  Leu Lys Asp
    1850                1855                1860

Leu Arg  Ser Gln Arg Arg Lys  Lys Ala Leu Glu Ile  Ser His Gln
```

-continued

```
    1865                1870                1875

Trp Tyr  Gln Tyr Lys Arg Gln  Ala Asp Asp Leu Leu  Lys Cys Leu
    1880                1885                1890

Asp Asp  Ile Glu Lys Lys Leu  Ala Ser Leu Pro Glu  Pro Arg Asp
    1895                1900                1905

Glu Arg  Lys Ile Lys Glu Ile  Asp Arg Glu Leu Gln  Lys Lys Lys
    1910                1915                1920

Glu Glu  Leu Asn Ala Val Arg  Arg Gln Ala Glu Gly  Leu Ser Glu
    1925                1930                1935

Asp Gly  Ala Ala Met Ala Val  Glu Pro Thr Gln Ile  Gln Leu Ser
    1940                1945                1950

Lys Arg  Trp Arg Glu Ile Glu  Ser Lys Phe Ala Gln  Phe Arg Arg
    1955                1960                1965

Leu Asn  Phe Ala Gln Ile His  Thr Val Arg Glu Glu  Thr Met Met
    1970                1975                1980

Val Met  Thr Glu Asp Met Pro  Leu Glu Ile Ser Tyr  Val Pro Ser
    1985                1990                1995

Thr Tyr  Leu Thr Glu Ile Thr  His Val Ser Gln Ala  Leu Leu Glu
    2000                2005                2010

Val Glu  Gln Leu Leu Asn Ala  Pro Asp Leu Cys Ala  Lys Asp Phe
    2015                2020                2025

Glu Asp  Leu Phe Lys Gln Glu  Glu Ser Leu Lys Asn  Ile Lys Asp
    2030                2035                2040

Ser Leu  Gln Gln Ser Ser Gly  Arg Ile Asp Ile Ile  His Ser Lys
    2045                2050                2055

Lys Thr  Ala Ala Leu Gln Ser  Ala Thr Pro Val Glu  Arg Val Lys
    2060                2065                2070

Leu Gln  Glu Ala Leu Ser Gln  Leu Asp Phe Gln Trp  Glu Lys Val
    2075                2080                2085

Asn Lys  Met Tyr Lys Asp Arg  Gln Gly Arg Phe Asp  Arg Ser Val
    2090                2095                2100

Glu Lys  Trp Arg Arg Phe His  Tyr Asp Ile Lys Ile  Phe Asn Gln
    2105                2110                2115

Trp Leu  Thr Glu Ala Glu Gln  Phe Leu Arg Lys Thr  Gln Ile Pro
    2120                2125                2130

Glu Asn  Trp Glu His Ala Lys  Tyr Lys Trp Tyr Leu  Lys Glu Leu
    2135                2140                2145

Gln Asp  Gly Ile Gly Gln Arg  Gln Thr Val Val Arg  Thr Leu Asn
    2150                2155                2160

Ala Thr  Gly Glu Glu Ile Ile  Gln Gln Ser Ser Lys  Thr Asp Ala
    2165                2170                2175

Ser Ile  Leu Gln Glu Lys Leu  Gly Ser Leu Asn Leu  Arg Trp Gln
    2180                2185                2190

Glu Val  Cys Lys Gln Leu Ser  Asp Arg Lys Lys Arg  Leu Glu Glu
    2195                2200                2205

Gln Lys  Asn Ile Leu Ser Glu  Phe Gln Arg Asp Leu  Asn Glu Phe
    2210                2215                2220

Val Leu  Trp Leu Glu Glu Ala  Asp Asn Ile Ala Ser  Ile Pro Leu
    2225                2230                2235

Glu Pro  Gly Lys Glu Gln Gln  Leu Lys Glu Lys Leu  Glu Gln Val
    2240                2245                2250
```

-continued

```
Lys Leu  Leu Val Glu Glu Leu  Pro Leu Arg Gln Gly  Ile Leu Lys
    2255                 2260                 2265

Gln Leu  Asn Glu Thr Gly Gly  Pro Val Leu Val Ser  Ala Pro Ile
    2270                 2275                 2280

Ser Pro  Glu Glu Gln Asp Lys  Leu Glu Asn Lys Leu  Lys Gln Thr
    2285                 2290                 2295

Asn Leu  Gln Trp Ile Lys Val  Ser Arg Ala Leu Pro  Glu Lys Gln
    2300                 2305                 2310

Gly Glu  Ile Glu Ala Gln Ile  Lys Asp Leu Gly Gln  Leu Glu Lys
    2315                 2320                 2325

Lys Leu  Glu Asp Leu Glu Glu  Gln Leu Asn His Leu  Leu Leu Trp
    2330                 2335                 2340

Leu Ser  Pro Ile Arg Asn Gln  Leu Glu Ile Tyr Asn  Gln Pro Asn
    2345                 2350                 2355

Gln Glu  Gly Pro Phe Asp Val  Gln Glu Thr Glu Ile  Ala Val Gln
    2360                 2365                 2370

Ala Lys  Gln Pro Asp Val Glu  Glu Ile Leu Ser Lys  Gly Gln His
    2375                 2380                 2385

Leu Tyr  Lys Glu Lys Pro Ala  Thr Gln Pro Val Lys  Arg Lys Leu
    2390                 2395                 2400

Glu Asp  Leu Ser Ser Glu Trp  Lys Ala Val Asn Arg  Leu Leu Gln
    2405                 2410                 2415

Glu Leu  Arg Ala Lys Gln Pro  Asp Leu Ala Pro Gly  Leu Thr Thr
    2420                 2425                 2430

Ile Gly  Ala Ser Pro Thr Gln  Thr Val Thr Leu Val  Thr Gln Pro
    2435                 2440                 2445

Val Val  Thr Lys Glu Thr Ala  Ile Ser Lys Leu Glu  Met Pro Ser
    2450                 2455                 2460

Ser Leu  Met Leu Glu Val Pro  Ala Leu Ala Asp Phe  Asn Arg Ala
    2465                 2470                 2475

Trp Thr  Glu Leu Thr Asp Trp  Leu Ser Leu Leu Asp  Gln Val Ile
    2480                 2485                 2490

Lys Ser  Gln Arg Val Met Val  Gly Asp Leu Glu Asp  Ile Asn Glu
    2495                 2500                 2505

Met Ile  Ile Lys Gln Lys Ala  Thr Met Gln Asp Leu  Glu Gln Arg
    2510                 2515                 2520

Arg Pro  Gln Leu Glu Glu Leu  Ile Thr Ala Ala Gln  Asn Leu Lys
    2525                 2530                 2535

Asn Lys  Thr Ser Asn Gln Glu  Ala Arg Thr Ile Ile  Thr Asp Arg
    2540                 2545                 2550

Ile Glu  Arg Ile Gln Asn Gln  Trp Asp Glu Val Gln  Glu His Leu
    2555                 2560                 2565

Gln Asn  Arg Arg Gln Gln Leu  Asn Glu Met Leu Lys  Asp Ser Thr
    2570                 2575                 2580

Gln Trp  Leu Glu Ala Lys Glu  Glu Ala Glu Gln Val  Leu Gly Gln
    2585                 2590                 2595

Ala Arg  Ala Lys Leu Glu Ser  Trp Lys Glu Gly Pro  Tyr Thr Val
    2600                 2605                 2610

Asp Ala  Ile Gln Lys Lys Ile  Thr Glu Thr Lys Gln  Leu Ala Lys
    2615                 2620                 2625
```

-continued

```
Asp Leu  Arg Gln Trp Gln Thr  Asn Val Asp Val Ala  Asn Asp Leu
    2630                 2635                 2640

Ala Leu  Lys Leu Leu Arg Asp  Tyr Ser Ala Asp Asp  Thr Arg Lys
    2645                 2650                 2655

Val His  Met Ile Thr Glu Asn  Ile Asn Ala Ser Trp  Arg Ser Ile
    2660                 2665                 2670

His Lys  Arg Val Ser Glu Arg  Glu Ala Ala Leu Glu  Glu Thr His
    2675                 2680                 2685

Arg Leu  Leu Gln Gln Phe Pro  Leu Asp Leu Glu Lys  Phe Leu Ala
    2690                 2695                 2700

Trp Leu  Thr Glu Ala Glu Thr  Thr Ala Asn Val Leu  Gln Asp Ala
    2705                 2710                 2715

Thr Arg  Lys Glu Arg Leu Leu  Glu Asp Ser Lys Gly  Val Lys Glu
    2720                 2725                 2730

Leu Met  Lys Gln Trp Gln Asp  Leu Gln Gly Glu Ile  Glu Ala His
    2735                 2740                 2745

Thr Asp  Val Tyr His Asn Leu  Asp Glu Asn Ser Gln  Lys Ile Leu
    2750                 2755                 2760

Arg Ser  Leu Glu Gly Ser Asp  Asp Ala Val Leu Leu  Gln Arg Arg
    2765                 2770                 2775

Leu Asp  Asn Met Asn Phe Lys  Trp Ser Glu Leu Arg  Lys Lys Ser
    2780                 2785                 2790

Leu Asn  Ile Arg Ser His Leu  Glu Ala Ser Ser Asp  Gln Trp Lys
    2795                 2800                 2805

Arg Leu  His Leu Ser Leu Gln  Glu Leu Leu Val Trp  Leu Gln Leu
    2810                 2815                 2820

Lys Asp  Asp Glu Leu Ser Arg  Gln Ala Pro Ile Gly  Gly Asp Phe
    2825                 2830                 2835

Pro Ala  Val Gln Lys Gln Asn  Asp Val His Arg Ala  Phe Lys Arg
    2840                 2845                 2850

Glu Leu  Lys Thr Lys Glu Pro  Val Ile Met Ser Thr  Leu Glu Thr
    2855                 2860                 2865

Val Arg  Ile Phe Leu Thr Glu  Gln Pro Leu Glu Gly  Leu Glu Lys
    2870                 2875                 2880

Leu Tyr  Gln Glu Pro Arg Glu  Leu Pro Pro Glu Glu  Arg Ala Gln
    2885                 2890                 2895

Asn Val  Thr Arg Leu Leu Arg  Lys Gln Ala Glu Glu  Val Asn Thr
    2900                 2905                 2910

Glu Trp  Glu Lys Leu Asn Leu  His Ser Ala Asp Trp  Gln Arg Lys
    2915                 2920                 2925

Ile Asp  Glu Thr Leu Glu Arg  Leu Gln Glu Leu Gln  Glu Ala Thr
    2930                 2935                 2940

Asp Glu  Leu Asp Leu Lys Leu  Arg Gln Ala Glu Val  Ile Lys Gly
    2945                 2950                 2955

Ser Trp  Gln Pro Val Gly Asp  Leu Leu Ile Asp Ser  Leu Gln Asp
    2960                 2965                 2970

His Leu  Glu Lys Val Lys Ala  Leu Arg Gly Glu Ile  Ala Pro Leu
    2975                 2980                 2985

Lys Glu  Asn Val Ser His Val  Asn Asp Leu Ala Arg  Gln Leu Thr
    2990                 2995                 3000

Thr Leu  Gly Ile Gln Leu Ser  Pro Tyr Asn Leu Ser  Thr Leu Glu
```

-continued

```
    3005                3010                3015

Asp Leu  Asn Thr Arg Trp Lys  Leu Leu Gln Val Ala  Val Glu Asp
    3020                3025                3030

Arg Val  Arg Gln Leu His Glu  Ala His Arg Asp Phe  Gly Pro Ala
    3035                3040                3045

Ser Gln  His Phe Leu Ser Thr  Ser Val Gln Gly Pro  Trp Glu Arg
    3050                3055                3060

Ala Ile  Ser Pro Asn Lys Val  Pro Tyr Tyr Ile Asn  His Glu Thr
    3065                3070                3075

Gln Thr  Thr Cys Trp Asp His  Pro Lys Met Thr Glu  Leu Tyr Gln
    3080                3085                3090

Ser Leu  Ala Asp Leu Asn Asn  Val Arg Phe Ser Ala  Tyr Arg Thr
    3095                3100                3105

Ala Met  Lys Leu Arg Arg Leu  Gln Lys Ala Leu Cys  Leu Asp Leu
    3110                3115                3120

Leu Ser  Leu Ser Ala Ala Cys  Asp Ala Leu Asp Gln  His Asn Leu
    3125                3130                3135

Lys Gln  Asn Asp Gln Pro Met  Asp Ile Leu Gln Ile  Ile Asn Cys
    3140                3145                3150

Leu Thr  Thr Ile Tyr Asp Arg  Leu Glu Gln Glu His  Asn Asn Leu
    3155                3160                3165

Val Asn  Val Pro Leu Cys Val  Asp Met Cys Leu Asn  Trp Leu Leu
    3170                3175                3180

Asn Val  Tyr Asp Thr Gly Arg  Thr Gly Arg Ile Arg  Val Leu Ser
    3185                3190                3195

Phe Lys  Thr Gly Ile Ile Ser  Leu Cys Lys Ala His  Leu Glu Asp
    3200                3205                3210

Lys Tyr  Arg Tyr Leu Phe Lys  Gln Val Ala Ser Ser  Thr Gly Phe
    3215                3220                3225

Cys Asp  Gln Arg Arg Leu Gly  Leu Leu Leu His Asp  Ser Ile Gln
    3230                3235                3240

Ile Pro  Arg Gln Leu Gly Glu  Val Ala Ser Phe Gly  Gly Ser Asn
    3245                3250                3255

Ile Glu  Pro Ser Val Arg Ser  Cys Phe Gln Phe Ala  Asn Asn Lys
    3260                3265                3270

Pro Glu  Ile Glu Ala Ala Leu  Phe Leu Asp Trp Met  Arg Leu Glu
    3275                3280                3285

Pro Gln  Ser Met Val Trp Leu  Pro Val Leu His Arg  Val Ala Ala
    3290                3295                3300

Ala Glu  Thr Ala Lys His Gln  Ala Lys Cys Asn Ile  Cys Lys Glu
    3305                3310                3315

Cys Pro  Ile Ile Gly Phe Arg  Tyr Arg Ser Leu Lys  His Phe Asn
    3320                3325                3330

Tyr Asp  Ile Cys Gln Ser Cys  Phe Phe Ser Gly Arg  Val Ala Lys
    3335                3340                3345

Gly His  Lys Met His Tyr Pro  Met Val Glu Tyr Cys  Thr Pro Thr
    3350                3355                3360

Thr Ser  Gly Glu Asp Val Arg  Asp Phe Ala Lys Val  Leu Lys Asn
    3365                3370                3375

Lys Phe  Arg Thr Lys Arg Tyr  Phe Ala Lys His Pro  Arg Met Gly
    3380                3385                3390
```

-continued

```
Tyr Leu  Pro Val Gln Thr Val  Leu Glu Gly Asp Asn  Met Glu Thr
    3395                 3400                 3405

Pro Val  Thr Leu Ile Asn Phe  Trp Pro Val Asp Ser  Ala Pro Ala
    3410                 3415                 3420

Ser Ser  Pro Gln Leu Ser His  Asp Asp Thr His Ser  Arg Ile Glu
    3425                 3430                 3435

His Tyr  Ala Ser Arg Leu Ala  Glu Met Glu Asn Ser  Asn Gly Ser
    3440                 3445                 3450

Tyr Leu  Asn Asp Ser Ile Ser  Pro Asn Glu Ser Ile  Asp Asp Glu
    3455                 3460                 3465

His Leu  Leu Ile Gln His Tyr  Cys Gln Ser Leu Asn  Gln Asp Ser
    3470                 3475                 3480

Pro Leu  Ser Gln Pro Arg Ser  Pro Ala Gln Ile Leu  Ile Ser Leu
    3485                 3490                 3495

Glu Ser  Glu Glu Arg Gly Glu  Leu Glu Arg Ile Leu  Ala Asp Leu
    3500                 3505                 3510

Glu Glu  Glu Asn Arg Asn Leu  Gln Ala Glu Tyr Asp  Arg Leu Lys
    3515                 3520                 3525

Gln Gln  His Glu His Lys Gly  Leu Ser Pro Leu Pro  Ser Pro Pro
    3530                 3535                 3540

Glu Met  Met Pro Thr Ser Pro  Gln Ser Pro Arg Asp  Ala Glu Leu
    3545                 3550                 3555

Ile Ala  Glu Ala Lys Leu Leu  Arg Gln His Lys Gly  Arg Leu Glu
    3560                 3565                 3570

Ala Arg  Met Gln Ile Leu Glu  Asp His Asn Lys Gln  Leu Glu Ser
    3575                 3580                 3585

Gln Leu  His Arg Leu Arg Gln  Leu Leu Glu Gln Pro  Gln Ala Glu
    3590                 3595                 3600

Ala Lys  Val Asn Gly Thr Thr  Val Ser Ser Pro Ser  Thr Ser Leu
    3605                 3610                 3615

Gln Arg  Ser Asp Ser Ser Gln  Pro Met Leu Leu Arg  Val Val Gly
    3620                 3625                 3630

Ser Gln  Thr Ser Asp Ser Met  Gly Glu Glu Asp Leu  Leu Ser Pro
    3635                 3640                 3645

Pro Gln  Asp Thr Ser Thr Gly  Leu Glu Glu Val Met  Glu Gln Leu
    3650                 3655                 3660

Asn Asn  Ser Phe Pro Ser Ser  Arg Gly Arg Asn Thr  Pro Gly Lys
    3665                 3670                 3675

Pro Met  Arg Glu Asp Thr Met
    3680                 3685


<210> SEQ ID NO 2
<211> LENGTH: 83
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 2

agauagucua caacaaagcu caggucggau ugacauuauu cauagcaaga agacagcagc     60

auugcaaagu gcaacgccug ugg                                             83
```

-continued

<210> SEQ ID NO 3
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 3

uuaugguugg aggaagcaga uaacauugcu aguaucccac uugaaccugg aaaagagcag 60

caacuaaaag aaaagc 76

<210> SEQ ID NO 4
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 4

ggcgguaaac cguuuacuuc aagagcugag ggcaaagcag ccugaccuag cuccuggacu 60

gaccacuauu gg 72

<210> SEQ ID NO 5
<211> LENGTH: 99
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 5

cuccuacuca gacuguuacu cuggugacac aaccuguggu uacuaaggaa acugccaucu 60

ccaaacuaga aaugccaucu uccuugaugu uggagguac 99

<210> SEQ ID NO 6
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 6

augcaggauu uggaacagag gcgucccag uuggaagaac ucauuaccgc ugcccaaaau 60

uugaaaaaca agaccagcaa ucaagaggcu 90

<210> SEQ ID NO 7
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 7

aaauguuaaa ggauucaaca caauggcugg aagcuaagga agaagcugag caggucuuag 60

gacaggccag ag 72

<210> SEQ ID NO 8
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 8

ccacaggcgu ugcacuuugc aaugc 25

<210> SEQ ID NO 9
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 9

cacaggcguu gcacuuugca augcu 25

<210> SEQ ID NO 10
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 10

acaggcguug cacuuugcaa ugcug 25

<210> SEQ ID NO 11
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 11

caggcguugc acuuugcaau gcugc 25

<210> SEQ ID NO 12
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 12

aggcguugca cuuugcaaug cugcu 25

<210> SEQ ID NO 13
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 13

ggcguugcac uuugcaaugc ugcug 25

<210> SEQ ID NO 14
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 14

gcguugcacu uugcaaugcu gcugu 25

-continued

<210> SEQ ID NO 15
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 15

cguugcacuu ugcaaugcug cuguc 25

<210> SEQ ID NO 16
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 16

cguugcacuu ugcaaugcug cug 23

<210> SEQ ID NO 17
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 17

guugcacuuu gcaaugcugc ugucu 25

<210> SEQ ID NO 18
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 18

uugcacuuug caaugcugcu gucuu 25

<210> SEQ ID NO 19
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 19

ugcacuuugc aaugcugcug ucuuc 25

<210> SEQ ID NO 20
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 20

gcacuuugca augcugcugu cuucu 25

<210> SEQ ID NO 21
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 21

cacuuugcaa ugcugcuguc uucuu 25

<210> SEQ ID NO 22
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 22

acuuugcaau gcugcugucu ucuug 25

<210> SEQ ID NO 23
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 23

cuuugcaaug cugcugucuu cuugc 25

<210> SEQ ID NO 24
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 24

uuugcaaugc ugcugucuuc uugcu 25

<210> SEQ ID NO 25
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 25

uugcaaugcu gcugucuucu ugcua 25

<210> SEQ ID NO 26
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 26

ugcaaugcug cugucuucuu gcuau 25

<210> SEQ ID NO 27
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 27

gcaaugcugc ugucuucuug cuaug 25

<210> SEQ ID NO 28
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 28

caaugcugcu gucuucuugc uauga 25

<210> SEQ ID NO 29
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: olignucleotide

<400> SEQUENCE: 29

aaugcugcug ucuucuugcu augaa 25

<210> SEQ ID NO 30
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 30

augcugcugu cuucuugcua ugaau 25

<210> SEQ ID NO 31
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 31

ugcugcuguc uucuugcuau gaaua 25

<210> SEQ ID NO 32
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 32

gcugcugucu ucuugcuaug aauaa 25

<210> SEQ ID NO 33
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 33

cugcugucuu cuugcuauga auaau 25

-continued

<210> SEQ ID NO 34
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 34

ugcugucuuc uugcuaugaa uaaug 25

<210> SEQ ID NO 35
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 35

gcugucuucu ugcuaugaau aaugu 25

<210> SEQ ID NO 36
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 36

cugucuucuu gcuaugaaua auguc 25

<210> SEQ ID NO 37
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 37

ugucuucuug cuaugaauaa uguca 25

<210> SEQ ID NO 38
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 38

gucuucuugc uaugaauaau gucaa 25

<210> SEQ ID NO 39
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 39

ucuucuugcu augaauaaug ucaau 25

<210> SEQ ID NO 40
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 40

cuucuugcua ugaauaaugu caauc 25

<210> SEQ ID NO 41
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 41

uucuugcuau gaauaauguc aaucc 25

<210> SEQ ID NO 42
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 42

ucuugcuaug aauaauguca auccg 25

<210> SEQ ID NO 43
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 43

cuugcuauga auaaugucaa uccga 25

<210> SEQ ID NO 44
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 44

uugcuaugaa uaaugucaau ccgac 25

<210> SEQ ID NO 45
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 45

ugcuaugaau aaugucaauc cgacc 25

<210> SEQ ID NO 46
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 46

gcuaugaaua augucaaucc gaccu 25

<210> SEQ ID NO 47
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 47

cuaugaauaa ugucaauccg accug 25

<210> SEQ ID NO 48
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 48

uaugaauaau gucaauccga ccuga 25

<210> SEQ ID NO 49
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 49

augaauaaug ucaauccgac cugag 25

<210> SEQ ID NO 50
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 50

ugaauaaugu caauccgacc ugagc 25

<210> SEQ ID NO 51
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 51

gaauaauguc aauccgaccu gagcu 25

<210> SEQ ID NO 52
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 52

aauaauguca auccgaccug agcuu 25

-continued

<210> SEQ ID NO 53
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 53

auaaugucaa uccgaccuga gcuuu 25

<210> SEQ ID NO 54
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 54

uaaugucaau ccgaccugag cuuug 25

<210> SEQ ID NO 55
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 55

aaugucaauc cgaccugagc uuugu 25

<210> SEQ ID NO 56
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 56

augucaaucc gaccugagcu uuguu 25

<210> SEQ ID NO 57
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 57

ugucaauccg accugagcuu uguug 25

<210> SEQ ID NO 58
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 58

gucaauccga ccugagcuuu guugu 25

<210> SEQ ID NO 59
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 59

ucaauccgac cugagcuuug uugua 25

<210> SEQ ID NO 60
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 60

caauccgacc ugagcuuugu uguag 25

<210> SEQ ID NO 61
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 61

aauccgaccu gagcuuuguu guaga 25

<210> SEQ ID NO 62
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: olignucleotide

<400> SEQUENCE: 62

auccgaccug agcuuuguug uagac 25

<210> SEQ ID NO 63
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 63

uccgaccuga gcuuuguugu agacu 25

<210> SEQ ID NO 64
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 64

ccgaccugag cuuuguugua gacua 25

<210> SEQ ID NO 65
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 65

cgaccugagc uuuguuguag 20

<210> SEQ ID NO 66
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 66

cgaccugagc uuuguuguag acuau 25

<210> SEQ ID NO 67
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 67

gaccugagcu uuguuguaga cuauc 25

<210> SEQ ID NO 68
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 68

accugagcuu uguuguagac uauca 25

<210> SEQ ID NO 69
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 69

ccugagcuuu guuguagacu auc 23

<210> SEQ ID NO 70
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 70

gcuuuucuuu uaguugcugc ucuuu 25

<210> SEQ ID NO 71
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 71

cuuuucuuuu aguugcugcu cuuuu 25

-continued

<210> SEQ ID NO 72
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 72

uuuucuuuua guugcugcuc uuuuc 25

<210> SEQ ID NO 73
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 73

uuucuuuuag uugcugcucu uuucc 25

<210> SEQ ID NO 74
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 74

uucuuuuagu ugcugcucuu uucca 25

<210> SEQ ID NO 75
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 75

ucuuuuaguu gcugcucuuu uccag 25

<210> SEQ ID NO 76
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 76

cuuuuaguug cugcucuuuu ccagg 25

<210> SEQ ID NO 77
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 77

uuuuaguugc ugcucuuuuc caggu 25

<210> SEQ ID NO 78
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 78

uuuaguugcu gcucuuuucc agguu 25

<210> SEQ ID NO 79
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 79

uuaguugcug cucuuuucca gguuc 25

<210> SEQ ID NO 80
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 80

uaguugcugc ucuuuuccag guuca 25

<210> SEQ ID NO 81
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 81

aguugcugcu cuuuuccagg uucaa 25

<210> SEQ ID NO 82
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 82

guugcugcuc uuuuccaggu ucaag 25

<210> SEQ ID NO 83
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 83

uugcugcucu uuuccagguu caagu 25

<210> SEQ ID NO 84
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 84

ugcugcucuu uuccagguuc aagug 25

<210> SEQ ID NO 85
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 85

gcugcucuuu uccagguuca agugg 25

<210> SEQ ID NO 86
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 86

cugcucuuuu ccagguucaa guggg 25

<210> SEQ ID NO 87
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 87

ugcucuuuuc cagguucaag uggga 25

<210> SEQ ID NO 88
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 88

gcucuuuucc agguucaagu gggac 25

<210> SEQ ID NO 89
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 89

cucuuuucca gguucaagug ggaua 25

<210> SEQ ID NO 90
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 90

ucuuuuccag guucaagugg gauac 25

-continued

<210> SEQ ID NO 91
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 91

ucuuuuccag guucaagugg 20

<210> SEQ ID NO 92
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 92

cuuuuccagg uucaaguggg auacu 25

<210> SEQ ID NO 93
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 93

uuuuccaggu ucaaguggga uacua 25

<210> SEQ ID NO 94
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 94

uuuccagguu caagugggau acuag 25

<210> SEQ ID NO 95
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 95

uuccagguuc aagugggaua cuagc 25

<210> SEQ ID NO 96
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 96

uccagguuca agugggauac uagca 25

<210> SEQ ID NO 97
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 97

ccagguucaa gugggauacu agcaa 25

<210> SEQ ID NO 98
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 98

cagguucaag ugggauacua gcaau 25

<210> SEQ ID NO 99
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 99

agguucaagu gggauacuag caaug 25

<210> SEQ ID NO 100
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 100

gguucaagug ggauacuagc aaugu 25

<210> SEQ ID NO 101
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 101

guucaagugg gauacuagca auguu 25

<210> SEQ ID NO 102
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 102

uucaaguggg auacuagcaa uguua 25

<210> SEQ ID NO 103
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 103

ucaaguggga uacuagcaau guuau 25

<210> SEQ ID NO 104
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 104

caagugggau acuagcaaug uuauc 25

<210> SEQ ID NO 105
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 105

aagugggaua cuagcaaugu uaucu 25

<210> SEQ ID NO 106
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 106

agugggauac uagcaauguu aucug 25

<210> SEQ ID NO 107
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 107

gugggauacu agcaauguua ucugc 25

<210> SEQ ID NO 108
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 108

ugggauacua gcaauguuau cugcu 25

<210> SEQ ID NO 109
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 109

gggauacuag caauguuauc ugcuu 25

-continued

<210> SEQ ID NO 110
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 110

ggauacuagc aauguuaucu gcuuc 25

<210> SEQ ID NO 111
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 111

gauacuagca auguuaucug cuucc 25

<210> SEQ ID NO 112
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 112

auacuagcaa uguuaucugc uuccu 25

<210> SEQ ID NO 113
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 113

uacuagcaau guuaucugcu uccuc 25

<210> SEQ ID NO 114
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 114

acuagcaaug uuaucugcuu ccucc 25

<210> SEQ ID NO 115
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 115

cuagcaaugu uaucugcuuc cucca 25

<210> SEQ ID NO 116
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 116

uagcaauguu aucugcuucc uccaa 25

<210> SEQ ID NO 117
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 117

agcaauguua ucugcuuccu ccaac 25

<210> SEQ ID NO 118
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 118

gcaauguuau cugcuuccuc caacc 25

<210> SEQ ID NO 119
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 119

caauguuauc ugcuuccucc aacca 25

<210> SEQ ID NO 120
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 120

aauguuaucu gcuuccucca accau 25

<210> SEQ ID NO 121
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 121

auguuaucug cuuccuccaa ccaua 25

<210> SEQ ID NO 122
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 122

uguuaucugc uuccuccaac cauaa 25

<210> SEQ ID NO 123
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 123

ccaauagugg ucaguccagg agcua 25

<210> SEQ ID NO 124
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 124

caauaguggu caguccagga gcuag 25

<210> SEQ ID NO 125
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 125

aauagugguc aguccaggag cuagg 25

<210> SEQ ID NO 126
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 126

auagugguca guccaggagc uaggu 25

<210> SEQ ID NO 127
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 127

auagugguca guccaggagc u 21

<210> SEQ ID NO 128
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 128

uaguggucag uccaggagcu agguc 25

-continued

<210> SEQ ID NO 129
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 129

aguggucagu ccaggagcua gguca 25

<210> SEQ ID NO 130
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 130

guggucaguc caggagcuag gucag 25

<210> SEQ ID NO 131
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 131

uggucagucc aggagcuagg ucagg 25

<210> SEQ ID NO 132
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 132

ggucagucca ggagcuaggu caggc 25

<210> SEQ ID NO 133
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 133

gucaguccag gagcuagguc aggcu 25

<210> SEQ ID NO 134
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 134

ucaguccagg agcuagguca ggcug 25

<210> SEQ ID NO 135
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 135

caguccagga gcuaggucag gcugc 25

<210> SEQ ID NO 136
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 136

aguccaggag cuaggucagg cugcu 25

<210> SEQ ID NO 137
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 137

guccaggagc uaggucaggc ugcuu 25

<210> SEQ ID NO 138
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 138

uccaggagcu aggucaggcu gcuuu 25

<210> SEQ ID NO 139
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 139

ccaggagcua ggucaggcug cuuug 25

<210> SEQ ID NO 140
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 140

caggagcuag gucaggcugc uuugc 25

<210> SEQ ID NO 141
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 141

aggagcuagg ucaggcugcu uugcc 25

<210> SEQ ID NO 142
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 142

ggagcuaggu caggcugcuu ugccc 25

<210> SEQ ID NO 143
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 143

gagcuagguc aggcugcuuu gcccu 25

<210> SEQ ID NO 144
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 144

agcuagguca ggcugcuuug cccuc 25

<210> SEQ ID NO 145
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 145

gcuaggucag gcugcuuugc ccuca 25

<210> SEQ ID NO 146
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 146

cuaggucagg cugcuuugcc cucag 25

<210> SEQ ID NO 147
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 147

uaggucaggc ugcuuugccc ucagc 25

-continued

<210> SEQ ID NO 148
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 148

aggucaggcu gcuuugcccu cagcu 25

<210> SEQ ID NO 149
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 149

ggucaggcug cuuugcccuc agcuc 25

<210> SEQ ID NO 150
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 150

gucaggcugc uuugcccuca gcucu 25

<210> SEQ ID NO 151
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 151

ucaggcugcu uugcccucag cucuu 25

<210> SEQ ID NO 152
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 152

caggcugcuu ugcccucagc ucuug 25

<210> SEQ ID NO 153
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 153

aggcugcuuu gcccucagcu cuuga 25

<210> SEQ ID NO 154
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 154

ggcugcuuug cccucagcuc uugaa 25

<210> SEQ ID NO 155
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 155

gcugcuuugc ccucagcucu ugaag 25

<210> SEQ ID NO 156
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 156

cugcuuugcc cucagcucuu gaagu 25

<210> SEQ ID NO 157
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 157

ugcuuugccc ucagcucuug aagua 25

<210> SEQ ID NO 158
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 158

gcuuugcccu cagcucuuga aguaa 25

<210> SEQ ID NO 159
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 159

cuuugcccuc agcucuugaa guaaa 25

<210> SEQ ID NO 160
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 160

uuugcccuca gcucuugaag uaaac 25

<210> SEQ ID NO 161
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 161

uugcccucag cucuugaagu aaacg 25

<210> SEQ ID NO 162
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 162

ugcccucagc ucuugaagua aacgg 25

<210> SEQ ID NO 163
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 163

gcccucagcu cuugaaguaa acggu 25

<210> SEQ ID NO 164
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 164

cccucagcuc uugaaguaaa cgguu 25

<210> SEQ ID NO 165
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 165

ccucagcucu ugaaguaaac 20

<210> SEQ ID NO 166
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 166

ccucagcucu ugaaguaaac g 21

-continued

<210> SEQ ID NO 167
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 167

cucagcucuu gaaguaaacg 20

<210> SEQ ID NO 168
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 168

guaccuccaa caucaaggaa gaugg 25

<210> SEQ ID NO 169
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 169

uaccuccaac aucaaggaag auggc 25

<210> SEQ ID NO 170
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 170

accuccaaca ucaaggaaga uggca 25

<210> SEQ ID NO 171
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 171

ccuccaacau caaggaagau ggcau 25

<210> SEQ ID NO 172
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 172

cuccaacauc aaggaagaug gcauu 25

<210> SEQ ID NO 173
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 173

uccaacauca aggaagaugg cauuu 25

<210> SEQ ID NO 174
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonuclelotide

<400> SEQUENCE: 174

ccaacaucaa ggaagauggc auuuc 25

<210> SEQ ID NO 175
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 175

caacaucaag gaagauggca uuucu 25

<210> SEQ ID NO 176
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 176

aacaucaagg aagauggcau uucua 25

<210> SEQ ID NO 177
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 177

acaucaagga agauggcauu ucuag 25

<210> SEQ ID NO 178
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 178

caucaaggaa gauggcauuu cuagu 25

<210> SEQ ID NO 179
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 179

aucaaggaag auggcauuuc uaguu 25

<210> SEQ ID NO 180
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 180

ucaaggaaga uggcauuucu aguuu 25

<210> SEQ ID NO 181
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 181

caaggaagau ggcauuucua guuug 25

<210> SEQ ID NO 182
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 182

aaggaagaug gcauuucuag uuugg 25

<210> SEQ ID NO 183
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 183

aggaagaugg cauuucuagu uugga 25

<210> SEQ ID NO 184
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 184

ggaagauggc auuucuaguu uggag 25

<210> SEQ ID NO 185
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 185

gaagauggca uuucuaguuu ggaga 25

-continued

<210> SEQ ID NO 186
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 186

aagauggcau uucuaguuug gagau 25

<210> SEQ ID NO 187
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 187

agauggcauu ucuaguuugg agaug 25

<210> SEQ ID NO 188
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 188

gauggcauuu cuaguuugga gaugg 25

<210> SEQ ID NO 189
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 189

auggcauuuc uaguuuggag auggc 25

<210> SEQ ID NO 190
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 190

uggcauuucu aguuuggaga uggca 25

<210> SEQ ID NO 191
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 191

ggcauuucua guuuggagau ggcag 25

<210> SEQ ID NO 192
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 192

gcauuucuag uuuggagaug gcagu 25

<210> SEQ ID NO 193
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 193

cauuucuagu uuggagaugg caguu 25

<210> SEQ ID NO 194
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 194

auuucuaguu uggagauggc aguuu 25

<210> SEQ ID NO 195
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 195

uuucuaguuu ggagauggca guuuc 25

<210> SEQ ID NO 196
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 196

uucuaguuug gagauggcag uuucc 25

<210> SEQ ID NO 197
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 197

ucuaguuugg agauggcagu uuccu 25

<210> SEQ ID NO 198
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 198

cuaguuugga gauggcaguu uccuu 25

<210> SEQ ID NO 199
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 199

uaguuuggag auggcaguuu ccuua 25

<210> SEQ ID NO 200
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 200

aguuuggaga uggcaguuuc cuuag 25

<210> SEQ ID NO 201
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 201

guuuggagau ggcaguuucc uuagu 25

<210> SEQ ID NO 202
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 202

uuuggagaug gcaguuuccu uagua 25

<210> SEQ ID NO 203
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 203

uuggagaugg caguuuccuu aguaa 25

<210> SEQ ID NO 204
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 204

uggagauggc aguuuccuua guaac 25

-continued

<210> SEQ ID NO 205
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 205

gagauggcag uuuccuuagu aacca 25

<210> SEQ ID NO 206
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 206

agauggcagu uuccuuagua accac 25

<210> SEQ ID NO 207
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 207

gauggcaguu uccuuaguaa ccaca 25

<210> SEQ ID NO 208
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 208

auggcaguuu ccuuaguaac cacag 25

<210> SEQ ID NO 209
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 209

uggcaguuuc cuuaguaacc acagg 25

<210> SEQ ID NO 210
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 210

ggcaguuucc uuaguaacca caggu 25

<210> SEQ ID NO 211
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 211

gcaguuuccu uaguaaccac agguu 25

<210> SEQ ID NO 212
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 212

caguuuccuu aguaaccaca gguug 25

<210> SEQ ID NO 213
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 213

aguuuccuua guaaccacag guugu 25

<210> SEQ ID NO 214
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 214

guuuccuuag uaaccacagg uugug 25

<210> SEQ ID NO 215
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 215

uuuccuuagu aaccacaggu ugugu 25

<210> SEQ ID NO 216
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 216

uuccuuagua accacagguu guguc 25

<210> SEQ ID NO 217
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 217

uccuuaguaa ccacagguug uguca 25

<210> SEQ ID NO 218
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 218

ccuuaguaac cacagguugu gucac 25

<210> SEQ ID NO 219
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 219

cuuaguaacc acagguugug ucacc 25

<210> SEQ ID NO 220
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 220

uuaguaacca cagguugugu cacca 25

<210> SEQ ID NO 221
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 221

uaguaaccac agguuguguc accag 25

<210> SEQ ID NO 222
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 222

aguaaccaca gguuguguca ccaga 25

<210> SEQ ID NO 223
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 223

guaaccacag guugugucac cagag 25

-continued

<210> SEQ ID NO 224
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 224

uaaccacagg uugugucacc agagu 25

<210> SEQ ID NO 225
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 225

aaccacaggu ugugucacca gagua 25

<210> SEQ ID NO 226
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 226

accacagguu gugucaccag aguaa 25

<210> SEQ ID NO 227
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 227

ccacagguug ugucaccaga guaac 25

<210> SEQ ID NO 228
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 228

cacagguugu gucaccagag uaaca 25

<210> SEQ ID NO 229
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 229

acagguugug ucaccagagu aacag 25

<210> SEQ ID NO 230
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 230

cagguugugu caccagagua acagu 25

<210> SEQ ID NO 231
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 231

agguuguguc accagaguaa caguc 25

<210> SEQ ID NO 232
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 232

gguuguguca ccagaguaac agucu 25

<210> SEQ ID NO 233
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 233

guugugucac cagaguaaca gucug 25

<210> SEQ ID NO 234
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 234

uugugucacc agaguaacag ucuga 25

<210> SEQ ID NO 235
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 235

ugugucacca gaguaacagu cugag 25

<210> SEQ ID NO 236
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 236

gugucaccag aguaacaguc ugagu 25

<210> SEQ ID NO 237
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 237

ugucaccaga guaacagucu gagua 25

<210> SEQ ID NO 238
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 238

gucaccagag uaacagucug aguag 25

<210> SEQ ID NO 239
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 239

ucaccagagu aacagucuga guagg 25

<210> SEQ ID NO 240
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 240

caccagagua acagucugag uagga 25

<210> SEQ ID NO 241
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 241

accagaguaa cagucugagu aggag 25

<210> SEQ ID NO 242
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 242

agccucuuga uugcuggucu uguuu 25

-continued

<210> SEQ ID NO 243
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 243

gccucuugau ugcuggucuu guuuu 25

<210> SEQ ID NO 244
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 244

ccucuugauu gcuggucuug uuuuu 25

<210> SEQ ID NO 245
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 245

ccucuugauu gcuggucuug 20

<210> SEQ ID NO 246
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 246

cucuugauug cuggucuugu uuuuc 25

<210> SEQ ID NO 247
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 247

ucuugauugc uggucuuguu uuuca 25

<210> SEQ ID NO 248
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 248

cuugauugcu ggucuuguuu uucaa 25

<210> SEQ ID NO 249
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 249

uugauugcug gucuuguuuu ucaaa 25

<210> SEQ ID NO 250
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 250

ugauugcugg ucuuguuuuu caaau 25

<210> SEQ ID NO 251
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 251

gauugcuggu cuuguuuuuc aaauu 25

<210> SEQ ID NO 252
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 252

gauugcuggu cuuguuuuuc 20

<210> SEQ ID NO 253
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 253

auugcugguc uuguuuuuca aauuu 25

<210> SEQ ID NO 254
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 254

uugcuggucu uguuuuucaa auuuu 25

<210> SEQ ID NO 255
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 255

ugcuggucuu guuuuucaaa uuuug 25

<210> SEQ ID NO 256
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 256

gcuggucuug uuuuucaaau uuugg 25

<210> SEQ ID NO 257
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 257

cuggucuugu uuuucaaauu uuggg 25

<210> SEQ ID NO 258
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 258

uggucuuguu uuucaaauuu ugggc 25

<210> SEQ ID NO 259
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 259

ggucuuguuu uucaaauuuu gggca 25

<210> SEQ ID NO 260
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 260

gucuuguuuu ucaaauuuug ggcag 25

<210> SEQ ID NO 261
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 261

ucuuguuuuu caaauuuugg gcagc 25

-continued

<210> SEQ ID NO 262
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 262

cuuguuuuuc aaauuuuggg cagcg 25

<210> SEQ ID NO 263
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 263

uuguuuuuca aauuuugggc agcgg 25

<210> SEQ ID NO 264
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 264

uguuuuucaa auuuugggca gcggu 25

<210> SEQ ID NO 265
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 265

guuuuucaaa uuuugggcag cggua 25

<210> SEQ ID NO 266
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 266

uuuuucaaau uuugggcagc gguaa 25

<210> SEQ ID NO 267
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 267

uuuucaaauu uugggcagcg guaau 25

<210> SEQ ID NO 268
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 268

uuucaaauuu ugggcagcgg uaaug 25

<210> SEQ ID NO 269
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 269

uucaaauuuu gggcagcggu aauga 25

<210> SEQ ID NO 270
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 270

ucaaauuuug ggcagcggua augag 25

<210> SEQ ID NO 271
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 271

caaauuuugg gcagcgguaa ugagu 25

<210> SEQ ID NO 272
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 272

aaauuuuggg cagcgguaau gaguu 25

<210> SEQ ID NO 273
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 273

aauuuugggc agcgguaaug aguuc 25

<210> SEQ ID NO 274
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 274

auuuugggca gcgguaauga guucu 25

<210> SEQ ID NO 275
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 275

uuuugggcag cgguaaugag uucuu 25

<210> SEQ ID NO 276
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 276

uuugggcagc gguaaugagu ucuuc 25

<210> SEQ ID NO 277
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 277

uugggcagcg guaaugaguu cuucc 25

<210> SEQ ID NO 278
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 278

ugggcagcgg uaaugaguuc uucca 25

<210> SEQ ID NO 279
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 279

gggcagcggu aaugaguucu uccaa 25

<210> SEQ ID NO 280
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 280

ggcagcggua augaguucuu ccaac 25

-continued

<210> SEQ ID NO 281
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 281

gcagcgguaa ugaguucuuc caacu 25

<210> SEQ ID NO 282
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 282

cagcgguaau gaguucuucc aacug 25

<210> SEQ ID NO 283
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 283

agcgguaaug aguucuucca acugg 25

<210> SEQ ID NO 284
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 284

gcgguaauga guucuuccaa cuggg 25

<210> SEQ ID NO 285
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 285

cgguaaugag uucuuccaac ugggg 25

<210> SEQ ID NO 286
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 286

gguaaugagu ucuuccaacu gggga 25

<210> SEQ ID NO 287
<211> LENGTH: 22

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 287

gguaaugagu ucuuccaacu gg 22

<210> SEQ ID NO 288
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 288

guaaugaguu cuuccaacug gggac 25

<210> SEQ ID NO 289
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 289

uaaugaguuc uuccaacugg ggacg 25

<210> SEQ ID NO 290
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 290

aaugaguucu uccaacuggg gacgc 25

<210> SEQ ID NO 291
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 291

augaguucuu ccaacugggg acgcc 25

<210> SEQ ID NO 292
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 292

ugaguucuuc caacugggga cgccu 25

<210> SEQ ID NO 293
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 293

gaguucuucc aacuggggac gccuc 25

<210> SEQ ID NO 294
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 294

aguucuucca acuggggacg ccucu 25

<210> SEQ ID NO 295
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 295

guucuuccaa cuggggacgc cucug 25

<210> SEQ ID NO 296
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 296

uucuuccaac uggggacgcc ucugu 25

<210> SEQ ID NO 297
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 297

ucuuccaacu ggggacgccu cuguu 25

<210> SEQ ID NO 298
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 298

cuuccaacug gggacgccuc uguuc 25

<210> SEQ ID NO 299
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 299

uuccaacugg ggacgccucu guucc 25

-continued

<210> SEQ ID NO 300
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 300

uccaacuggg gacgccucug uucca 25

<210> SEQ ID NO 301
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 301

ccaacugggg acgccucugu uccaa 25

<210> SEQ ID NO 302
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 302

caacugggga cgccucuguu ccaaa 25

<210> SEQ ID NO 303
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 303

aacuggggac gccucuguuc caaau 25

<210> SEQ ID NO 304
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 304

acuggggacg ccucuguucc aaauc 25

<210> SEQ ID NO 305
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 305

cuggggacgc cucuguucca aaucc 25

<210> SEQ ID NO 306
<211> LENGTH: 25

-continued

<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 306

uggggacgcc ucuguuccaa auccu 25

<210> SEQ ID NO 307
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 307

ggggacgccu cuguuccaaa uccug 25

<210> SEQ ID NO 308
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 308

gggacgccuc uguuccaaau ccugc 25

<210> SEQ ID NO 309
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 309

ggacgccucu guuccaaauc cugca 25

<210> SEQ ID NO 310
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 310

gacgccucug uuccaaaucc ugcau 25

<210> SEQ ID NO 311
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 311

cucuggccug uccuaagacc ugcuc 25

<210> SEQ ID NO 312
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 312

ucuggccugu ccuaagaccu gcuca 25

<210> SEQ ID NO 313

<400> SEQUENCE: 313

000

<210> SEQ ID NO 314
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 314

uggccugucc uaagaccugc ucagc 25

<210> SEQ ID NO 315
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 315

ggccuguccu aagaccugcu cagcu 25

<210> SEQ ID NO 316
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 316

gccuguccua agaccugcuc agcuu 25

<210> SEQ ID NO 317
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 317

ccuguccuaa gaccugcuca gcuuc 25

<210> SEQ ID NO 318
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 318

cuguccuaag accugcucag cuucu 25

<210> SEQ ID NO 319
<211> LENGTH: 25
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 319

uguccuaaga ccugcucagc uucuu 25

<210> SEQ ID NO 320
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 320

guccuaagac cugcucagcu ucuuc 25

<210> SEQ ID NO 321
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 321

uccuaagacc ugcucagcuu cuucc 25

<210> SEQ ID NO 322
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 322

ccuaagaccu gcucagcuuc uuccu 25

<210> SEQ ID NO 323
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 323

cuaagaccug cucagcuucu uccuu 25

<210> SEQ ID NO 324
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 324

uaagaccugc ucagcuucuu ccuua 25

<210> SEQ ID NO 325
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 325

aagaccugcu cagcuucuuc cuuag 25

<210> SEQ ID NO 326
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 326

agaccugcuc agcuucuucc uuagc 25

<210> SEQ ID NO 327
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 327

gaccugcuca gcuucuuccu uagcu 25

<210> SEQ ID NO 328
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 328

accugcucag cuucuuccuu agcuu 25

<210> SEQ ID NO 329
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 329

ccugcucagc uucuuccuua gcuuc 25

<210> SEQ ID NO 330
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 330

cugcucagcu ucuuccuuag cuucc 25

<210> SEQ ID NO 331
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 331

ugcucagcuu cuuccuuagc uucca 25

-continued

<210> SEQ ID NO 332
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 332

gcucagcuuc uuccuuagcu uccag 25

<210> SEQ ID NO 333
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 333

cucagcuucu uccuuagcuu ccagc 25

<210> SEQ ID NO 334
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 334

ucagcuucuu ccuuagcuuc cagcc 25

<210> SEQ ID NO 335
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 335

cagcuucuuc cuuagcuucc agcca 25

<210> SEQ ID NO 336
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 336

agcuucuucc uuagcuucca gccau 25

<210> SEQ ID NO 337
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 337

gcuucuuccu uagcuuccag ccauu 25

<210> SEQ ID NO 338
<211> LENGTH: 25
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 338

cuucuuccuu agcuuccagc cauug 25

<210> SEQ ID NO 339
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 339

uucuuccuua gcuuccagcc auugu 25

<210> SEQ ID NO 340
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 340

ucuuccuuag cuuccagcca uugug 25

<210> SEQ ID NO 341
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 341

cuuccuuagc uuccagccau ugugu 25

<210> SEQ ID NO 342
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 342

uuccuuagcu uccagccauu guguu 25

<210> SEQ ID NO 343
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 343

uccuuagcuu ccagccauug uguug 25

<210> SEQ ID NO 344
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 344

ccuuagcuuc cagccauugu guuga 25

<210> SEQ ID NO 345
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 345

cuuagcuucc agccauugug uugaa 25

<210> SEQ ID NO 346
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 346

uuagcuucca gccauugugu ugaau 25

<210> SEQ ID NO 347
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 347

uagcuuccag ccauuguguu gaauc 25

<210> SEQ ID NO 348
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 348

agcuuccagc cauuguguug aaucc 25

<210> SEQ ID NO 349
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 349

gcuuccagcc auuguguuga auccu 25

<210> SEQ ID NO 350
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 350

cuuccagcca uuguguugaa uccuu 25

-continued

<210> SEQ ID NO 351
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 351

uuccagccau uguguugaau ccuuu 25

<210> SEQ ID NO 352
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 352

uccagccauu guguugaauc cuuua 25

<210> SEQ ID NO 353
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 353

ccagccauug uguugaaucc uuuaa 25

<210> SEQ ID NO 354
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 354

cagccauugu guugaauccu uuaac 25

<210> SEQ ID NO 355
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 355

agccauugug uugaauccuu uaaca 25

<210> SEQ ID NO 356
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 356

gccauugugu ugaauccuuu aacau 25

<210> SEQ ID NO 357
<211> LENGTH: 25
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 357

ccauuguguu gaauccuuua acauu 25

<210> SEQ ID NO 358
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 358

cauuguguug aauccuuuaa cauuu 25

<210> SEQ ID NO 359
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 359

cauuuuugac cuacaugugg 20

<210> SEQ ID NO 360
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 360

uuugaccuac auguggaaag 20

<210> SEQ ID NO 361
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 361

uacauuuuug accuacaugu ggaaag 26

<210> SEQ ID NO 362
<211> LENGTH: 17
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 362

ggucuccuua ccuauga 17

<210> SEQ ID NO 363
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 363

ucuuaccuau gacuauggau gaga 24

<210> SEQ ID NO 364
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 364

auuuuugacc uacaugggaa ag 22

<210> SEQ ID NO 365
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 365

uacgaguuga uugucggacc cag 23

<210> SEQ ID NO 366
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 366

guggucuccu uaccuaugac ugugg 25

<210> SEQ ID NO 367
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 367

ugucucagua aucuucuuac cuau 24

<210> SEQ ID NO 368
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 368

ugcauguucc agucguugug ugg 23

<210> SEQ ID NO 369
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 369

cacuauucca gucaaauagg ucugg 25

-continued

<210> SEQ ID NO 370
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 370

auuuaccaac cuucaggauc gagua 25

<210> SEQ ID NO 371
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 371

ggccuaaaac acauacacau a 21

<210> SEQ ID NO 372
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 372

cccugaggca uucccaucuu gaau 24

<210> SEQ ID NO 373
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 373

aggacuuacu ugcuuuguuu 20

<210> SEQ ID NO 374
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 374

cuugaauuua ggagauucau cug 23

<210> SEQ ID NO 375
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 375

caucuucuga uaauuuuccu guu 23

<210> SEQ ID NO 376
<211> LENGTH: 20
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 376

ccauuacagu ugucuguguu 20

<210> SEQ ID NO 377
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 377

ugacagccug ugaaaucugu gag 23

<210> SEQ ID NO 378
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 378

uaaucugccu cuucuuuugg 20

<210> SEQ ID NO 379
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 379

cagcaguagu ugucaucugc 20

<210> SEQ ID NO 380
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 380

gccugagcug aucugcuggc aucuugc 27

<210> SEQ ID NO 381
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 381

gccugagcug aucugcuggc aucuugcagu u 31

<210> SEQ ID NO 382
<211> LENGTH: 16
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 382

ucugcuggca ucuugc 16

<210> SEQ ID NO 383
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 383

gccgguugac uucauccugu gc 22

<210> SEQ ID NO 384
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 384

gucugcaucc aggaacaugg guc 23

<210> SEQ ID NO 385
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 385

uacuuacugu cuguagcucu uucu 24

<210> SEQ ID NO 386
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 386

cugcauccag gaacaugggu cc 22

<210> SEQ ID NO 387
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 387

guugaagauc ugauagccgg uuga 24

<210> SEQ ID NO 388
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 388

ucagcuucug uuagccacug 20

-continued

<210> SEQ ID NO 389
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 389

uucagcuucu guuagccacu 20

<210> SEQ ID NO 390
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 390

uucagcuucu guuagccacu g 21

<210> SEQ ID NO 391
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 391

ucagcuucug uuagccacug a 21

<210> SEQ ID NO 392
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 392

uucagcuucu guuagccacu ga 22

<210> SEQ ID NO 393
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 393

ucagcuucug uuagccacug a 21

<210> SEQ ID NO 394
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 394

uucagcuucu guuagccacu ga 22

<210> SEQ ID NO 395
<211> LENGTH: 22
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 395

ucagcuucug uuagccacug au 22

<210> SEQ ID NO 396
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 396

uucagcuucu guuagccacu gau 23

<210> SEQ ID NO 397
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 397

ucagcuucug uuagccacug auu 23

<210> SEQ ID NO 398
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 398

uucagcuucu guuagccacu gauu 24

<210> SEQ ID NO 399
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 399

ucagcuucug uuagccacug auua 24

<210> SEQ ID NO 400
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 400

uucagcuucu guuagccacu gaua 24

<210> SEQ ID NO 401
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 401

ucagcuucug uuagccacug auuaa 25

<210> SEQ ID NO 402
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 402

uucagcuucu guuagccacu gauuaa 26

<210> SEQ ID NO 403
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 403

ucagcuucug uuagccacug auuaaa 26

<210> SEQ ID NO 404
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 404

uucagcuucu guuagccacu gauuaaa 27

<210> SEQ ID NO 405
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 405

cagcuucugu uagccacug 19

<210> SEQ ID NO 406
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 406

cagcuucugu uagccacuga u 21

<210> SEQ ID NO 407
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 407

agcuucuguu agccacugau u 21

-continued

<210> SEQ ID NO 408
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 408

cagcuucugu uagccacuga uu 22

<210> SEQ ID NO 409
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 409

agcuucuguu agccacugau ua 22

<210> SEQ ID NO 410
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 410

cagcuucugu uagccacuga uua 23

<210> SEQ ID NO 411
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 411

agcuucuguu agccacugau uaa 23

<210> SEQ ID NO 412
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 412

cagcuucugu uagccacuga uuaa 24

<210> SEQ ID NO 413
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 413

agcuucuguu agccacugau uaaa 24

<210> SEQ ID NO 414
<211> LENGTH: 25
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 414

cagcuucugu uagccacuga uuaaa 25

<210> SEQ ID NO 415
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 415

agcuucuguu agccacugau uaaa 24

<210> SEQ ID NO 416
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 416

agcuucuguu agccacugau 20

<210> SEQ ID NO 417
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 417

gcuucuguua gccacugauu 20

<210> SEQ ID NO 418
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 418

agcuucuguu agccacugau u 21

<210> SEQ ID NO 419
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 419

gcuucuguua gccacugauu a 21

<210> SEQ ID NO 420
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 420

agcuucuguu agccacugau ua 22

<210> SEQ ID NO 421
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 421

gcuucuguua gccacugauu aa 22

<210> SEQ ID NO 422
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 422

agcuucuguu agccacugau uaa 23

<210> SEQ ID NO 423
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 423

gcuucuguua gccacugauu aaa 23

<210> SEQ ID NO 424
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 424

agcuucuguu agccacugau uaaa 24

<210> SEQ ID NO 425
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 425

gcuucuguua gccacugauu aaa 23

<210> SEQ ID NO 426
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 426

ccauuuguau uuagcauguu ccc 23

-continued

<210> SEQ ID NO 427
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligoucleotide

<400> SEQUENCE: 427

agauaccauu uguauuuagc 20

<210> SEQ ID NO 428
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 428

gccauuucuc aacagaucu 19

<210> SEQ ID NO 429
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 429

gccauuucuc aacagaucug uca 23

<210> SEQ ID NO 430
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 430

auucucagga auuugugucu uuc 23

<210> SEQ ID NO 431
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 431

ucucaggaau uugugucuuu c 21

<210> SEQ ID NO 432
<211> LENGTH: 18
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 432

guucagcuuc uguuagcc 18

<210> SEQ ID NO 433
<211> LENGTH: 21
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 433

cugauuaaau aucuuuauau c 21

<210> SEQ ID NO 434
<211> LENGTH: 18
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 434

gccgccauuu cucaacag 18

<210> SEQ ID NO 435
<211> LENGTH: 18
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 435

gccgccauuu cucaacag 18

<210> SEQ ID NO 436
<211> LENGTH: 18
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 436

caggaauuug ugucuuuc 18

<210> SEQ ID NO 437
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 437

uuugccgcug cccaaugcca uccug 25

<210> SEQ ID NO 438
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 438

auucaauguu cugacaacag uuugc 25

<210> SEQ ID NO 439
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 439

ccaguugcau ucaauguucu gacaa 25

<210> SEQ ID NO 440
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 440

caguugcauu caauguucug ac 22

<210> SEQ ID NO 441
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 441

aguugcauuc aauguucuga 20

<210> SEQ ID NO 442
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 442

gauugcugaa uuauuucuuc c 21

<210> SEQ ID NO 443
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 443

gauugcugaa uuauuucuuc cccag 25

<210> SEQ ID NO 444
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 444

auugcugaau uauuucuucc ccagu 25

<210> SEQ ID NO 445
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 445

uugcugaauu auuucuuccc caguu 25

-continued

<210> SEQ ID NO 446
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 446

ugcugaauua uuucuucccc aguug 25

<210> SEQ ID NO 447
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 447

gcugaauuau uucuucccca guugc 25

<210> SEQ ID NO 448
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 448

cugaauuauu ucuuccccag uugca 25

<210> SEQ ID NO 449
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 449

ugaauuauuu cuuccccagu ugcau 25

<210> SEQ ID NO 450
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 450

gaauuauuuc uuccccaguu gcauu 25

<210> SEQ ID NO 451
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 451

aauuauuucu uccccaguug cauuc 25

<210> SEQ ID NO 452
<211> LENGTH: 25
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 452

auuauuucuu ccccaguugc auuca 25

<210> SEQ ID NO 453
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 453

uuauuucuuc cccaguugca uucaa 25

<210> SEQ ID NO 454
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 454

uauuucuucc ccaguugcau ucaau 25

<210> SEQ ID NO 455
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 455

auuucuuccc caguugcauu caaug 25

<210> SEQ ID NO 456
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 456

uuucuucccc aguugcauuc aaugu 25

<210> SEQ ID NO 457
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 457

uucuucccca guugcauuca auguu 25

<210> SEQ ID NO 458
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 458

ucuuccccag uugcauucaa uguuc 25

<210> SEQ ID NO 459
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 459

cuuccccagu ugcauucaau guucu 25

<210> SEQ ID NO 460
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 460

uuccccaguu gcauucaaug uucug 25

<210> SEQ ID NO 461
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 461

uccccaguug cauucaaugu ucuga 25

<210> SEQ ID NO 462
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 462

ccccaguugc auucaauguu cugac 25

<210> SEQ ID NO 463
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 463

cccaguugca uucaauguuc ugaca 25

<210> SEQ ID NO 464
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 464

ccaguugcau ucaauguucu gacaa 25

-continued

<210> SEQ ID NO 465
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 465

caguugcauu caauguucug acaac 25

<210> SEQ ID NO 466
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 466

aguugcauuc aauguucuga caaca 25

<210> SEQ ID NO 467
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 467

uccuguagaa uacuggcauc 20

<210> SEQ ID NO 468
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 468

ugcagaccuc cugccaccgc agauuca 27

<210> SEQ ID NO 469
<211> LENGTH: 34
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 469

uugcagaccu ccugccaccg cagauucagg cuuc 34

<210> SEQ ID NO 470
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 470

guugcauuca auguucugac aacag 25

<210> SEQ ID NO 471
<211> LENGTH: 25
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 471

uugcauucaa uguucugaca acagu 25

<210> SEQ ID NO 472
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 472

ugcauucaau guucugacaa caguu 25

<210> SEQ ID NO 473
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 473

gcauucaaug uucugacaac aguuu 25

<210> SEQ ID NO 474
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 474

cauucaaugu ucugacaaca guuug 25

<210> SEQ ID NO 475
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 475

auucaauguu cugacaacag uuugc 25

<210> SEQ ID NO 476
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 476

ucaauguucu gacaacaguu ugccg 25

<210> SEQ ID NO 477
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 477

caauguucug acaacaguuu gccgc 25

<210> SEQ ID NO 478
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 478

aauguucuga caacaguuug ccgcu 25

<210> SEQ ID NO 479
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 479

auguucugac aacaguuugc cgcug 25

<210> SEQ ID NO 480
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 480

uguucugaca acaguuugcc gcugc 25

<210> SEQ ID NO 481
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 481

guucugacaa caguuugccg cugcc 25

<210> SEQ ID NO 482
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 482

uucugacaac aguuugccgc ugccc 25

<210> SEQ ID NO 483
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 483

ucugacaaca guuugccgcu gccca 25

-continued

<210> SEQ ID NO 484
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 484

cugacaacag uuugccgcug cccaa 25

<210> SEQ ID NO 485
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 485

ugacaacagu uugccgcugc ccaau 25

<210> SEQ ID NO 486
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 486

gacaacaguu ugccgcugcc caaug 25

<210> SEQ ID NO 487
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 487

acaacaguuu gccgcugccc aaugc 25

<210> SEQ ID NO 488
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonculeotide

<400> SEQUENCE: 488

caacaguuug ccgcugccca augcc 25

<210> SEQ ID NO 489
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 489

aacaguuugc cgcugcccaa ugcca 25

<210> SEQ ID NO 490
<211> LENGTH: 25
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 490

acaguuugcc gcugcccaau gccau 25

<210> SEQ ID NO 491
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 491

caguuugccg cugcccaaug ccauc 25

<210> SEQ ID NO 492
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 492

aguuugccgc ugcccaaugc caucc 25

<210> SEQ ID NO 493
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 493

guuugccgcu gcccaaugcc auccu 25

<210> SEQ ID NO 494
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 494

uuugccgcug cccaaugcca uccug 25

<210> SEQ ID NO 495
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 495

uugccgcugc ccaaugccau ccugg 25

<210> SEQ ID NO 496
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 496

ugccgcugcc caaugccauc cugga 25

<210> SEQ ID NO 497
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 497

gccgcugccc aaugccaucc uggag 25

<210> SEQ ID NO 498
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 498

ccgcugccca augccauccu ggagu 25

<210> SEQ ID NO 499
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 499

cgcugcccaa ugccauccug gaguu 25

<210> SEQ ID NO 500
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 500

uguuuuugag gauugcugaa 20

<210> SEQ ID NO 501
<211> LENGTH: 40
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 501

uguucugaca acaguuugcc gcugcccaau gccauccugg 40

<210> SEQ ID NO 502
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 502

cuguugcagu aaucuaugag 20

-continued

<210> SEQ ID NO 503
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 503

ugcaguaauc uaugaguuuc 20

<210> SEQ ID NO 504
<211> LENGTH: 18
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 504

gagucuucua ggagccuu 18

<210> SEQ ID NO 505
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 505

ugccauuguu ucaucagcuc uuu 23

<210> SEQ ID NO 506
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 506

uccuguagga cauuggcagu 20

<210> SEQ ID NO 507
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 507

cuuggagucu ucuaggagcc 20

<210> SEQ ID NO 508
<211> LENGTH: 17
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 508

uaggugccug ccggcuu 17

<210> SEQ ID NO 509
<211> LENGTH: 18
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 509

uucagcugua gccacacc 18

<210> SEQ ID NO 510
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 510

cugaacugcu ggaaagucgc c 21

<210> SEQ ID NO 511
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 511

cuggcuucca aaugggaccu gaaaaagaac 30

<210> SEQ ID NO 512
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 512

caauuuuucc cacucaguau u 21

<210> SEQ ID NO 513
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 513

uugaaguucc uggagucuu 19

<210> SEQ ID NO 514
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 514

uccucaggag gcagcucuaa au 22

<210> SEQ ID NO 515
<211> LENGTH: 16
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 515

uggcucucuc ccaggg 16

<210> SEQ ID NO 516
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 516

gagauggcuc ucucccaggg acccugg 27

<210> SEQ ID NO 517
<211> LENGTH: 17
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 517

gggcacuuug uuuggcg 17

<210> SEQ ID NO 518
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 518

ggucccagca aguuguuug 19

<210> SEQ ID NO 519
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 519

ugggaugguc ccagcaaguu guuug 25

<210> SEQ ID NO 520
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 520

guagagcucu gucauuuugg g 21

<210> SEQ ID NO 521
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 521

gcucaagaga uccacugcaa aaaac 25

-continued

<210> SEQ ID NO 522
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 522

gccauacgua cguaucauaa acauuc 26

<210> SEQ ID NO 523
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 523

ucugcaggau auccaugggc ugguc 25

<210> SEQ ID NO 524
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 524

gauccucccu guucgucccc uauuaug 27

<210> SEQ ID NO 525
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 525

ugcuuuagac uccuguaccu gaua 24

<210> SEQ ID NO 526
<211> LENGTH: 18
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 526

ggcggccuuu guguugac 18

<210> SEQ ID NO 527
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 527

ggacaggccu uuauguucgu gcugc 25

<210> SEQ ID NO 528
<211> LENGTH: 19
<212> TYPE: RNA

-continued

<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 528

ccuuuauguu cgugcugcu 19

<210> SEQ ID NO 529
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 529

ccucagcucu ugaaguaaac gguuu 25

<210> SEQ ID NO 530
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 530

cucagcucuu gaaguaaacg guuua 25

<210> SEQ ID NO 531
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 531

ucagcucuug aaguaaacgg uuuac 25

<210> SEQ ID NO 532
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 532

cagcucuuga aguaaacggu uuacc 25

<210> SEQ ID NO 533
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 533

agcucuugaa guaaacgguu uaccg 25

<210> SEQ ID NO 534
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

-continued

<400> SEQUENCE: 534

gcucuugaag uaaacgguuu accgc 25

<210> SEQ ID NO 535
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: oligonucleotide

<400> SEQUENCE: 535

cucuugaagu aaacgguuua ccgcc 25

1. A molecule, which binds to a continuous stretch of at least 8 nucleotides within one of the following nucleotide sequences selected from:

(SEQ ID NO: 4)
5'-GGCGGTAAACCGUUUACUUCAAGAGCUGAGGGCAAAGCAGCCUGA

CCUAGCUCCUGGACUGACCACUAUUGG-3'
for skipping of exon 50;

(SEQ ID NO: 2)
5'AGAUAGUCUACAACAAAGCUCAGGUCGGAUUGACAUUAUUCAUAGC

AAGAAGACAGCAGCAUUGCAAAGUGCAACGCCUGUGG-3'
for skipping of exon 43

(SEQ ID NO: 3)
5'UUAUGGUUGGAGGAAGCAGAUAACAUUGCUAGUAUCCCACUUGAAC

CUGGAAAAGAGCAGCAACUAAAAGAAAAGC-3'
for skipping of exon 46;

(SEQ ID NO: 5)
5'CUCCUACUCAGACUGUUACUCUGGUGACACAACCUGUGGUUACUAA

GGAAACUGCCAUCUCCAAACUAGAAAUGCCAUCUUCCUUGAUG UUGG

AGGUAC-3'
for skipping of exon 51;

(SEQ ID NO: 6)
5'AUGCAGGAUUUGGAACAGAGGCGUCCCCAGUUGGAAGAACUCAUUA

CCGCUGCCCAAAAUUUGAAAAACAAGACCAGCAAUCAAGAGGCU-3'
for skipping of exon 52,
and

(SEQ ID NO: 7)
5'AAAUGUUAAAGGAUUCAACACAAUGGCUGGAAGCUAAGGAAAA GC

UGAGCAGGUCUUAGGACAGGCCAGAG-3'
for skipping of exon 53.

2. A molecule according to claim 1, wherein the molecule comprises or consists of the antisense nucleotide sequence selected from SEQ ID NO: 8-358, and/or SEQ ID NO 529-535 as depicted in tables 1 to 6.

3. A molecule according to claim 2, wherein the molecule comprises or consists of the antisense nucleotide sequence selected from SEQ ID NO:16, SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:91, SEQ ID NO:110, SEQ ID NO:117, SEQ ID NO:127, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:246, SEQ ID NO:299 and SEQ ID NO:357.

4. A molecule according to claim 1, comprising a 2'-O-alkyl phosphorothioate antisense oligonucleotide.

5. A molecule according to claim 4, comprising a 2'-O methyl phosphorothioate ribose.

6. A viral-based vector, comprising an expression cassette that drives expression of a molecule as defined in claim 1.

7. A molecule according to claim 1 for use as a medicament, preferably for modulating splicing of the DMD pre-mRNA of a DMD or BMD patient or for the treatment of a DMD or BMD patient.

8. A pharmaceutical composition comprising a molecule as defined in claim 1, a pharmaceutical acceptable carrier, and optionally combined with a molecule which is able to induce or promote skipping of at least one of exon 6, 7, 11, 17, 19, 21, 43, 44, 45, 50-53, 55, 57, 59, 62, 63, 65, 66, 69, or 75 of the DMD pre-mRNA of a patient.

9. A method for inducing and/or promoting skipping of at least one of exon 43, exon 46, and exons 50-53 of the DMD pre-mRNA in a patient, preferably in an isolated cell of a patient, the method comprising providing said cell and/or said patient with a molecule as defined in claim 1.

10. A method according to claim 9, wherein an additional molecule is used which is able to induce or promote skipping of at least one of exon 6, 7, 11, 17, 19, 21, 43, 44, 45, 50-53, 55, 57, 59, 62, 63, 65, 66, 69, or 75 of the DMD pre-mRNA of a patient.

11. A method of treating a patient with DMD or BMD comprising administering the molecule of claim 1, wherein following administration, splicing of the DMD pre-mRNA of said patient is modulated, thereby treating said patient.

* * * * *