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(54) **COMPOSITIONS FOR TREATING
MUSCULAR DYSTROPHY**

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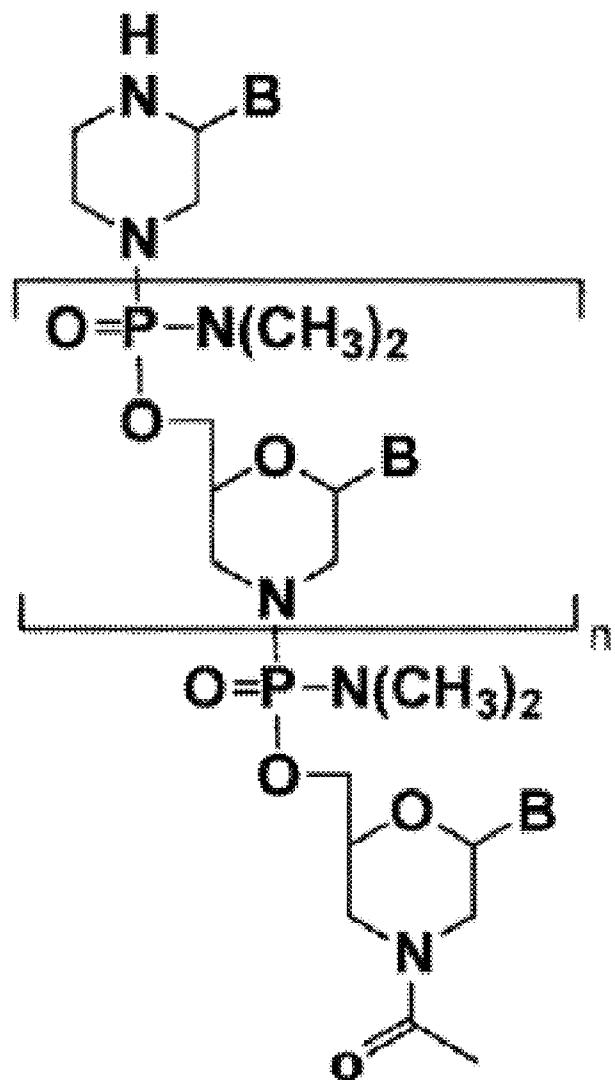
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(57)

ABSTRACT

Improved compositions and methods for treating muscular dystrophy by administering antisense molecules capable of binding to a selected target site in the human dystrophin gene to induce exon skipping are described.



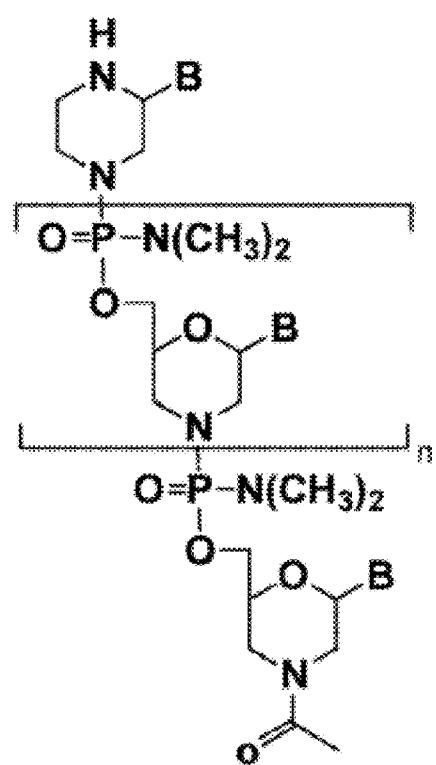


Fig. 1A

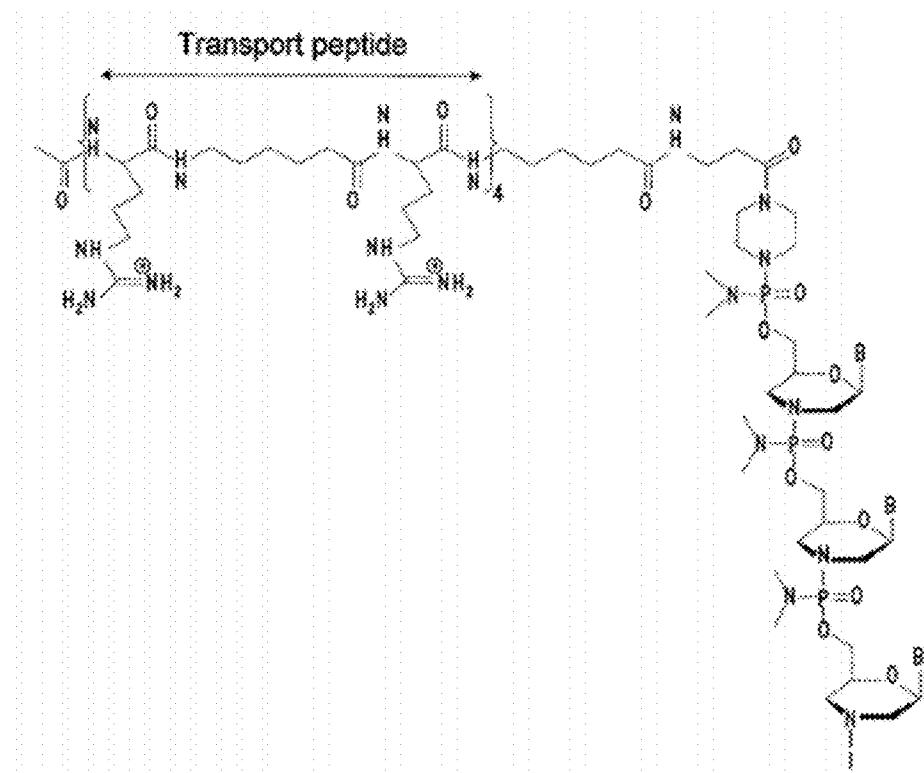


Fig. 1B

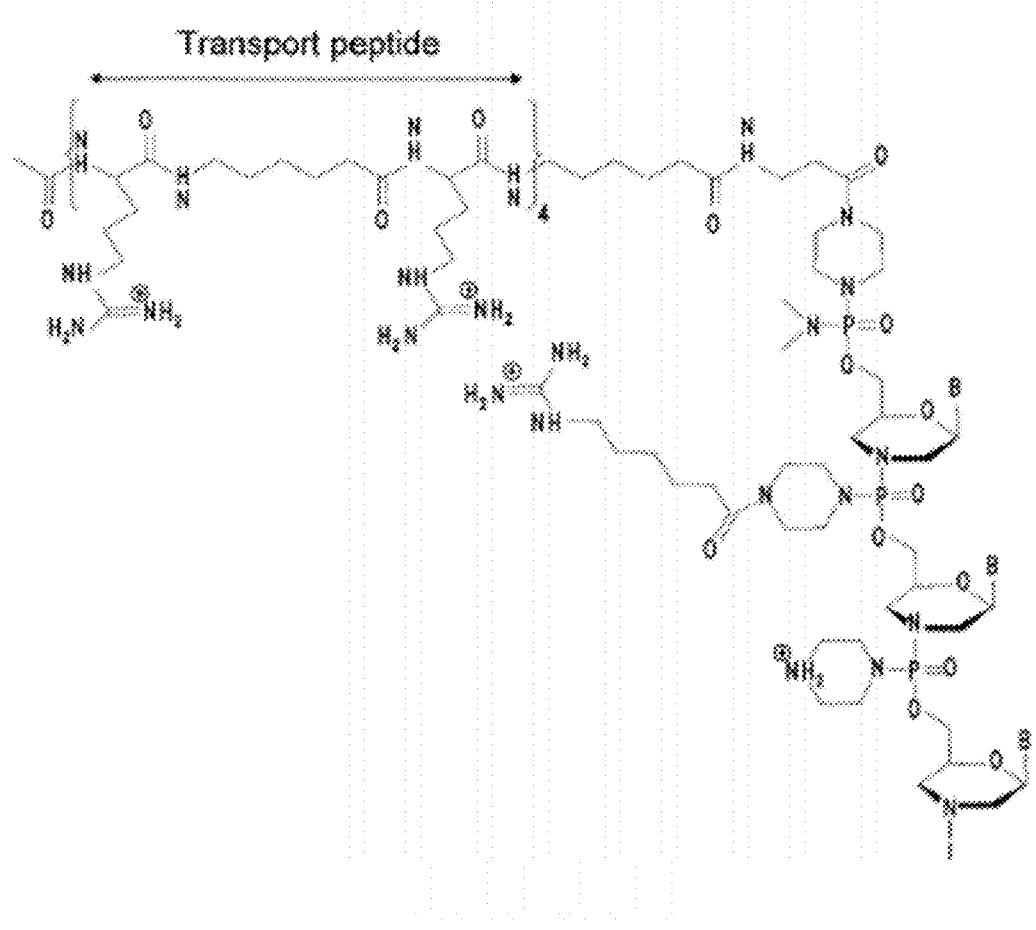


Fig. 1C

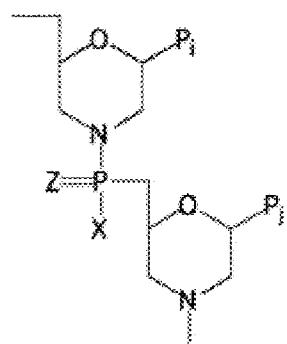


Fig. 1D

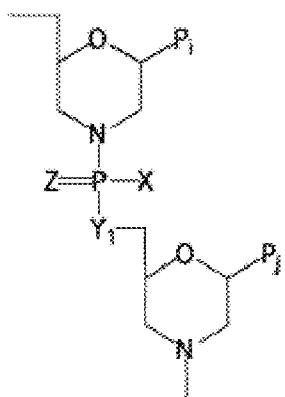


Fig. 1E

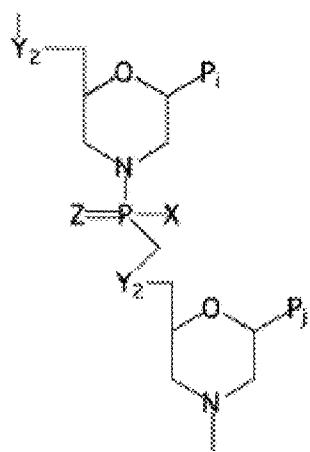


Fig. 1F

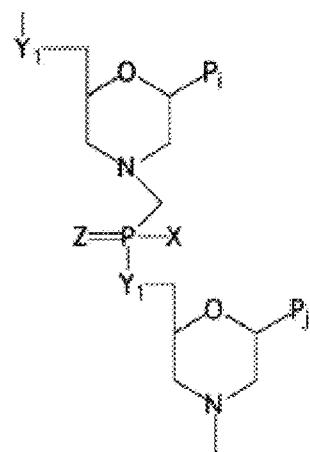


Fig. 1G

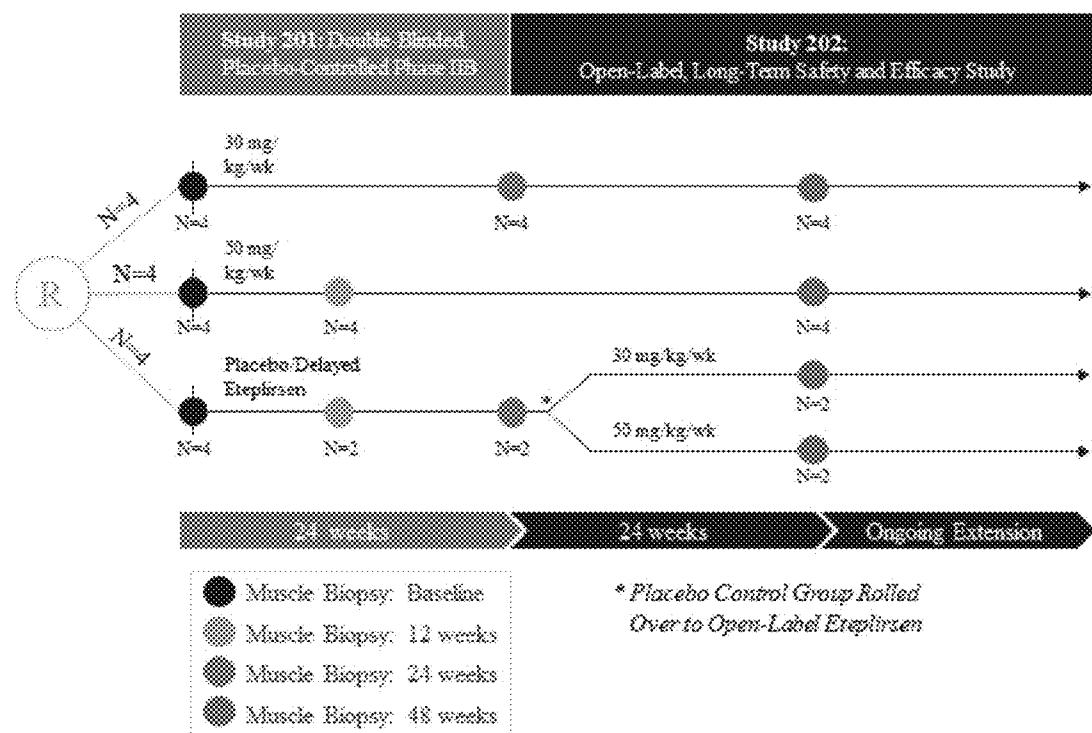


Fig. 2

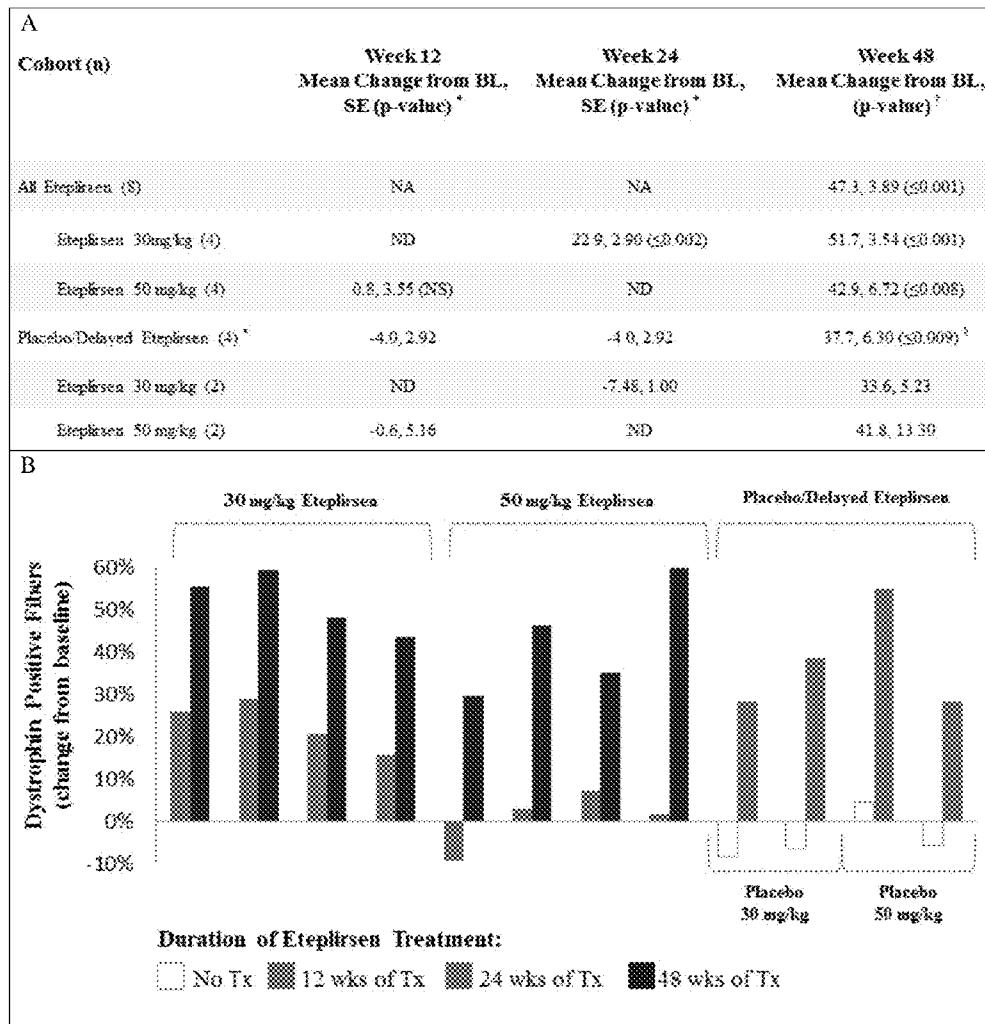
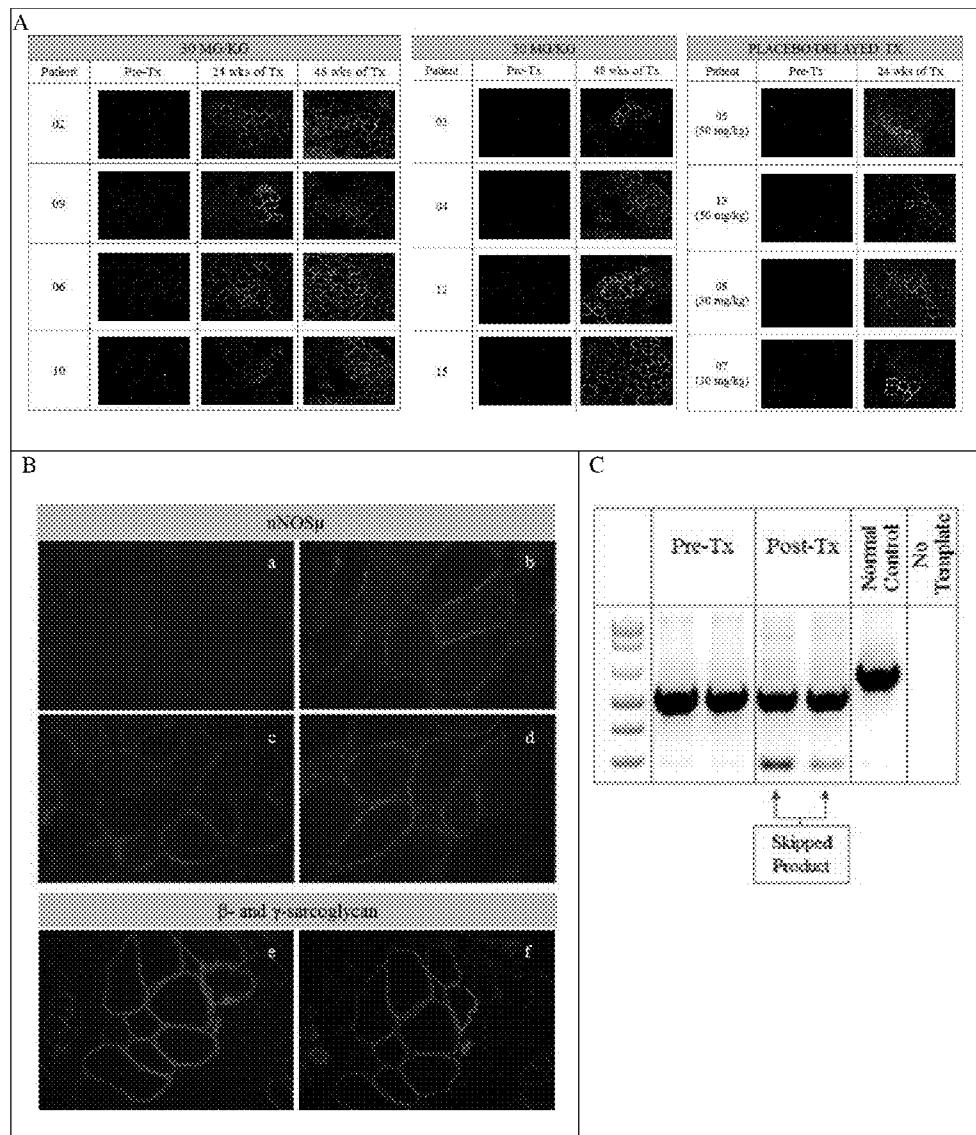


Fig. 3



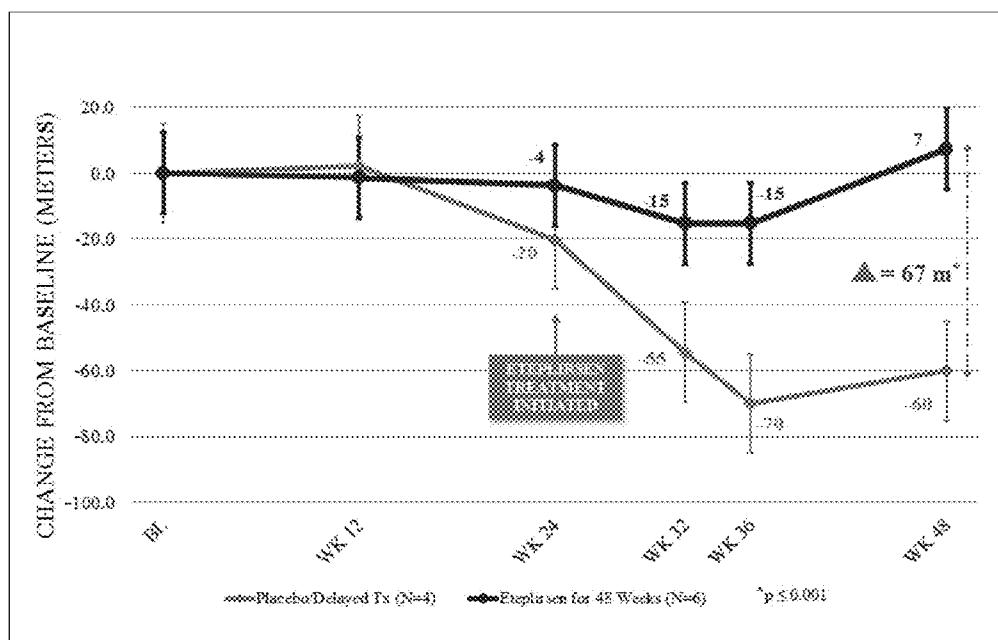


Fig. 5

COMPOSITIONS FOR TREATING MUSCULAR DYSTROPHY

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 61/793,463, filed on Mar. 15, 2013, entitled "COMPOSITIONS FOR TREATING MUSCULAR DYSTROPHY". The entire contents of the foregoing application are incorporated herein by reference.

STATEMENT REGARDING SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted in computer readable form (CRF) via EFS-Web and is hereby incorporated by reference in its entirety. Said CRF, created on Jul. 22, 2014, is named AVN_012A_Sequence_Listing.txt and is 187 Kilobytes in size. The Sequence Listing is being submitted by EFS Web and is hereby incorporated by reference into the specification.

FIELD OF THE INVENTION

[0003] The present invention relates to improved methods for treating muscular dystrophy in a patient. It also provides compositions suitable for facilitating exon skipping in the human dystrophin gene.

BACKGROUND OF THE INVENTION

[0004] Antisense technologies are being developed using a range of chemistries to affect gene expression at a variety of different levels (transcription, splicing, stability, translation). Much of that research has focused on the use of antisense compounds to correct or compensate for abnormal or disease-associated genes in a wide range of indications. Antisense molecules are able to inhibit gene expression with specificity, and because of this, many research efforts concerning oligonucleotides as modulators of gene expression have focused on inhibiting the expression of targeted genes or the function of cis-acting elements. The antisense oligonucleotides are typically directed against RNA, either the sense strand (e.g., mRNA), or minus-strand in the case of some viral RNA targets. To achieve a desired effect of specific gene down-regulation, the oligonucleotides generally either promote the decay of the targeted mRNA, block translation of the mRNA or block the function of cis-acting RNA elements, thereby effectively preventing either de novo synthesis of the target protein or replication of the viral RNA.

[0005] However, such techniques are not useful where the object is to up-regulate production of the native protein or compensate for mutations that induce premature termination of translation, such as nonsense or frame-shifting mutations. In these cases, the defective gene transcript should not be subjected to targeted degradation or steric inhibition, so the antisense oligonucleotide chemistry should not promote target mRNA decay or block translation.

[0006] In a variety of genetic diseases, the effects of mutations on the eventual expression of a gene can be modulated through a process of targeted exon skipping during the splicing process. The splicing process is directed by complex multi-component machinery that brings adjacent exon-intron junctions in pre-mRNA into close proximity and performs cleavage of phosphodiester bonds at the ends of the introns with their subsequent reformation between exons that are to be spliced together. This complex and highly precise process

is mediated by sequence motifs in the pre-mRNA that are relatively short, semi-conserved RNA segments to which various nuclear splicing factors that are then involved in the splicing reactions bind. By changing the way the splicing machinery reads or recognizes the motifs involved in pre-mRNA processing, it is possible to create differentially spliced mRNA molecules. It has now been recognized that the majority of human genes are alternatively spliced during normal gene expression, although the mechanisms involved have not been identified. Bennett et al. (U.S. Pat. No. 6,210,892) describe antisense modulation of wild-type cellular mRNA processing using antisense oligonucleotide analogs that do not induce RNase H-mediated cleavage of the target RNA. This finds utility in being able to generate alternatively spliced mRNAs that lack specific exons (e.g., as described by (Sazani, Kole, et al. 2007) for the generation of soluble TNF superfamily receptors that lack exons encoding membrane spanning domains.

[0007] In cases where a normally functional protein is prematurely terminated because of mutations therein, a means for restoring some functional protein production through antisense technology has been shown to be possible through intervention during the splicing processes, and that if exons associated with disease-causing mutations can be specifically deleted from some genes, a shortened protein product can sometimes be produced that has similar biological properties of the native protein or has sufficient biological activity to ameliorate the disease caused by mutations associated with the exon (see e.g., Sierakowska, Sambade et al. 1996; Wilton, Lloyd et al. 1999; van Deutekom, Bremmer-Bout et al. 2001; Lu, Mann et al. 2003; Aartsma-Rus, Janson et al. 2004). Kole et al. (U.S. Pat. Nos. 5,627,274; 5,916,808; 5,976,879; and 5,665,593) disclose methods of combating aberrant splicing using modified antisense oligonucleotide analogs that do not promote decay of the targeted pre-mRNA. Bennett et al. (U.S. Pat. No. 6,210,892) describe antisense modulation of wild-type cellular mRNA processing also using antisense oligonucleotide analogs that do not induce RNase H-mediated cleavage of the target RNA.

[0008] The process of targeted exon skipping is likely to be particularly useful in long genes where there are many exons and introns, where there is redundancy in the genetic constitution of the exons or where a protein is able to function without one or more particular exons. Efforts to redirect gene processing for the treatment of genetic diseases associated with truncations caused by mutations in various genes have focused on the use of antisense oligonucleotides that either: (1) fully or partially overlap with the elements involved in the splicing process; or (2) bind to the pre-mRNA at a position sufficiently close to the element to disrupt the binding and function of the splicing factors that would normally mediate a particular splicing reaction which occurs at that element.

[0009] Duchenne muscular dystrophy (DMD) is caused by a defect in the expression of the protein dystrophin. The gene encoding the protein contains 79 exons spread out over more than 2 million nucleotides of DNA. Any exonic mutation that changes the reading frame of the exon, or introduces a stop codon, or is characterized by removal of an entire out of frame exon or exons, or duplications of one or more exons, has the potential to disrupt production of functional dystrophin, resulting in DMD.

[0010] Disease onset can be documented at birth with elevated creatine kinase levels, and significant motor deficits may be present in the first year of life. By the age of seven or

eight, most patients with DMD have an increasingly labored gait and are losing the ability to rise from the floor and climb stairs; by ages 10 to 14, most are wheelchair-dependent. DMD is uniformly fatal; affected individuals typically die of respiratory and/or cardiac failure in their late teens or early 20s. The continuous progression of DMD allows for therapeutic intervention at all stages of the disease; however, treatment is currently limited to glucocorticoids, which are associated with numerous side effects including weight gain, behavioral changes, pubertal changes, osteoporosis, Cushingoid facies, growth inhibition, and cataracts. Consequently, developing better therapies to treat the underlying cause of this disease is imperative.

[0011] A less severe form of muscular dystrophy, Becker muscular dystrophy (BMD) has been found to arise where a mutation, typically a deletion of one or more exons, results in a correct reading frame along the entire dystrophin transcript, such that translation of mRNA into protein is not prematurely terminated. If the joining of the upstream and downstream exons in the processing of a mutated dystrophin pre-mRNA maintains the correct reading frame of the gene, the result is an mRNA coding for a protein with a short internal deletion that retains some activity, resulting in a Becker phenotype.

[0012] For many years it has been known that deletions of an exon or exons which do not alter the reading frame of a dystrophin protein would give rise to a BMD phenotype, whereas an exon deletion that causes a frame-shift will give rise to DMD (Monaco, Bertelson et al. 1988). In general, dystrophin mutations including point mutations and exon deletions that change the reading frame and thus interrupt proper protein translation result in DMD. It should also be noted that some BMD and DMD patients have exon deletions covering multiple exons.

[0013] Modulation of mutant dystrophin pre-mRNA splicing with antisense oligoribonucleotides has been reported both in vitro and in vivo (see e.g., Matsuo, Masumura et al. 1991; Takeshima, Nishio et al. 1995; Pramono, Takeshima et al. 1996; Dunckley, Eperon et al. 1997; Dunckley, Manoharan et al. 1998; Errington, Mann et al. 2003).

[0014] The first example of specific and reproducible exon skipping in the mdx mouse model was reported by Wilton et al. (Wilton, Lloyd et al. 1999). By directing an antisense molecule to the donor splice site, consistent and efficient exon 23 skipping was induced in the dystrophin mRNA within 6 hours of treatment of the cultured cells. Wilton et al. also describe targeting the acceptor region of the mouse dystrophin pre-mRNA with longer antisense oligoribonucleotides. While the first antisense oligoribonucleotide directed at the intron 23 donor splice site induced consistent exon skipping in primary cultured myoblasts, this compound was found to be much less efficient in immortalized cell cultures expressing higher levels of dystrophin. However, with refined targeting and antisense oligoribonucleotide design, the efficiency of specific exon removal was increased by almost an order of magnitude (Mann, Honeyman et al. 2002).

[0015] Recent studies have begun to address the challenge of achieving sustained dystrophin expression accompanied by minimal adverse effects in tissues affected by the absence of dystrophin. Intramuscular injection of an antisense oligonucleotide targeted to exon 51 (PRO051) into the tibialis anterior muscle in four patients with DMD resulted in specific skipping of exon 51 without any clinically apparent adverse effects (Mann, Honeyman et al. 2002; van Deutekom, Janson et al. 2007). Studies looking at systemic delivery of an anti-

sense phosphorodiamidate morpholino oligomer conjugated to a cell-penetrating peptide (PPMO) targeted to exon 23 in mdx mice produced high and sustained dystrophin protein production in skeletal and cardiac muscles without detectable toxicity (Jearawiriyapaisarn, Moulton et al. 2008; Wu, Moulton et al. 2008; Yin, Moulton et al. 2008).

[0016] Recent clinical trials testing the safety and efficacy of splice switching oligonucleotides (SSOs) for the treatment of DMD are based on SSO technology to induce alternative splicing of pre-mRNAs by steric blockade of the spliceosome (Cirak et al., 2011; Goemans et al., 2011; Kinalli et al., 2009; van Deutekom et al., 2007). However, despite these successes, the pharmacological options available for treating DMD are limited. Notably, an antisense oligonucleotide (drisapersen), which utilizes a negatively charged phosphorothioate backbone, has been associated in clinical trials with proteinuria, increased urinary al-microglobulin, thrombocytopenia and injection site reactions, such as erythema and inflammation.

[0017] Thus, there remains a need for improved compositions and methods for treating muscular dystrophy, such as DMD and BMD in patients.

SUMMARY OF THE INVENTION

[0018] The present invention is based, at least in part, on compelling evidence of a therapeutic effect of an exon skipping antisense oligonucleotide, eteplirsen, which represents a major advance in the treatment of DMD by addressing the underlying cause of the disease. The novel finding that treatment with an exon 51 skipping antisense oligonucleotide, eteplirsen, produced reliable increases in novel dystrophin and stabilized walking ability (e.g., stabilization of ambulation), as measured by the 6 Minute Walk Test (6MWT), underscores the potential alter the course of the disease. Significantly, no drug-related adverse events were seen in 576 infusions administered over one year. When applied to other exons, the use of exon skipping antisense oligonucleotides could treat an estimated 70% to 80% of patients who have DMD due to a deletion in the dystrophin gene.

[0019] Accordingly, the present invention relates to methods of treating Duchenne muscular dystrophy (DMD) or Becker muscular dystrophy (BMD) in patients by administering an effective amount of a composition comprising an antisense oligonucleotide of 20 to 50 nucleotides in length comprising at least 10 consecutive nucleotides complementary to a target region in an exon of the human dystrophin gene to specifically hybridize to the target region, induce exon skipping, and thereby treat the disease. In one embodiment, an effective amount is at least 20 mg/kg for a period of time sufficient to increase the number of dystrophin-positive fibers in a subject to at least 20% of normal, and stabilize, maintain, or improve walking distance from a 20% deficit, for example in a 6 MWT, in the patient, relative to a healthy peer. In another embodiment, an effective amount is at least 20 mg/kg to about 30 mg/kg, about 25 mg/kg to about 30 mg/kg, or about 30 mg/kg to about 50 mg/kg. In yet another embodiment, an effective amount is about 30 mg/kg or about 50 mg/kg.

[0020] In another aspect, an effective amount is at least 20 mg/kg, about 25 mg/kg, about 30 mg/kg, or about 30 mg/kg to about 50 mg/kg, for at least 24 weeks, at least 36 weeks, or at least 48 weeks, to thereby increase the number of dystrophin-positive fibers in a subject to at least 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about

90%, about 95% of normal, and stabilize or improve walking distance from a 20% deficit, for example in a 6 MWT, in the patient relative to a healthy peer. In one embodiment, treatment increases the number of dystrophin-positive fibers to 20-60%, or 30-50% of normal in the patient. In some embodiments, treatment is by systemic administration, such as once weekly by infusion. In other embodiments, treatment includes administering another therapeutic agent, such as a steroid to the subject.

[0021] In another aspect, the present invention provides a method of treating DMD or BMD in a patient by administering about 30 mg/kg to about 50 mg/kg of a composition comprising an antisense oligonucleotide of 20 to 50 nucleotides in length comprising at least 10 consecutive nucleotides complementary to a target region in an exon of the human dystrophin gene, wherein the antisense oligonucleotide specifically hybridizes to the target region inducing exon skipping, thereby treating the subject. In one embodiment, the antisense oligonucleotide is substantially uncharged. In another embodiment, the antisense oligonucleotide comprises morpholino subunits linked by phosphorus-containing intersubunit linkages joining a morpholino nitrogen of one subunit to a 5' exocyclic carbon of an adjacent subunit. In yet another embodiment, the antisense oligonucleotide comprises morpholino subunits linked by substantially uncharged phosphorus-containing intersubunit linkages joining a morpholino nitrogen of one subunit to a 5' exocyclic carbon of an adjacent subunit. In other aspects, the antisense oligonucleotide comprises morpholino subunits and phosphorodiamide intersubunit linkages.

[0022] In some embodiments, the antisense oligonucleotide is 20 to 50, 30 to 50, or 20 to 30 nucleotides in length comprising at least 10, 12, 15, 17, or 20 consecutive nucleotides complementary to a target region in an exon of the human dystrophin gene selected from the group consisting of exon 51, exon 50, exon 53, exon 45, exon 46, exon 44, exon 52, exon 55 and exon 8. In one embodiment, the antisense is 20 to 50, 30 to 50, or 20 to 30 nucleotides in length and includes at least 20 consecutive nucleotides eteplirsen (SEQ ID NO: 1). In another embodiment, the antisense oligonucleotide is 20 to 50, 30 to 50, or 20 to 30 nucleotides in length and includes at least 10, 12, 15, 17, or 20 consecutive nucleotides of the antisense oligonucleotide set forth as SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID NO: 9. In yet another embodiment, the antisense oligonucleotide is 20 to 50, 30 to 50, or 20 to 30 nucleotides in length and includes at least 10, 12, 15, 17, or 20 consecutive nucleotides of a nucleotide sequences set forth in Tables 3 and 4, wherein uracil bases in the antisense oligonucleotide are optionally thymine bases.

[0023] In one embodiment, the composition includes eteplirsen (SEQ ID NO: 1), and, optionally, a pharmaceutically acceptable carrier. In another embodiment, the composition includes an antisense oligonucleotide selected from the group consisting of SEQ ID NOS: 1-9, such as SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9. In yet another embodiment, the antisense oligonucleotide is any one or a combination of the nucleotide sequences set forth in Tables 3 and 4, wherein uracil bases in the antisense oligonucleotide are optionally thymine bases. In some aspects, the antisense oligonucleotide is chemically linked to one or more moieties or conjugates that enhance the activity, cellular

distribution, or cellular uptake of the antisense oligonucleotide, such as an arginine-rich peptide.

[0024] In another aspect, the present invention provides a method of treating DMD or BMD in a patient by administering at least 20 mg/kg of a composition comprising eteplirsen (SEQ ID NO: 1) for a period of time sufficient to increase the number of dystrophin-positive fibers in a subject to at least about 20% of normal, and stabilize or improve walking distance from a 20% deficit, for example in a 6 MWT, in the patient, relative to a healthy peer. In another embodiment, an effective amount is at least 20 mg/kg to about 30 mg/kg, about 25 mg/kg to about 30 mg/kg, or about 30 mg/kg to about 50 mg/kg of a composition comprising eteplirsen (SEQ ID NO: 1), and, optionally, a pharmaceutically acceptable carrier, such as phosphate-buffered saline.

[0025] In another aspect, an effective amount of a composition comprising eteplirsen (SEQ ID NO: 1) is at least 20 mg/kg, about 25 mg/kg, about 30 mg/kg, or about 30 mg/kg to about 50 mg/kg, for at least 24 weeks, at least 36 weeks, or at least 48 weeks, to thereby increase the number of dystrophin-positive fibers in a subject to at least about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95% of normal, and stabilize or improve walking distance from a 20% deficit, for example in a 6 MWT, in the patient relative to a healthy peer. In some embodiments, treatment with antisense oligonucleotides of the present invention slows or reduces the loss of ambulation that would be expected without treatment. In some embodiments, treatment with the antisense oligonucleotides of the present invention stabilizes, maintains, or increases a stable walking distance in a patient. For example, treatment may increase the stable walking distance in the patient from baseline to greater than 3, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30 or 50 meters (including all integers in between).

BRIEF DESCRIPTION OF THE FIGURES

[0026] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0027] FIG. 1A shows an exemplary morpholino oligomer structure with a phosphorodiamide linkage.

[0028] FIG. 1B shows a conjugate of an arginine-rich peptide and an antisense oligomer, in accordance with an embodiment of the invention.

[0029] FIG. 1C shows a conjugate as in FIG. 1B, wherein the backbone linkages contain one or more positively charged groups.

[0030] FIGS. 1D-G show the repeating subunit segment of exemplary morpholino oligonucleotides, designated D through G.

[0031] FIG. 2 is a schematic representation of the study design for treating DMD patients. Twelve DMD patients were randomized to one of three cohorts in the double-blind, placebo-controlled study, 201: Cohort 1, eteplirsen 30 mg/kg/wk; Cohort 2, eteplirsen 50 mg/kg/wk; and Cohort 3, placebo/delayed eteplirsen. At week 25, placebo-treated patients in Cohort 3 switched to open-label treatment with 30 or 50 mg/kg/week eteplirsen. Patients were maintained on their same dose of eteplirsen under the open-label extension study, 202. Muscle Biopsies. Patients underwent biceps biopsies at baseline and deltoid biopsies at week 48 for analysis of dystrophin. Additional biceps biopsies were obtained at week 12

(from patients in Cohort 2 and two patients in Cohort 3) or week 24 (from patients in Cohort 1 and two patients in Cohort 3). Efficacy Evaluations. The 6MWT was used as a functional outcome measure and was performed pre-treatment and every 12 weeks post treatment through week 48.

[0032] FIG. 3 depicts dystrophin-positive muscle fibers after 12, 24, and 48 weeks of eteplirsen. Panels A and B show the mean absolute change from baseline in the percentage of dystrophin-positive fibers at weeks 12, 24, and week 48 by treatment group. In Panel A: *P-value is for comparison between eteplirsen and placebo using the pooled results from weeks 12 and 24, and is based on an analysis of covariance model for ranked data with treatment as a fixed effect and baseline value and time since DMD diagnosis as covariates. Mean changes shown are based on descriptive statistics. [†]P-value is from a paired t-test comparing the week 48 value to baseline. [‡]Results from the placebo-treated patients biopsied at weeks 12 and 24 are pooled. §Placebo/delayed eteplirsen patients began receiving eteplirsen at week 25 and had received a total of 24 doses at week 48. Abbreviations: BL=baseline; NA=not applicable; ND=not done; NS=not significant; SE=standard error.

[0033] FIG. 4 shows the effects of eteplirsen on the dystrophin-associated glycoprotein complex. (A) Representative examples of time-dependent increases in dystrophin-positive fibers in relation to treatment for all participating study patients. (B) nNOS μ staining in muscle from DMD (a) and normal (c) control patients (not in study), and from patient 6 at baseline (b) and week 48 (d), demonstrates restoration of nNOS μ binding with eteplirsen. β -sarcoglycan (e) and γ -sarcoglycan (f) staining in patient 6 at week 48 demonstrate restoration of the sarcoglycan complex with eteplirsen. (C) RT-PCR shows skipped product (289 bp) post-treatment in the muscle of patient 12.

[0034] FIG. 5 graphically depicts the functional efficacy of eteplirsen. The dark purple line shows the change from baseline in distance walked on the 6MWT over time for the 6 evaluable patients who received eteplirsen from the start of 201 (two boys were unable to at or beyond week 24 were excluded from this analysis). The gray line shows change from baseline in distance walked on the 6MWT for the 4 patients who received placebo for the first 24 weeks and eteplirsen for the last 24 weeks.

DETAILED DESCRIPTION

[0035] Embodiments of the present invention relate to improved methods for treating muscular dystrophy, such as DMD and BMD, by administering antisense compounds that are specifically designed to induce exon skipping in the human dystrophin gene. Dystrophin plays a vital role in muscle function, and various muscle-related diseases are characterized by mutated forms of this gene. Hence, in certain embodiments, the improved methods described herein may be used for inducing exon skipping in mutated forms of the human dystrophin gene, such as the mutated dystrophin genes found in DMD and BMD.

[0036] Due to aberrant mRNA splicing events caused by mutations, these mutated human dystrophin genes either express defective dystrophin protein or express no measurable dystrophin at all, a condition that leads to various forms of muscular dystrophy. To remedy this condition, the antisense compounds of the present invention hybridize to selected regions of a pre-processed RNA of a mutated human dystrophin gene, induce exon skipping and differential splicing

in that otherwise aberrantly spliced dystrophin mRNA, and thereby allow muscle cells to produce an mRNA transcript that encodes a functional dystrophin protein. In certain embodiments, the resulting dystrophin protein is not necessarily the “wild-type” form of dystrophin, but is rather a truncated, yet functional or semi-functional, form of dystrophin.

[0037] By increasing the levels of functional dystrophin protein in muscle cells, these and related embodiments are useful in the prophylaxis and treatment of muscular dystrophy, especially those forms of muscular dystrophy, such as DMD and BMD, that are characterized by the expression of defective dystrophin proteins due to aberrant mRNA splicing. The methods described herein further provide improved treatment options for patients with muscular dystrophy and offer significant and practical advantages over alternate methods of treating relevant forms of muscular dystrophy. For example, in some embodiments, the improved methods relate to the administration of an antisense compound for inducing exon skipping in the human dystrophin gene at a higher dose and/or for a longer duration than prior approaches.

[0038] Thus, the invention relates to improved methods for treating muscular dystrophy such as DMD and BMD, by inducing exon skipping in a patient. In some embodiments, exon skipping is induced by administering an effective amount of a composition which includes a charge-neutral, phosphorodiamidate morpholino oligomer (PMO), such as eteplirsen, which selectively binds to a target sequence in an exon of dystrophin pre-mRNA. In some embodiments, the invention relates to methods of treating DMD or BMD in which an effective amount of a composition e.g., at least 20 mg/kg, about 25 mg/kg, about 30 mg/kg or about 30 mg/kg to about 50 mg/kg, which includes an antisense as described herein, such as eteplirsen, over a period of time sufficient to treat the disease.

[0039] Some embodiments of the present invention relate to the use of eteplirsen as a disease-modifying therapy for treating DMD. In a clinical study described in the Examples, no drug-related adverse events were seen in 576 infusions of eteplirsen administered over one year, nor were there any infusion-associated reactions, cardiac abnormalities, or any other organ system involvement. There was also no evidence of glomerular or renal tubular dysfunction in eteplirsen-treated patients over the course of the study (e.g., no proteinuria, elevations in serum cystatin C, or urine cystatin C or KIM-1). Without being bound by theory, the safety profile of eteplirsen and other exon-skipping antisense oligonucleotides described herein may be attributed to its unique chemical composition, which is characterized by nucleotides bound to morpholine rings linked through charge-neutral phosphorodiamidate moieties.

[0040] In DMD patients treated with eteplirsen for one year, the mean percentage of dystrophin-positive fibers was increased to 47% of normal, relative to baseline. The magnitude of the increase was dependent upon treatment duration. Significant increases in dystrophin levels were observed in the 24-week biopsies taken from patients in Cohort 1 (30 mg/kg) and in the 48-week biopsies from patients in Cohort 3 (who started eteplirsen at week 25).

[0041] Eteplirsen's clinical benefit mirrored its ability to induce exon skipping and restore functional dystrophin production. Clinical effect was assessed with the 6MWT, a measure of endurance and muscular capacity that goes beyond the assessment of strength in individual muscle groups. Patients

who received 30 or 50 mg/kg eteplirsen from the beginning maintained a stable walking distance over 48 weeks, consistent with eteplirsen-induced increases in novel dystrophin expression between weeks 12 and 24. In contrast, patients in the placebo/delayed eteplirsen cohort lost 70 meters by week 36, but appeared to stabilize by week 48 (24 weeks after initiating eteplirsen). This is the same timeframe in which a clinical impact was seen in patients who received 30 or 50 mg/kg eteplirsen once a week from the start of the study.

[0042] The present invention is based, at least in part, on the evidence of a therapeutic effect of eteplirsen, which represents a major advance in the treatment of DMD by addressing the underlying cause of the disease. Accordingly, the invention relates to methods of treating DMD or BMD in patients by administering an effective amount of a composition which includes an antisense oligonucleotide, such as eteplirsen, which is complementary to a target region in an exon of the human dystrophin gene to specifically hybridize to the target region, induce exon skipping, and treat the disease. In one embodiment, treatment is by administering one or more antisense oligonucleotides of the present invention (e.g., a nucleotide sequence shown in Tables 3 and 4), optionally as part of a pharmaceutical formulation or dosage form, to a subject in need thereof. Treatment includes inducing exon-skipping in a subject by administering an effective amount of one or more antisense oligonucleotides, in which the exon is any one or more of exons 1-79 from the dystrophin gene. Preferably, the exon is exon 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 8 from the human dystrophin gene.

[0043] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by those of ordinary skill in the art to which the invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, preferred methods and materials are described. For the purposes of the present invention, the following terms are defined below.

I. DEFINITIONS

[0044] By "about" is meant a quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length that varies by as much as 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1% to a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length.

[0045] The terms "complementary" and "complementarity" refer to polynucleotides (i.e., a sequence of nucleotides) related by base-pairing rules. For example, the sequence "T-G-A (5'-3')," is complementary to the sequence "T-C-A (5'-3')." Complementarity may be "partial," in which only some of the nucleic acids' bases are matched according to base pairing rules. Or, there may be "complete" or "total" complementarity between the nucleic acids. The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of hybridization between nucleic acid strands. While perfect complementarity is often desired, some embodiments can include one or more but preferably 6, 5, 4, 3, 2, or 1 mismatches with respect to the target RNA. Variations at any location within the oligomer are included. In certain embodiments, variations in sequence near the termini of an oligomer are generally preferable to variations in the interior, and if present are typically within about 6, 5, 4, 3, 2, or 1 nucleotides of the 5' and/or 3' terminus.

[0046] The terms "cell penetrating peptide" and "CPP" are used interchangeably and refer to cationic cell penetrating peptides, also called transport peptides, carrier peptides, or peptide transduction domains. The peptides, as shown herein, have the capability of inducing cell penetration within 100% of cells of a given cell culture population and allow macromolecular translocation within multiple tissues *in vivo* upon systemic administration. A preferred CPP embodiment is an arginine-rich peptide as described further below.

[0047] The terms "antisense oligomer" and "antisense compound" and "antisense oligonucleotide" are used interchangeably and refer to a sequence of cyclic subunits, each bearing a base-pairing moiety, linked by intersubunit linkages that allow the base-pairing moieties to hybridize to a target sequence in a nucleic acid (typically an RNA) by Watson-Crick base pairing, to form a nucleic acid:oligomer heteroduplex within the target sequence. The cyclic subunits are based on ribose or another pentose sugar or, in a preferred embodiment, a morpholino group (see description of morpholino oligomers below). The oligomer may have exact or near sequence complementarity to the target sequence; variations in sequence near the termini of an oligomer are generally preferable to variations in the interior.

[0048] Such an antisense oligomer can be designed to block or inhibit translation of mRNA or to inhibit natural pre-mRNA splice processing, and may be said to be "directed to" or "targeted against" a target sequence with which it hybridizes. The target sequence is typically a region including an AUG start codon of an mRNA, a Translation Suppressing Oligomer, or splice site of a pre-processed mRNA, a Splice Suppressing Oligomer (SSO). The target sequence for a splice site may include an mRNA sequence having its 5' end 1 to about 25 base pairs downstream of a normal splice acceptor junction in a preprocessed mRNA. A preferred target sequence is any region of a preprocessed mRNA that includes a splice site or is contained entirely within an exon coding sequence or spans a splice acceptor or donor site. An oligomer is more generally said to be "targeted against" a biologically relevant target, such as a protein, virus, or bacteria, when it is targeted against the nucleic acid of the target in the manner described above.

[0049] The terms "morpholino oligomer" or "PMO" (phosphoramidate- or phosphorodiamidate morpholino oligomer) refer to an oligonucleotide analog composed of morpholino subunit structures, where (i) the structures are linked together by phosphorus-containing linkages, one to three atoms long, preferably two atoms long, and preferably uncharged or cationic, joining the morpholino nitrogen of one subunit to a 5' exocyclic carbon of an adjacent subunit, and (ii) each morpholino ring bears a purine or pyrimidine base-pairing moiety effective to bind, by base specific hydrogen bonding, to a base in a polynucleotide. See, for example, the structure in FIG. 1A, which shows a preferred phosphorodiamidate linkage type. Variations can be made to this linkage as long as they do not interfere with binding or activity. For example, the oxygen attached to phosphorus may be substituted with sulfur (thiophosphorodiamidate). The 5' oxygen may be substituted with amino or lower alkyl substituted amino. The pendant nitrogen attached to phosphorus may be unsubstituted, monosubstituted, or disubstituted with (optionally substituted) lower alkyl. The purine or pyrimidine base pairing moiety is typically adenine, cytosine, guanine, uracil, thymine or inosine. The synthesis, structures, and binding characteristics of morpholino oligomers are detailed in U.S. Pat. Nos. 5,698,685,

5,217,866, 5,142,047, 5,034,506, 5,166,315, 5,521,063, 5,506,337, 8,076,476, 8,299,206 and 7,943,762 (cationic linkages), all of which are incorporated herein by reference. Modified intersubunit linkages and terminal groups are detailed in PCT application US2011/038459 and publication WO/2011/150408 which are incorporated herein by reference in their entirety.

[0050] An “amino acid subunit” or “amino acid residue” can refer to an α -amino acid residue (—CO—CHR—NH—) or a β - or other amino acid residue (e.g. —CO—(CH₂)_nCHR—NH—), where R is a side chain (which may include hydrogen) and n is 1 to 6, preferably 1 to 4.

[0051] The term “naturally occurring amino acid” refers to an amino acid present in proteins found in nature. The term “non-natural amino acids” refers to those amino acids not present in proteins found in nature, examples include beta-alanine (β -Ala), 6-aminohexanoic acid (Ahx) and 6-amino-pentanoic acid.

[0052] An “exon” refers to a defined section of nucleic acid that encodes for a protein, or a nucleic acid sequence that is represented in the mature form of an RNA molecule after either portions of a pre-processed (or precursor) RNA have been removed by splicing. The mature RNA molecule can be a messenger RNA (mRNA) or a functional form of a non-coding RNA, such as rRNA or tRNA. The human dystrophin gene has about 79 exons.

[0053] An “intron” refers to a nucleic acid region (within a gene) that is not translated into a protein. An intron is a non-coding section that is transcribed into a precursor mRNA (pre-mRNA), and subsequently removed by splicing during formation of the mature RNA.

[0054] An “effective amount” or “therapeutically effective amount” refers to an amount of therapeutic compound, such as an antisense oligonucleotide, administered to a human subject, either as a single dose or as part of a series of doses, which is effective to produce a desired therapeutic effect. For an antisense oligonucleotide, this effect is typically brought about by inhibiting translation or natural splice-processing of a selected target sequence. In some embodiments, an effective amount is at least 20 mg/kg of a composition including an antisense oligonucleotide for a period of time to treat the subject. In one embodiment, an effective amount is at least 20 mg/kg of a composition including an antisense oligonucleotide to increase the number of dystrophin-positive fibers in a subject to at least 20% of normal. In another embodiment, an effective amount is at least 20 mg/kg of a composition including an antisense oligonucleotide to stabilize, maintain, or improve walking distance from a 20% deficit, for example in a 6 MWT, in a patient, relative to a healthy peer. In another embodiment, an effective amount is at least 20 mg/kg to about 30 mg/kg, about 25 mg/kg to about 30 mg/kg, or about 30 mg/kg to about 50 mg/kg. In yet another embodiment, an effective amount is about 30 mg/kg or about 50 mg/kg. In another aspect, an effective amount is at least 20 mg/kg, about 25 mg/kg, about 30 mg/kg, or about 30 mg/kg to about 50 mg/kg, for at least 24 weeks, at least 36 weeks, or at least 48 weeks, to thereby increase the number of dystrophin-positive fibers in a subject to at least 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95% of normal, and stabilize or improve walking distance from a 20% deficit, for example in a 6 MWT, in the patient relative to a healthy peer. In one embodiment, treatment increases the number of dystrophin-positive fibers to 20-60%, or 30-50% of normal in the patient.

[0055] “Exon skipping” refers generally to the process by which an entire exon, or a portion thereof, is removed from a given pre-processed RNA, and is thereby excluded from being present in the mature RNA, such as the mature mRNA that is translated into a protein. Hence, the portion of the protein that is otherwise encoded by the skipped exon is not present in the expressed form of the protein, typically creating an altered, though still functional, form of the protein. In certain embodiments, the exon being skipped is an aberrant exon from the human dystrophin gene, which may contain a mutation or other alteration in its sequence that otherwise causes aberrant splicing. In certain embodiments, the exon being skipped is any one or more of exons 1-79 of the human dystrophin gene, such as 3-8, 10-16, 19-40, 42-47, and 50-55, though exons 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 and 8 of the human dystrophin gene are preferred.

[0056] “Dystrophin” is a rod-shaped cytoplasmic protein, and a vital part of the protein complex that connects the cytoskeleton of a muscle fiber to the surrounding extracellular matrix through the cell membrane. Dystrophin contains multiple functional domains. For instance, dystrophin contains an actin binding domain at about amino acids 14-240 and a central rod domain at about amino acids 253-3040. This large central domain is formed by 24 spectrin-like triple-helical elements of about 109 amino acids, which have homology to alpha-actinin and spectrin. The repeats are typically interrupted by four proline-rich non-repeat segments, also referred to as hinge regions. Repeats 15 and 16 are separated by an 18 amino acid stretch that appears to provide a major site for proteolytic cleavage of dystrophin. The sequence identity between most repeats ranges from 10-25%. One repeat contains three alpha-helices: 1, 2 and 3. Alpha-helices 1 and 3 are each formed by 7 helix turns, probably interacting as a coiled-coil through a hydrophobic interface. Alpha-helix 2 has a more complex structure and is formed by segments of four and three helix turns, separated by a Glycine or Proline residue. Each repeat is encoded by two exons, typically interrupted by an intron between amino acids 47 and 48 in the first part of alpha-helix 2. The other intron is found at different positions in the repeat, usually scattered over helix-3. Dystrophin also contains a cysteine-rich domain at about amino acids 3080-3360), including a cysteine-rich segment (i.e., 15 Cysteines in 280 amino acids) showing homology to the C-terminal domain of the slime mold (*Dictyostelium discoideum*) alpha-actinin. The carboxy-terminal domain is at about amino acids 3361-3685.

[0057] The amino-terminus of dystrophin binds to F-actin and the carboxy-terminus binds to the dystrophin-associated protein complex (DAPC) at the sarcolemma. The DAPC includes the dystroglycans, sarcoglycans, integrins and caveolin, and mutations in any of these components cause autosomally inherited muscular dystrophies. The DAPC is destabilized when dystrophin is absent, which results in diminished levels of the member proteins, and in turn leads to progressive fibre damage and membrane leakage. In various forms of muscular dystrophy, such as Duchenne’s muscular dystrophy (DMD) and Becker’s muscular dystrophy (BMD), muscle cells produce an altered and functionally defective form of dystrophin, or no dystrophin at all, mainly due to mutations in the gene sequence that lead to incorrect splicing. The predominant expression of the defective dystrophin protein, or the complete lack of dystrophin or a dystrophin-like protein, leads to rapid progression of muscle degeneration, as noted above. In this regard, a “defective” dystrophin protein

may be characterized by the forms of dystrophin that are produced in certain subjects with DMD or BMD, as known in the art, or by the absence of detectable dystrophin.

[0058] As used herein, the terms "function" and "functional" and the like refer to a biological, enzymatic, or therapeutic function.

[0059] A "functional" dystrophin protein refers generally to a dystrophin protein having sufficient biological activity to reduce the progressive degradation of muscle tissue that is otherwise characteristic of muscular dystrophy, typically as compared to the altered or "defective" form of dystrophin protein that is present in certain subjects with DMD or BMD. In certain embodiments, a functional dystrophin protein may have about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% (including all integers in between) of the in vitro or in vivo biological activity of wild-type dystrophin, as measured according to routine techniques in the art. As one example, dystrophin-related activity in muscle cultures in vitro can be measured according to myotube size, myofibril organization (or disorganization), contractile activity, and spontaneous clustering of acetylcholine receptors (see, e.g., Brown et al., *Journal of Cell Science*. 112:209-216, 1999). Animal models are also valuable resources for studying the pathogenesis of disease, and provide a means to test dystrophin-related activity. Two of the most widely used animal models for DMD research are the mdx mouse and the golden retriever muscular dystrophy (GRMD) dog, both of which are dystrophin negative (see, e.g., Collins & Morgan, *Int J Exp Pathol* 84: 165-172, 2003). These and other animal models can be used to measure the functional activity of various dystrophin proteins. Included are truncated forms of dystrophin, such as those forms that are produced by certain of the exon-skipping antisense compounds of the present invention.

[0060] The term "restoration" of dystrophin synthesis or production refers generally to the production of a dystrophin protein including truncated forms of dystrophin in a patient with muscular dystrophy following treatment with an antisense oligonucleotide as described herein. In some embodiments, treatment results in an increase in novel dystrophin production in a patient by 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100% (including all integers in between). In some embodiments, treatment increases the number of dystrophin-positive fibers to at least 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90% or about 95% to 100% of normal in the subject. In other embodiments, treatment increases the number of dystrophin-positive fibers to about 20% to about 60%, or about 30% to about 50% of normal in the subject. The percent of dystrophin-positive fibers in a patient following treatment can be determined by a muscle biopsy using known techniques. For example, a muscle biopsy may be taken from a suitable muscle, such as the biceps brachii muscle in a patient.

[0061] Analysis of the percentage of positive dystrophin fibers may be performed pre-treatment and/or post-treatment or at time points throughout the course of treatment. In some embodiments, a post-treatment biopsy is taken from the contralateral muscle from the pre-treatment biopsy. Pre- and post-treatment dystrophin expression studies may be performed using any suitable assay for dystrophin. In one embodiment, immunohistochemical detection is performed on tissue sections from the muscle biopsy using an antibody that is a marker for dystrophin, such as a monoclonal or a polyclonal antibody. For example, the MANDYS106 anti-

body can be used which is a highly sensitive marker for dystrophin. Any suitable secondary antibody may be used.

[0062] In some embodiments, the percent dystrophin-positive fibers are calculated by dividing the number of positive fibers by the total fibers counted. Normal muscle samples have 100% dystrophin-positive fibers. Therefore, the percent dystrophin-positive fibers can be expressed as a percentage of normal. To control for the presence of trace levels of dystrophin in the pretreatment muscle as well as revertant fibers a baseline can be set using sections of pre-treatment muscles from each patient when counting dystrophin-positive fibers in post-treatment muscles. This may be used as a threshold for counting dystrophin-positive fibers in sections of post-treatment muscle in that patient. In other embodiments, antibody-stained tissue sections can also be used for dystrophin quantification using Bioquant image analysis software (Bioquant Image Analysis Corporation, Nashville, Tenn.). The total dystrophin fluorescence signal intensity can be reported as a percentage of normal. In addition, Western blot analysis with monoclonal or polyclonal anti-dystrophin antibodies can be used to determine the percentage of dystrophin positive fibers. For example, the anti-dystrophin antibody NCL-Dysl from Novacastra may be used. The percentage of dystrophin-positive fibers can also be analyzed by determining the expression of the components of the sarcoglycan complex (β, γ) and/or neuronal NOS.

[0063] By "isolated" is meant material that is substantially or essentially free from components that normally accompany it in its native state. For example, an "isolated polynucleotide," as used herein, may refer to a polynucleotide that has been purified or removed from the sequences that flank it in a naturally-occurring state, e.g., a DNA fragment that has been removed from the sequences that are normally adjacent to the fragment.

[0064] As used herein, "sufficient length" refers to an antisense oligonucleotide that is complementary to at least 8, more typically 8-30, contiguous nucleobases in a target dystrophin pre-mRNA. In some embodiments, an antisense of sufficient length includes at least 8, 9, 10, 11, 12, 13, 14, or 15 contiguous nucleobases in the target dystrophin pre-mRNA. In other embodiments an antisense of sufficient length includes at least 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous nucleobases in the target dystrophin pre-mRNA. An antisense oligonucleotide of sufficient length has at least a minimal number of nucleotides to be capable of specifically hybridizing to any one or more of exons 1-79 of the dystrophin gene. Preferably, the antisense oligonucleotide of the invention has a minimal number of nucleotides to be capable of specifically hybridizing to any one or more of exons 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 8 of the human dystrophin gene. Preferably an oligonucleotide of sufficient length is from about 10 to about 50 nucleotides in length, including oligonucleotides of 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 and 40 or more nucleotides. In one embodiment, an oligonucleotide of sufficient length is from 10 to about 30 nucleotides in length. In another embodiment, an oligonucleotide of sufficient length is from 15 to about 25 nucleotides in length. In yet another embodiment, an oligonucleotide of sufficient length is from 20 to 30, or 20 to 50, nucleotides in length. In yet another embodiment, an oligonucleotide of sufficient length is from 25 to 28 nucleotides in length.

[0065] By “enhance” or “enhancing,” or “increase” or “increasing,” or “stimulate” or “stimulating,” refers generally to the ability of one or antisense compounds or compositions to produce or cause a greater physiological response (i.e., downstream effects) in a cell or a subject, as compared to the response caused by either no antisense compound or a control compound. A measurable physiological response may include increased expression of a functional form of a dystrophin protein, or increased dystrophin-related biological activity in muscle tissue, among other responses apparent from the understanding in the art and the description herein. Increased muscle function can also be measured, including increases or improvements in muscle function by about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%. The percentage of muscle fibers that express a functional dystrophin can also be measured, including increased dystrophin expression in about 1%, 2%, %, 15%, 16%, 17%, 18%, 19%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% of muscle fibers. For instance, it has been shown that around 40% of muscle function improvement can occur if 25-30% of fibers express dystrophin (see, e.g., Dell'Osso et al, Proc Natl Acad Sci USA 99: 12979-12984, 2002). An “increased” or “enhanced” amount is typically a “statistically significant” amount, and may include an increase that is 1.1, 1.2, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50 or more times (e.g., 500, 1000 times) (including all integers and decimal points in between and above 1), e.g., 1.5, 1.6, 1.7, 1.8, etc.) the amount produced by no antisense compound (the absence of an agent) or a control compound.

[0066] The term “reduce” or “inhibit” may relate generally to the ability of one or more antisense compounds of the invention to “decrease” a relevant physiological or cellular response, such as a symptom of a disease or condition described herein, as measured according to routine techniques in the diagnostic art. Relevant physiological or cellular responses (in vivo or in vitro) will be apparent to persons skilled in the art, and may include reductions in the symptoms or pathology of muscular dystrophy, or reductions in the expression of defective forms of dystrophin, such as the altered forms of dystrophin that are expressed in individuals with DMD or BMD. A “decrease” in a response may be statistically significant as compared to the response produced by no antisense compound or a control composition, and may include a 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% decrease, including all integers in between.

[0067] Also included are vector delivery systems that are capable of expressing the oligomeric, dystrophin-targeting sequences of the present invention, such as vectors that express a polynucleotide sequence comprising any one or more of the sequences shown in Tables 3 and 4, and variants thereof, as described herein. By “vector” or “nucleic acid construct” is meant a polynucleotide molecule, preferably a DNA molecule derived, for example, from a plasmid, bacteriophage, yeast or virus, into which a polynucleotide can be inserted or cloned. A vector preferably contains one or more unique restriction sites and can be capable of autonomous replication in a defined host cell including a target cell or tissue or a progenitor cell or tissue thereof, or be integrated

with the genome of the defined host such that the cloned sequence is reproducible. Accordingly, the vector can be an autonomously replicating vector, i.e., a vector that exists as an extra-chromosomal entity, the replication of which is independent of chromosomal replication, e.g., a linear or closed circular plasmid, an extra-chromosomal element, a mini-chromosome, or an artificial chromosome. The vector can contain any means for assuring self-replication. Alternatively, the vector can be one which, when introduced into the host cell, is integrated into the genome and replicated together with the chromosome(s) into which it has been integrated.

[0068] “Treatment” of an individual (e.g. a mammal, such as a human) or a cell is any type of intervention used in an attempt to alter the natural course of the individual or cell. Treatment includes, but is not limited to, administration of a pharmaceutical composition, and may be performed either prophylactically or subsequent to the initiation of a pathologic event or contact with an etiologic agent. Treatment includes any desirable effect on the symptoms or pathology of a disease or condition associated with the dystrophin protein, as in certain forms of muscular dystrophy, and may include, for example, minimal changes or improvements in one or more measurable markers of the disease or condition being treated. Also included are “prophylactic” treatments, which can be directed to reducing the rate of progression of the disease or condition being treated, delaying the onset of that disease or condition, or reducing the severity of its onset. “Treatment” or “prophylaxis” does not necessarily indicate complete eradication, cure, or prevention of the disease or condition, or associated symptoms thereof.

[0069] In one embodiment, treatment with an antisense oligonucleotide of the invention increases novel dystrophin production and slows or reduces the loss of ambulation that would be expected without treatment. For example, treatment may stabilize, maintain, improve or increase walking ability (e.g., stabilization of ambulation) in the subject. In some embodiments, treatment maintains or increases a stable walking distance in a patient, as measured by, for example, the 6 Minute Walk Test (6MWT), described by McDonald, et al. (Muscle Nerve, 2010; 42:966-74, herein incorporated by reference). A change in the 6 Minute Walk Distance (6MWD) may be expressed as an absolute value, a percentage change or a change in the %-predicted value. In some embodiments, treatment maintains or improves a stable walking distance in a 6MWT from a 20% deficit in the subject relative to a healthy peer. The performance of a DMD patient in the 6MWT relative to the typical performance of a healthy peer can be determined by calculating a %-predicted value. For example, the %-predicted 6MWD may be calculated using the following equation for males: $196.72 + (39.81 \times \text{age}) - (1.36 \times \text{age}^2) + (132.28 \times \text{height in meters})$. For females, the %-predicted 6MWD may be calculated using the following equation: $188.61 + (51.50 \times \text{age}) - (1.86 \times \text{age}^2) + (86.10 \times \text{height in meters})$ (Henricson et al. PLoS Curr., 2012, version 2, herein incorporated by reference). In some embodiments, treatment with an antisense oligonucleotide increases the stable walking distance in the patient from baseline to greater than 3, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30 or 50 meters (including all integers in between).

[0070] Loss of muscle function in patients with DMD may occur against the background of normal childhood growth and development. Indeed, younger children with DMD may show an increase in distance walked during 6MWT over the course of about 1 year despite progressive muscular impairment. In some embodiments, the 6MWD from patients with

DMD is compared to typically developing control subjects and to existing normative data from age and sex matched subjects. In some embodiments, normal growth and development can be accounted for using an age and height based equation fitted to normative data. Such an equation can be used to convert 6MWD to a percent-predicted (%-predicted) value in subjects with DMD. In certain embodiments, analysis of %-predicted 6MWD data represents a method to account for normal growth and development, and may show that gains in function at early ages (e.g., less than or equal to age 7) represent stable rather than improving abilities in patients with DMD (Henricson et al. PLoS Curr., 2012, version 2, herein incorporated by reference).

[0071] A “subject,” as used herein, includes any animal that exhibits a symptom, or is at risk for exhibiting a symptom, which can be treated with an antisense compound of the invention, such as a subject that has or is at risk for having DMD or BMD, or any of the symptoms associated with these conditions (e.g., muscle fibre loss). Suitable subjects (patients) include laboratory animals (such as mouse, rat, rabbit, or guinea pig), farm animals, and domestic animals or pets (such as a cat or dog). Non-human primates and, preferably, human patients, are included.

[0072] “Alkyl” or “alkylene” both refer to a saturated straight or branched chain hydrocarbon radical containing from 1 to 18 carbons. Examples include without limitation methyl, ethyl, propyl, iso-propyl, butyl, iso-butyl, tert-butyl, n-pentyl and n-hexyl. The term “lower alkyl” refers to an alkyl group, as defined herein, containing between 1 and 8 carbons.

[0073] “Alkenyl” refers to an unsaturated straight or branched chain hydrocarbon radical containing from 2 to 18 carbons and comprising at least one carbon to carbon double bond. Examples include without limitation ethenyl, propenyl, iso-propenyl, butenyl, iso-butenyl, tert-butenyl, n-pentenyl and n-hexenyl. The term “lower alkenyl” refers to an alkenyl group, as defined herein, containing between 2 and 8 carbons.

[0074] “Alkynyl” refers to an unsaturated straight or branched chain hydrocarbon radical containing from 2 to 18 carbons comprising at least one carbon to carbon triple bond. Examples include without limitation ethynyl, propynyl, iso-propynyl, butynyl, iso-butynyl, tert-butynyl, pentynyl and hexynyl. The term “lower alkynyl” refers to an alkynyl group, as defined herein, containing between 2 and 8 carbons.

[0075] “Cycloalkyl” refers to a mono- or poly-cyclic alkyl radical. Examples include without limitation cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

[0076] “Aryl” refers to a cyclic aromatic hydrocarbon moiety containing from 10 to 18 carbons having one or more closed ring(s). Examples include without limitation phenyl, benzyl, naphthyl, anthracenyl, phenanthracenyl and biphenyl.

[0077] “Aralkyl” refers to a radical of the formula RaRb where Ra is an alkylene chain as defined above and Rb is one or more aryl radicals as defined above, for example, benzyl, diphenylmethyl and the like.

[0078] “Thioalkoxy” refers to a radical of the formula —SRC where Rc is an alkyl radical as defined herein. The term “lower thioalkoxy” refers to an alkoxy group, as defined herein, containing between 1 and 8 carbons.

[0079] “Alkoxy” refers to a radical of the formula —ORd where Rd is an alkyl radical as defined herein. The term “lower alkoxy” refers to an alkoxy group, as defined herein, containing between 1 and 8 carbons. Examples of alkoxy groups include, without limitation, methoxy and ethoxy.

[0080] “Alkoxyalkyl” refers to an alkyl group substituted with an alkoxy group.

[0081] “Carbonyl” refers to the C(=O)— radical.

[0082] “Guanidynyl” refers to the H₂N(C=NH₂)—NH— radical.

[0083] “Amidinyl” refers to the H₂N(C=NH₂)CH— radical.

[0084] “Amino” refers to the NH₂ radical.

[0085] “Alkylamino” refers to a radical of the formula —NRd or —NRdRd where each Rd is, independently, an alkyl radical as defined herein. The term “lower alkylamino” refers to an alkylamino group, as defined herein, containing between 1 and 8 carbons.

[0086] “Heterocycle” means a 5- to 7-membered monocyclic, or 7- to 10-membered bicyclic, heterocyclic ring which is either saturated, unsaturated, or aromatic, and which contains from 1 to 4 heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the nitrogen and sulfur heteroatoms may be optionally oxidized, and the nitrogen heteroatom may be optionally quaternized, including bicyclic rings in which any of the above heterocycles are fused to a benzene ring. The heterocycle may be attached via any heteroatom or carbon atom. Heterocycles include heteroaryls as defined below. Thus, in addition to the heteroaryls listed below, heterocycles also include morpholinyl, pyrrolidinyl, pyrrolidinyl, piperidinyl, piperizinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyridinyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, tetrahydropyrimidinyl, tetrahydrothiopyranyl, and the like.

[0087] “Heteroaryl” means an aromatic heterocycle ring of 5- to 10 members and having at least one heteroatom selected from nitrogen, oxygen and sulfur, and containing at least 1 carbon atom, including both mono- and bicyclic ring systems. Representative heteroaryls are pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, and quinazolinyl.

[0088] The terms “optionally substituted alkyl”, “optionally substituted alkenyl”, “optionally substituted alkoxy”, “optionally substituted thioalkoxy”, “optionally substituted alkyl amino”, “optionally substituted lower alkyl”, “optionally substituted lower alkenyl”, “optionally substituted lower alkoxy”, “optionally substituted lower thioalkoxy”, “optionally substituted lower alkyl amino” and “optionally substituted heterocyclyl” mean that, when substituted, at least one hydrogen atom is replaced with a substituent. In the case of an oxo substituent (=O) two hydrogen atoms are replaced. In this regard, substituents include: deuterium, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted heterocycle, optionally substituted cycloalkyl, oxo, halogen, —CN, —ORx, NRxRy, NRxC(=O)Ry, NRxSO2Ry, NRxC(=O)NRxRy, C(=O)Rx, C(=O)ORx, C(=O)NRxRy, —S0mRx and —S0mNRxRy, wherein m is 0, 1 or 2, Rx and Ry are the same or different and independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heterocycle or optionally substituted cycloalkyl and each of said optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, option-

ally substituted heterocycle and optionally substituted cycloalkyl substituents may be further substituted with one or more of oxo, halogen, —CN, —ORx, NRxRy, NRxC(=O)Ry, NRxSO2Ry, —NRxC(=O)NRxRy, C(=O)Rx, C(=O)ORx, C(=O)NRxRy, —SOMRx and —SOMNRxRy.

[0089] An antisense molecule nomenclature system was proposed and published to distinguish between the different antisense molecules (see Mann et al., (2002) *J Gen Med* 4, 644-654). This nomenclature became especially relevant when testing several slightly different antisense molecules, all directed at the same target region, as shown below:

H#A/D(x:y).

[0090] The first letter designates the species (e.g. H: human, M: murine, C: canine). “#” designates target dystrophin exon number. “A/D” indicates acceptor or donor splice site at the beginning and end of the exon, respectively. (x y) represents the annealing coordinates where “-” or “+” indicate intronic or exonic sequences respectively. For example, A(-6+18) would indicate the last 6 bases of the intron preceding the target exon and the first 18 bases of the target exon. The closest splice site would be the acceptor so these coordinates would be preceded with an “A”. Describing annealing coordinates at the donor splice site could be D(+2-18) where the last 2 exonic bases and the first 18 intronic bases correspond to the annealing site of the antisense molecule. Entirely exonic annealing coordinates that would be represented by A(+65+85), that is the site between the 65th and 85th nucleotide from the start of that exon.

II. CONSTRUCTING THE ANTISENSE OLIGONUCLEOTIDE

[0091] Exemplary embodiments of the invention relate to morpholino oligonucleotides having phosphorus-containing backbone linkages are illustrated in FIGS. 1A-1C. Preferred is a phosphorodiamide-linked morpholino oligonucleotide such as shown in FIG. 1C, which is modified, in accordance with one aspect of the present invention, to contain positively charged groups at preferably 10%-50% of its backbone linkages. Morpholino oligonucleotides with uncharged backbone linkages, including antisense oligonucleotides, are detailed, for example, in (Summerton and Weller 1997) and in co-owned U.S. Pat. Nos. 5,698,685, 5,217,866, 5,142,047, 5,034,506, 5,166,315, 5,185, 444, 5,521,063, 5,506,337, 8,076,476, 8,299,206 and 7,943,762 all of which are expressly incorporated by reference herein.

[0092] Important properties of the morpholino-based sub-units include: 1) the ability to be linked in a oligomeric form by stable, uncharged or positively charged backbone linkages; 2) the ability to support a nucleotide base (e.g. adenine, cytosine, guanine, thymidine, uracil and inosine) such that the polymer formed can hybridize with a complementary-base target nucleic acid, including target RNA, T_m values above about 45° C. in relatively short oligonucleotides (e.g., 10-15 bases); 3) the ability of the oligonucleotide to be actively or passively transported into mammalian cells; and 4) the ability of the antisense oligonucleotide:RNA heteroduplex to resist RNase and RNase H degradation, respectively.

[0093] Exemplary backbone structures for antisense oligonucleotides of the claimed subject matter include the morpholino subunit types shown in FIGS. 1D-G, each linked by an uncharged or positively charged, phosphorus-containing subunit linkage. FIG. 1D shows a phosphorus-containing linkage which forms the five atom repeating-unit backbone,

where the morpholino rings are linked by a 1-atom phosphoamide linkage. FIG. 1E shows a linkage which produces a 6-atom repeating-unit backbone. In this structure, the atom Y linking the 5' morpholino carbon to the phosphorus group may be sulfur, nitrogen, carbon or, preferably, oxygen. The X moiety pendant from the phosphorus may be fluorine, an alkyl or substituted alkyl, an alkoxy or substituted alkoxy, a thioalkoxy or substituted thioalkoxy, or unsubstituted, mono-substituted, or disubstituted nitrogen, including cyclic structures, such as morpholines or piperidines. Alkyl, alkoxy and thioalkoxy preferably include 1-6 carbon atoms. The Z moieties are sulfur or oxygen, and are preferably oxygen.

[0094] The linkages shown in FIGS. 1F and 1G are designed for 7-atom unit-length linkages. In structure 1F, the X moiety is as in Structure 1E, and the Y moiety may be methylene, sulfur, or, preferably, oxygen. In Structure 1G, the X and Y moieties are as in Structure 1E. Particularly preferred morpholino oligonucleotides include those composed of morpholino subunit structures of the form shown in FIG. 1E, where X=NH₂, N(CH₃)₂, or 1-piperazine or other charged group, Y=O, and Z=O.

[0095] A substantially uncharged oligonucleotide may be modified, in accordance with an aspect of the invention, to include charged linkages, e.g., up to about 1 per every 2-5 uncharged linkages, such as about 4-5 per every 10 uncharged linkages. In certain embodiments, optimal improvement in antisense activity may be seen when about 25% of the backbone linkages are cationic. In certain embodiments, enhancement may be seen with a small number e.g., 10-20% cationic linkages, or where the number of cationic linkages are in the range 50-80%, such as about 60%.

[0096] Oligomers having any number of cationic linkages are provided, including fully cationic-linked oligomers. Preferably, however, the oligomers are partially charged, having, for example, 10%-80%. In preferred embodiments, about 10% to 60%, and preferably 20% to 50% of the linkages are cationic.

[0097] In one embodiment, the cationic linkages are interspersed along the backbone. The partially charged oligomers preferably contain at least two consecutive uncharged linkages; that is, the oligomer preferably does not have a strictly alternating pattern along its entire length.

[0098] Also considered are oligomers having blocks of cationic linkages and blocks of uncharged linkages; for example, a central block of uncharged linkages may be flanked by blocks of cationic linkages, or vice versa. In one embodiment, the oligomer has approximately equal-length 5', 3' and center regions, and the percentage of cationic linkages in the center region is greater than about 50%, preferably greater than about 70%.

[0099] In certain embodiments, the antisense compounds can be prepared by stepwise solid-phase synthesis, employing methods detailed in the references cited above, and below with respect to the synthesis of oligonucleotides having a mixture of uncharged and cationic backbone linkages. In some cases, it may be desirable to add additional chemical moieties to the antisense compound, e.g., to enhance pharmacokinetics or to facilitate capture or detection of the compound. Such a moiety may be covalently attached, according to standard synthetic methods. For example, addition of a polyethylene glycol moiety or other hydrophilic polymer, e.g., one having 1-100 monomeric subunits, may be useful in enhancing solubility.

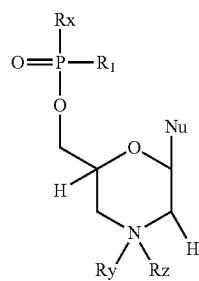
[0100] A reporter moiety, such as fluorescein or a radiolabeled group, may be attached for purposes of detection. Alternatively, the reporter label attached to the oligomer may be a ligand, such as an antigen or biotin, capable of binding a labeled antibody or streptavidin. In selecting a moiety for attachment or modification of an antisense compound, it is generally of course desirable to select chemical compounds or groups that are biocompatible and likely to be tolerated by a subject without undesirable side effects.

[0101] Oligomers for use in antisense applications generally range in length from about 10 to about 50 subunits, more preferably about 10 to 30 subunits, and typically 15-25 bases. For example, an oligomer of the invention having 19-20 subunits, a useful length for an antisense compound, may ideally have two to ten, e.g., four to eight, cationic linkages, and the remainder uncharged linkages. An oligomer having 14-15 subunits may ideally have two to seven, e.g., 3, 4, or 5, cationic linkages and the remainder uncharged linkages. In a preferred embodiment, the oligomers have 25 to 28 subunits.

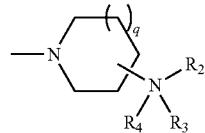
[0102] Each morpholino ring structure supports a base pairing moiety, to form a sequence of base pairing moieties which is typically designed to hybridize to a selected antisense target in a cell or in a subject being treated. The base pairing moiety may be a purine or pyrimidine found in native DNA or RNA (e.g., A, G, C, T or U) or an analog, such as hypoxanthine (the base component of the nucleoside inosine) or 5-methyl cytosine.

[0103] As noted above, certain embodiments are directed to oligomers comprising novel intersubunit linkages, including PMO-X oligomers and those having modified terminal groups. In some embodiments, these oligomers have higher affinity for DNA and RNA than do the corresponding unmodified oligomers and demonstrate improved cell delivery, potency, and/or tissue distribution properties compared to oligomers having other intersubunit linkages. The structural features and properties of the various linkage types and oligomers are described in more detail in the following discussion. The synthesis of these and related oligomers is described in co-owned U.S. application Ser. No. 13/118,298, which is incorporated by reference in its entirety.

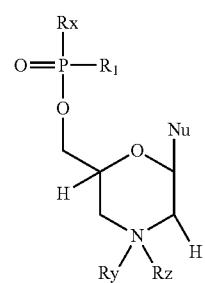
[0104] In certain embodiments, the invention provides for an oligonucleotide having a sequence complementary to the target sequence which is associated with a human disease, and comprises a sequence of nucleotides having a formula:



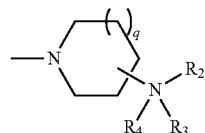
[0105] wherein Nu is a nucleobase;
[0106] R₁ has the formula



[0107] q is 0, 1, or 2;
[0108] R₂ is selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₁-C₅ aralkyl, and a formamidinyl group, and
[0109] R₃ is selected from the group consisting of hydrogen, C₁-C₁₀ acyl, C₁-C₁₀ aminoacyl, acyl moiety of a natural or unnatural alpha or beta amino acid, C₁-C₁₀ aralkyl, and C₁-C₁₀ alkyl, or
[0110] R₂ and R₃ are joined to form a 5-7 membered ring where the ring may be optionally substituted with a substituent selected from the group consisting of C₁-C₁₀ alkyl, phenyl, halogen, and C₁-C₁₀ aralkyl;
[0111] R₄ is selected from the group consisting of an electron pair, hydrogen, a C₁-C₆ alkyl and C₁-C₆ aralkyl;
[0112] Rx is selected from the group consisting of sarcosinamide, hydroxyl, a nucleotide, a cell penetrating peptide moiety, and piperazinyl;
[0113] Ry is selected from the group consisting of hydrogen, a C₁-C₆ alkyl, a nucleotide a cell penetrating peptide moiety, an amino acid, a formamidinyl group, and C₁-C₆ acyl; and,
[0114] Rz is selected from the group consisting of an electron pair, hydrogen, a C₁-C₆ alkyl, and C₁-C₆ acyl pharmaceutically acceptable salts thereof.
[0115] Nu may be selected from the group consisting of adenine, guanine, thymine, uracil, cytosine, and hypoxanthine. More preferably Nu is thymine or uracil.
[0116] In preferred embodiments, the invention provides an oligonucleotide having a sequence of nucleotides having a formula:



[0117] wherein Nu is a nucleobase;
[0118] R₁ is selected from the group consisting of R₁' and R₁'' wherein R₁' is dimethylamino and R₁'' has the formula



[0119] wherein at least one R_1 is R_1'' ;

[0120] q is 0, 1, or 2; with the proviso that at least one of R_1 is a piperidinyl moiety;

[0121] R_2 is selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_1 - C_5 aralkyl, and a formamidinyl group, and

[0122] R_3 is selected from the group consisting of hydrogen, C_1 - C_{10} acyl, C_1 - C_{10} aminoacyl, acyl moiety of a natural or unnatural alpha or beta amino acid, C_1 - C_{10} aralkyl, and C_1 - C_{10} alkyl, or

[0123] R_2 and R_3 are joined to form a 5-7 membered ring where the ring may be optionally substituted with a substituent selected from the group consisting of C_1 - C_{10} alkyl, phenyl, halogen, and C_1 - C_{10} aralkyl;

[0124] R_4 is selected from the group consisting of an electron pair, hydrogen, a C_1 - C_6 alkyl and aralkyl;

[0125] Rx is selected from the group consisting of sarcosinamide, hydroxyl, a nucleotide, a cell penetrating peptide moiety, and piperazinyl;

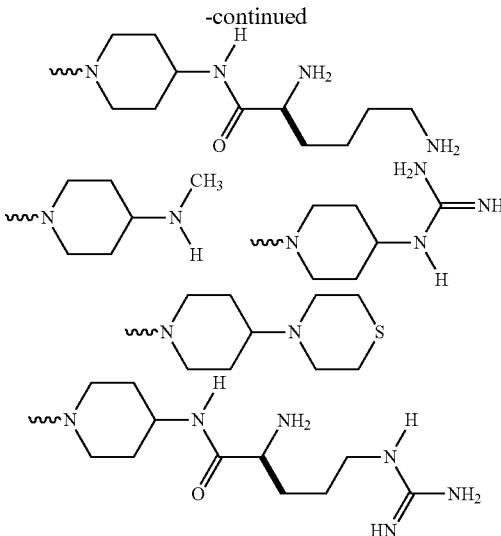
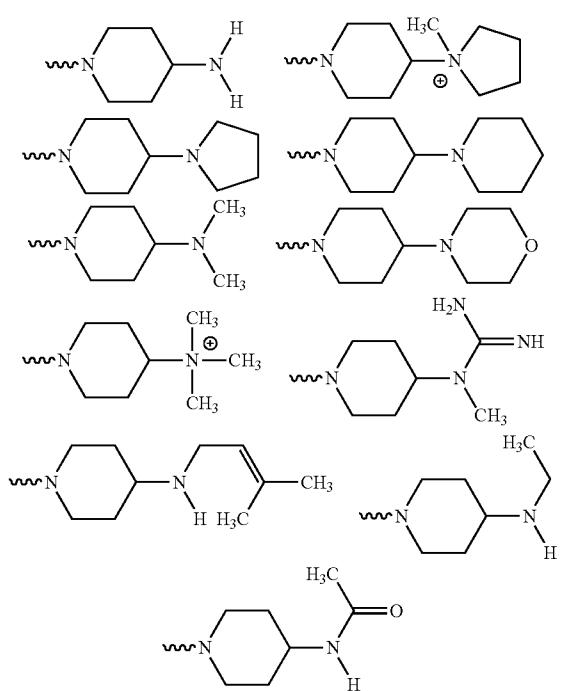
[0126] Ry is selected from the group consisting of hydrogen, a C_1 - C_6 alkyl, a nucleotide a cell penetrating peptide moiety, an amino acid, a formamidinyl group, and C_1 - C_6 acyl; and,

[0127] Rz is selected from the group consisting of an electron pair, hydrogen, a C_1 - C_6 alkyl, and C_1 - C_6 acyl pharmaceutically acceptable salts thereof.

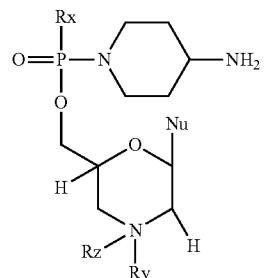
[0128] Nu may be selected from the group consisting of adenine, guanine, thymine, uracil, cytosine, and hypoxanthine. More preferably Nu is thymine or uracil.

[0129] About 90-50% of the R_1 groups are dimethylamino (i.e. R_1'). More, preferably, 90-50% of the R_1 groups are dimethylamino. Most, preferably about 66% of the R_1 groups are dimethylamino.

[0130] R_1'' may be selected from the group consisting of



[0131] Preferably, at least one nucleotide of the oligonucleotide has the formula:



[0132] wherein Rx, Ry, Rz, and Nu are as stated above. Most preferably, Nu is thymine or uracil.

[0133] Although thymine (T) is the preferred base pairing moiety (Nu or Pi) containing the chemical modifications described above, any base subunit known to a person of skill in the art can be used as the base pairing moiety.

[0134] The oligonucleotide and the DNA or RNA are complementary to each other when a sufficient number of corresponding positions in each molecule are occupied by nucleotides which can hydrogen bond with each other. Thus, "specifically hybridizable" and "complementary" are terms which are used to indicate a sufficient degree of complementarity or precise pairing such that stable and specific binding occurs between the oligonucleotide and the DNA or RNA target. It is understood in the art that the sequence of an antisense molecule need not be 100% complementary to that of its target sequence to be specifically hybridizable. An antisense molecule is specifically hybridizable when binding of the compound to the target DNA or RNA molecule interferes with the normal function of the target DNA or RNA to cause a loss of utility, and there is a sufficient degree of complementarity to avoid non-specific binding of the antisense compound to non-target sequences under conditions in which specific binding is desired, i.e., under physiological conditions.

tions in the case of in vivo assays or therapeutic treatment, and in the case of in vitro assays, under conditions in which the assays are performed.

[0135] While the above method may be used to select anti-sense molecules capable of deleting any exon from within a protein that is capable of being shortened without affecting its biological function, the exon deletion should not lead to a reading frame shift in the shortened transcribed mRNA. Thus, if in a linear sequence of three exons the end of the first exon encodes two of three nucleotides in a codon and the next exon is deleted then the third exon in the linear sequence must start with a single nucleotide that is capable of completing the nucleotide triplet for a codon. If the third exon does not commence with a single nucleotide there will be a reading frame shift that would lead to the generation of truncated or a non-functional protein.

[0136] It will be appreciated that the codon arrangements at the end of exons in structural proteins may not always break at the end of a codon, consequently there may be a need to delete more than one exon from the pre-mRNA to ensure in-frame reading of the mRNA. In such circumstances, a plurality of antisense oligonucleotides may need to be selected by the method of the invention wherein each is directed to a different region responsible for inducing splicing in the exons that are to be deleted.

[0137] The length of an antisense molecule may vary so long as it is capable of binding selectively to the intended location within the pre-mRNA molecule. The length of such sequences can be determined in accordance with selection procedures described herein. Generally, the antisense molecule will be from about 10 nucleotides in length up to about 50 nucleotides in length. It will be appreciated however that any length of nucleotides within this range may be used in the method. Preferably, the length of the antisense molecule is between 10-30 nucleotides in length.

[0138] The most common method for producing antisense molecules is the methylation of the 2' hydroxyribose position and the incorporation of a phosphorothioate backbone produces molecules that superficially resemble RNA but that are much more resistant to nuclease degradation.

[0139] To avoid degradation of pre-mRNA during duplex formation with the antisense molecules, the antisense molecules used in the method may be adapted to minimize or prevent cleavage by endogenous RNase H. This property is highly preferred as the treatment of the RNA with the unmodified oligonucleotides either intracellularly or in crude extracts that contain RNase H leads to degradation of the pre-mRNA: antisense oligonucleotide duplexes. Any form of modified antisense molecules that is capable of bypassing or not inducing such degradation may be used in the present method. An example of antisense molecules which when duplexed with RNA are not cleaved by cellular RNase H is 2'-O-methyl derivatives. 2'-O-methyl-oligoribonucleotides are very stable in a cellular environment and in animal tissues, and their duplexes with RNA have higher Tm values than their ribo- or deoxyribo-counterparts.

[0140] Antisense molecules that do not activate RNase H can be made in accordance with known techniques (see, e.g., U.S. Pat. No. 5,149,797). Such antisense molecules, which may be deoxyribonucleotide or ribonucleotide sequences, simply contain any structural modification which sterically hinders or prevents binding of RNase H to a duplex molecule containing the oligonucleotide as one member thereof, which structural modification does not substantially hinder or dis-

rupt duplex formation. Because the portions of the oligonucleotide involved in duplex formation are substantially different from those portions involved in RNase H binding thereto, numerous antisense molecules that do not activate RNase H are available. For example, such antisense molecules may be oligonucleotides wherein at least one, or all, of the inter-nucleotide bridging phosphate residues are modified phosphates, such as methyl phosphonates, methyl phosphorothioates, phosphoromorpholides, phosphoropiperazines and phosphoramidates. For example, every other one of the internucleotide bridging phosphate residues may be modified as described. In another non-limiting example, such antisense molecules are molecules wherein at least one, or all, of the nucleotides contain a 2' lower alkyl moiety (e.g., C₁-C₄, linear or branched, saturated or unsaturated alkyl, such as methyl, ethyl, ethenyl, propyl, 1-propenyl, 2-propenyl, and isopropyl). For example, every other one of the nucleotides may be modified as described.

[0141] While antisense oligonucleotides are a preferred form of the antisense molecules, the present invention comprehends other oligomeric antisense molecules, including but not limited to oligonucleotide mimetics such as are described below.

[0142] Specific examples of preferred antisense compounds useful in this invention include oligonucleotides containing modified backbones or non-natural inter-nucleoside linkages. As defined in this specification, oligonucleotides having modified backbones include those that retain a phosphorus atom in the backbone and those that do not have a phosphorus atom in the backbone. For the purposes of this specification, and as sometimes referenced in the art, modified oligonucleotides that do not have a phosphorus atom in their inter-nucleoside backbone can also be considered to be oligonucleosides.

[0143] In other preferred oligonucleotide mimetics, both the sugar and the inter-nucleoside linkage, i.e., the backbone, of the nucleotide units are replaced with novel groups. The base units are maintained for hybridization with an appropriate nucleic acid target compound. One such oligomeric compound, an oligonucleotide mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar-backbone of an oligonucleotide is replaced with an amide containing backbone, in particular an aminoethylglycine backbone. The nucleo-bases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone.

[0144] Modified oligonucleotides may also contain one or more substituted sugar moieties. Oligonucleotides may also include nucleobase (often referred to in the art simply as "base") modifications or substitutions. Certain nucleo-bases are particularly useful for increasing the binding affinity of the oligomeric compounds of the invention. These include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and O-6 substituted purines, including 2-aminopropyladenine, 5-propynyluracil and 5-propynylcytosine. 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2° C. and are presently preferred base substitutions, even more particularly when combined with 2'-O-methoxyethyl sugar modifications.

[0145] Another modification of the oligonucleotides of the invention involves chemically linking to the oligonucleotide one or more moieties or conjugates that enhance the activity, cellular distribution or cellular uptake of the oligonucleotide.

Such moieties include but are not limited to lipid moieties such as a cholesterol moiety, cholic acid, a thioether, e.g., hexyl-5-tritylthiol, a thiocholesterol, an aliphatic chain, e.g., dodecandiol or undecyl residues, a phospholipid, e.g., dihexadecyl-rac-glycerol or triethylammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate, a polyamine or a polyethylene glycol chain, or adamantane acetic acid, a palmitoyl moiety, or an octadecylamine or hexylamino-carbonyl-oxy-cholesterol moiety.

[0146] It is not necessary for all positions in a given compound to be uniformly modified, and in fact more than one of the aforementioned modifications may be incorporated in a single compound or even at a single nucleoside within an oligonucleotide. The present invention also includes anti-sense compounds that are chimeric compounds. "Chimeric" antisense compounds or "chimeras," in the context of this invention, are antisense molecules, particularly oligonucleotides, which contain two or more chemically distinct regions, each made up of at least one monomer unit, i.e., a nucleotide in the case of an oligonucleotide compound. These oligonucleotides typically contain at least one region wherein the oligonucleotide is modified so as to confer upon the increased resistance to nuclease degradation, increased cellular uptake, and an additional region for increased binding affinity for the target nucleic acid.

III. PEPTIDE TRANSPORTERS

[0147] The antisense compounds of the invention may include an oligonucleotide moiety conjugated to a CPP, preferably an arginine-rich peptide transport moiety effective to enhance transport of the compound into cells. The transport moiety is preferably attached to a terminus of the oligomer, as shown, for example, in FIGS. 1B and 1C. The peptides have the capability of inducing cell penetration within 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100% of cells of a given cell culture population, including all integers in between, and allow macromolecular translocation within multiple tissues in vivo upon systemic administration. In one embodiment, the cell-penetrating peptide may be an arginine-rich peptide transporter. In another embodiment, the cell-penetrating peptide may be Penetratin or the Tat peptide. These peptides are well known in the art and are disclosed, for example, in US Publication No. 2010-0016215 A1, incorporated by reference in its entirety. A particularly preferred approach to conjugation of peptides to antisense oligonucleotides can be found in PCT publication WO2012/150960, which is incorporated by reference in its entirety. A preferred embodiment of a peptide conjugated oligonucleotide of the present invention utilizes glycine as the linker between the CPP and the antisense oligonucleotide. For example, a preferred peptide conjugated PMO consists of R_n-G-PMO.

[0148] The transport moieties as described above have been shown to greatly enhance cell entry of attached oligomers, relative to uptake of the oligomer in the absence of the attached transport moiety. Uptake is preferably enhanced at least ten fold, and more preferably twenty fold, relative to the unconjugated compound.

[0149] The use of arginine-rich peptide transporters (i.e., cell-penetrating peptides) are particularly useful in practicing the present invention. Certain peptide transporters have been shown to be highly effective at delivery of antisense compounds into primary cells including muscle cells (Marshall, Oda et al. 2007; Jearawiriyapaisarn, Moulton et al. 2008; Wu, Moulton et al. 2008). Furthermore, compared to other known

peptide transporters such as Penetratin and the Tat peptide, the peptide transporters described herein, when conjugated to an antisense PMO, demonstrate an enhanced ability to alter splicing of several gene transcripts (Marshall, Oda et al. 2007).

[0150] Exemplary peptide transporters, excluding linkers are given below in Table 1.

TABLE 1

⁴Sequences assigned to SEQ ID NOS do not include the linkage portion (e.g., C, G, P, Ahx, B, AhxB where Ahx and B refer to 6-aminohexanoic acid and beta-alanine, respectively).

IV. FORMULATIONS AND TREATMENT

[0151] In certain embodiments, the present invention provides formulations or compositions suitable for the therapeutic delivery of antisense oligomers, as described herein. Hence, in certain embodiments, the present invention provides pharmaceutically acceptable compositions that comprise a therapeutically-effective amount of one or more of the oligomers described herein, formulated together with one or more pharmaceutically acceptable carriers (additives) and/or diluents. While it is possible for an oligomer of the present invention to be administered alone, it is preferable to administer the compound as a pharmaceutical formulation (composition).

[0152] The compositions of the present invention may be administered alone or in combination with another therapeutic. The additional therapeutic may be administered prior, concurrently or subsequently to the administration of the composition of the present invention. For example, the compositions may be administered in combination with a steroid and/or an antibiotic. The steroid may be a glucocorticoid or

prednisone. Other agents which can be administered include an antagonist of the ryanodine receptor, such as dantrolene, which has been shown to enhance antisense-mediated exon skipping in patient cells and a mouse model of DMD (G. Kendall et al. *Sci Transl Med* 4 164ra160 (2012), incorporated herein by reference).

[0153] Methods for the delivery of nucleic acid molecules are described, for example, in Akhtar et al., 1992, *Trends Cell Bio.*, 2:139; and *Delivery Strategies for Antisense Oligonucleotide Therapeutics*, ed. Akhtar; Sullivan et al., PCT WO 94/02595. These and other protocols can be utilized for the delivery of virtually any nucleic acid molecule, including the isolated oligomers of the present invention.

[0154] As detailed below, the pharmaceutical compositions of the present invention may be specially formulated for administration in solid or liquid form, including those adapted for the following: (1) oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, e.g., those targeted for buccal, sublingual, and systemic absorption, boluses, powders, granules, pastes for application to the tongue; (2) parenteral administration, for example, by subcutaneous, intramuscular, intravenous or epidural injection as, for example, a sterile solution or suspension, or sustained-release formulation; (3) topical application, for example, as a cream, ointment, or a controlled-release patch or spray applied to the skin; (4) intravaginally or intrarectally, for example, as a pessary, cream or foam; (5) sublingually; (6) ocularly; (7) transdermally; or (8) nasally.

[0155] The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[0156] The phrase "pharmaceutically-acceptable carrier" as used herein means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, manufacturing aid (e.g., lubricant, talc magnesium, calcium or zinc stearate, or steric acid), or solvent encapsulating material, involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient.

[0157] Some examples of materials that can serve as pharmaceutically-acceptable carriers include, without limitation: (1) sugars, such as lactose, glucose and sucrose; (2) starches, such as corn starch and potato starch; (3) cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; (4) powdered tragacanth; (5) malt; (6) gelatin; (7) talc; (8) excipients, such as cocoa butter and suppository waxes; (9) oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; (10) glycols, such as propylene glycol; (11) polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; (12) esters, such as ethyl oleate and ethyl laurate; (13) agar; (14) buffering agents, such as magnesium hydroxide and aluminum hydroxide; (15) alginic acid; (16) pyrogen-free water; (17) isotonic saline; (18) Ringer's solution; (19) ethyl alcohol; (20) pH buffered solutions; (21) polyesters, polycarbon-

ates and/or polyanhydrides; and (22) other non-toxic compatible substances employed in pharmaceutical formulations.

[0158] Additional non-limiting examples of agents suitable for formulation with the antisense oligomers of the instant invention include: PEG conjugated nucleic acids, phospholipid conjugated nucleic acids, nucleic acids containing lipophilic moieties, phosphorothioates, P-glycoprotein inhibitors (such as Pluronic P85) which can enhance entry of drugs into various tissues; biodegradable polymers, such as poly (DL-lactide-coglycolide) microspheres for sustained release delivery after implantation (Emerich, D F et al., 1999, *Cell Transplant*, 8, 47-58) Alkermes, Inc. Cambridge, Mass.; and loaded nanoparticles, such as those made of polybutylcyanoacrylate, which can deliver drugs across the blood brain barrier and can alter neuronal uptake mechanisms (*Prog Neuropsychopharmacol Biol Psychiatry*, 23, 941-949, 1999).

[0159] The invention also features the use of the composition comprising surface-modified liposomes containing poly (ethylene glycol) lipids (PEG-modified, branched and unbranched or combinations thereof, or long-circulating liposomes or stealth liposomes). Oligomers of the invention can also comprise covalently attached PEG molecules of various molecular weights. These formulations offer a method for increasing the accumulation of drugs in target tissues. This class of drug carriers resists opsonization and elimination by the mononuclear phagocytic system (MPS or RES), thereby enabling longer blood circulation times and enhanced tissue exposure for the encapsulated drug (Lasic et al. *Chem. Rev.* 1995, 95, 2601-2627; Ishiwata et al., *Chem. Pharm. Bull.* 1995, 43, 1005-1011). Such liposomes have been shown to accumulate selectively in tumors, presumably by extravasation and capture in the neovascularized target tissues (Lasic et al., *Science* 1995, 267, 1275-1276; Oku et al., 1995, *Biochim. Biophys. Acta*, 1238, 86-90). The long-circulating liposomes enhance the pharmacokinetics and pharmacodynamics of DNA and RNA, particularly compared to conventional cationic liposomes which are known to accumulate in tissues of the MPS (Liu et al., *J. Biol. Chem.* 1995, 42, 24864-24870; Choi et al., International PCT Publication No. WO 96/10391; Ansell et al., International PCT Publication No. WO 96/10390; Holland et al., International PCT Publication No. WO 96/10392). Long-circulating liposomes are also likely to protect drugs from nuclease degradation to a greater extent compared to cationic liposomes, based on their ability to avoid accumulation in metabolically aggressive MPS tissues such as the liver and spleen.

[0160] In a further embodiment, the present invention includes oligomer compositions prepared for delivery as described in U.S. Pat. Nos. 6,692,911, 7,163,695 and 7,070,807. In this regard, in one embodiment, the present invention provides an oligomer of the present invention in a composition comprising copolymers of lysine and histidine (HK) (as described in U.S. Pat. Nos. 7,163,695, 7,070,807, and 6,692,911) either alone or in combination with PEG (e.g., branched or unbranched PEG or a mixture of both), in combination with PEG and a targeting moiety or any of the foregoing in combination with a crosslinking agent. In certain embodiments, the present invention provides antisense oligomers in compositions comprising gluconic-acid-modified polyhistidine or gluconylated-polyhistidine/transferrin-polylysine. One skilled in the art will also recognize that amino acids with properties similar to His and Lys may be substituted within the composition.

[0161] Certain embodiments of the oligomers described herein may contain a basic functional group, such as amino or alkylamino, and are, thus, capable of forming pharmaceutically-acceptable salts with pharmaceutically-acceptable acids. The term "pharmaceutically-acceptable salts" in this respect, refers to the relatively non-toxic, inorganic and organic acid addition salts of compounds of the present invention. These salts can be prepared in situ in the administration vehicle or the dosage form manufacturing process, or by separately reacting a purified compound of the invention in its free base form with a suitable organic or inorganic acid, and isolating the salt thus formed during subsequent purification. Representative salts include the hydrobromide, hydrochloride, sulfate, bisulfate, phosphate, nitrate, acetate, valerate, oleate, palmitate, stearate, laurate, benzoate, lactate, phosphate, tosylate, citrate, maleate, fumarate, succinate, tartrate, naphthylate, mesylate, glucoheptonate, lactobionate, and laurylsulphonate salts and the like. (See, e.g., Berge et al. (1977) "Pharmaceutical Salts", *J. Pharm. Sci.* 66:1-19).

[0162] The pharmaceutically acceptable salts of the subject oligomers include the conventional nontoxic salts or quaternary ammonium salts of the compounds, e.g., from non-toxic organic or inorganic acids. For example, such conventional nontoxic salts include those derived from inorganic acids such as hydrochloride, hydrobromic, sulfuric, sulfamic, phosphoric, nitric, and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, palmitic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicyclic, sulfanilic, 2-acetoxybenzoic, fumaric, toluene-sulfonic, methanesulfonic, ethane disulfonic, oxalic, isothionic, and the like.

[0163] In certain embodiments, the oligomers of the present invention may contain one or more acidic functional groups and, thus, are capable of forming pharmaceutically-acceptable salts with pharmaceutically-acceptable bases. The term "pharmaceutically-acceptable salts" in these instances refers to the relatively non-toxic, inorganic and organic base addition salts of compounds of the present invention. These salts can likewise be prepared in situ in the administration vehicle or the dosage form manufacturing process, or by separately reacting the purified compound in its free acid form with a suitable base, such as the hydroxide, carbonate or bicarbonate of a pharmaceutically-acceptable metal cation, with ammonia, or with a pharmaceutically-acceptable organic primary, secondary or tertiary amine. Representative alkali or alkaline earth salts include the lithium, sodium, potassium, calcium, magnesium, and aluminum salts and the like. Representative organic amines useful for the formation of base addition salts include ethylamine, diethylamine, ethylenediamine, ethanolamine, diethanolamine, piperazine and the like. (See, e.g., Berge et al., *supra*).

[0164] Wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions.

[0165] Examples of pharmaceutically-acceptable antioxidants include: (1) water soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; (2) oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol, and the like; and (3) metal chelat-

ing agents, such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

[0166] Formulations of the present invention include those suitable for oral, nasal, topical (including buccal and sublingual), rectal, vaginal and/or parenteral administration. The formulations may conveniently be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. The amount of active ingredient that can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, the particular mode of administration. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect. Generally, out of one hundred percent, this amount will range from about 0.1 percent to about ninety-nine percent of active ingredient, preferably from about 5 percent to about 70 percent, most preferably from about 10 percent to about 30 percent.

[0167] In certain embodiments, a formulation of the present invention comprises an excipient selected from cyclodextrins, celluloses, liposomes, micelle forming agents, e.g., bile acids, and polymeric carriers, e.g., polyesters and poly-anhydrides; and an oligomer of the present invention. In certain embodiments, an aforementioned formulation renders orally bioavailable an oligomer of the present invention.

[0168] Methods of preparing these formulations or compositions include the step of bringing into association an oligomer of the present invention with the carrier and, optionally, one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association a compound of the present invention with liquid carriers, or finely divided solid carriers, or both, and then, if necessary, shaping the product.

[0169] Formulations of the invention suitable for oral administration may be in the form of capsules, cachets, pills, tablets, lozenges (using a flavored basis, usually sucrose and acacia or tragacanth), powders, granules, or as a solution or a suspension in an aqueous or non-aqueous liquid, or as an oil-in-water or water-in-oil liquid emulsion, or as an elixir or syrup, or as pastilles (using an inert base, such as gelatin and glycerin, or sucrose and acacia) and/or as mouth washes and the like, each containing a predetermined amount of a compound of the present invention as an active ingredient. An oligomer of the present invention may also be administered as a bolus, electuary or paste.

[0170] In solid dosage forms of the invention for oral administration (capsules, tablets, pills, dragees, powders, granules, trouches and the like), the active ingredient may be mixed with one or more pharmaceutically-acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: (1) fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and/or silicic acid; (2) binders, such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; (3) humectants, such as glycerol; (4) disintegrating agents, such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; (5) solution retarding agents, such as paraffin; (6) absorption accelerators, such as quaternary ammonium compounds and surfactants, such as poloxamer and sodium lauryl sulfate; (7) wetting agents, such as, for example, cetyl alcohol, glycerol monostearate, and non-ionic surfactants; (8) absorbents, such as kaolin and bentonite clay; (9) lubricants, such as talc,

calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, zinc stearate, sodium stearate, stearic acid, and mixtures thereof; (10) coloring agents; and (11) controlled release agents such as crospovidone or ethyl cellulose. In the case of capsules, tablets and pills, the pharmaceutical compositions may also comprise buffering agents. Solid compositions of a similar type may also be employed as fillers in soft and hard-shelled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like.

[0171] A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using binder (e.g., gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Molded tablets may be made by molding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent.

[0172] The tablets, and other solid dosage forms of the pharmaceutical compositions of the present invention, such as dragees, capsules, pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethyl cellulose in varying proportions to provide the desired release profile, other polymer matrices, liposomes and/or microspheres. They may be formulated for rapid release, e.g., freeze-dried. They may be sterilized by, for example, filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved in sterile water, or some other sterile injectable medium immediately before use. These compositions may also optionally contain opacifying agents and may be of a composition that they release the active ingredient(s) only, or preferentially, in a certain portion of the gastrointestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes. The active ingredient can also be in micro-encapsulated form, if appropriate, with one or more of the above-described excipients.

[0173] Liquid dosage forms for oral administration of the compounds of the invention include pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredient, the liquid dosage forms may contain inert diluents commonly used in the art, such as, for example, water or other solvents, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

[0174] Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, coloring, perfume and preservative agents.

[0175] Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan

esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, and mixtures thereof.

[0176] Formulations for rectal or vaginal administration may be presented as a suppository, which may be prepared by mixing one or more compounds of the invention with one or more suitable nonirritating excipients or carriers comprising, for example, cocoa butter, polyethylene glycol, a suppository wax or a salicylate, and which is solid at room temperature, but liquid at body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active compound.

[0177] Formulations or dosage forms for the topical or transdermal administration of an oligomer as provided herein include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. The active oligomers may be mixed under sterile conditions with a pharmaceutically-acceptable carrier, and with any preservatives, buffers, or propellants which may be required. The ointments, pastes, creams and gels may contain, in addition to an active compound of this invention, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

[0178] Powders and sprays can contain, in addition to an oligomer of the present invention, excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates and polyamide powder, or mixtures of these substances. Sprays can additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

[0179] Transdermal patches have the added advantage of providing controlled delivery of an oligomer of the present invention to the body. Such dosage forms can be made by dissolving or dispersing the oligomer in the proper medium. Absorption enhancers can also be used to increase the flux of the agent across the skin. The rate of such flux can be controlled by either providing a rate controlling membrane or dispersing the agent in a polymer matrix or gel, among other methods known in the art.

[0180] Pharmaceutical compositions suitable for parenteral administration may comprise one or more oligomers of the invention in combination with one or more pharmaceutically-acceptable sterile isotonic aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions just prior to use, which may contain sugars, alcohols, antioxidants, buffers, bacteriostats, solutes which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents. Examples of suitable aqueous and nonaqueous carriers which may be employed in the pharmaceutical compositions of the invention include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

[0181] These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms upon the subject oligomers may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the

like. It may also be desirable to include isotonic agents, such as sugars, sodium chloride, and the like into the compositions. In addition, prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents which delay absorption such as aluminum monostearate and gelatin.

[0182] In some cases, in order to prolong the effect of a drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material having poor water solubility, among other methods known in the art. The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally-administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

[0183] Injectable depot forms may be made by forming microencapsule matrices of the subject oligomers in biodegradable polymers such as polylactide-polyglycolide. Depending on the ratio of oligomer to polymer, and the nature of the particular polymer employed, the rate of oligomer release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations may also be prepared by entrapping the drug in liposomes or microemulsions that are compatible with body tissues.

[0184] When the oligomers of the present invention are administered as pharmaceuticals, to humans and animals, they can be given per se or as a pharmaceutical composition containing, for example, 0.1 to 99% (more preferably, 10 to 30%) of active ingredient in combination with a pharmaceutically acceptable carrier.

[0185] As noted above, the formulations or preparations of the present invention may be given orally, parenterally, systemically, topically, rectally or intramuscular administration. They are typically given in forms suitable for each administration route. For example, they are administered in tablets or capsule form, by injection, inhalation, eye lotion, ointment, suppository, etc. administration by injection, infusion or inhalation; topical by lotion or ointment; and rectal by suppositories.

[0186] The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal and intrasternal injection and infusion.

[0187] The phrases "systemic administration," "administered systemically," "peripheral administration" and "administered peripherally" as used herein mean the administration of a compound, drug or other material other than directly into the central nervous system, such that it enters the patient's system and, thus, is subject to metabolism and other like processes, for example, subcutaneous administration.

[0188] Regardless of the route of administration selected, the oligomers of the present invention, which may be used in a suitable hydrated form, and/or the pharmaceutical compositions of the present invention, may be formulated into pharmaceutically-acceptable dosage forms by conventional methods known to those of skill in the art. Actual dosage levels of

the active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active ingredient which is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being unacceptably toxic to the patient.

[0189] The selected dosage level will depend upon a variety of factors including the activity of the particular oligomer of the present invention employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of excretion or metabolism of the particular oligomer being employed, the rate and extent of absorption, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular oligomer employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts.

[0190] A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the compounds of the invention employed in the pharmaceutical composition at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved. In general, a suitable daily dose of a compound of the invention will be that amount of the compound which is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above. Generally, oral, intravenous, intracerebroventricular, intramuscular and subcutaneous doses of the compounds of this invention for a patient, when used for the indicated effects, will range from about 0.0001 to about 100 mg per kilogram of body weight per day.

[0191] Preferred doses of the oligomers of the present invention (e.g., phosphorodiamidate morpholino oligomers; eteplirsen) are administered generally from about 20-100 mg/kg. In some cases, doses of greater than 100 mg/kg may be necessary. For i.v. administration, preferred doses are from about 0.5 mg to 100 mg/kg. In some embodiments, the oligomers are administered at doses of about 20 mg/kg, 21 mg/kg, 25 mg/kg, 26 mg/kg, 27 mg/kg, 28 mg/kg, 29 mg/kg, 30 mg/kg, 31 mg/kg, 32 mg/kg, 33 mg/kg, 34 mg/kg, 35 mg/kg, 36 mg/kg, 37 mg/kg, 38 mg/kg, 39 mg/kg, 40 mg/kg, 41 mg/kg, 42 mg/kg, 43 mg/kg, 44 mg/kg, 45 mg/kg, 46 mg/kg, 47 mg/kg, 48 mg/kg, 49 mg/kg 50 mg/kg, 51 mg/kg, 52 mg/kg, 53 mg/kg, 54 mg/kg, 55 mg/kg, 56 mg/kg, 57 mg/kg, 58 mg/kg, 59 mg/kg, 60 mg/kg, 65 mg/kg, 70 mg/kg, 75 mg/kg, 80 mg/kg, 85 mg/kg, 90 mg/kg, 95 mg/kg, 100 mg/kg, including all integers in between. In a preferred embodiment, the oligomer is administered at 30 mg/kg. In another preferred embodiment, the oligomer is administered at 50 mg/kg.

[0192] If desired, the effective daily dose of the active compound may be administered as two, three, four, five, six or more sub-doses administered separately at appropriate intervals throughout the day, optionally, in unit dosage forms. In certain situations, dosing is one administration per day. In certain embodiments, dosing is one or more administration per every 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 days, or every 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 weeks, or every 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 months, as needed, to maintain the desired expression of a functional dystrophin protein.

[0193] In some embodiments, the oligomers of the present invention (e.g., phosphorodiamide morpholino oligomers; eteplirsen) are administered, generally at regular intervals (e.g., daily, weekly, biweekly, monthly, bimonthly). The oligomers may be administered at regular intervals, e.g., daily; once every two days; once every three days; once every 3 to 7 days; once every 3 to 10 days; once every 7 to 10 days; once every week; once every two weeks; once monthly. For example, the oligomers may be administered once weekly by intravenous infusion. The oligomers may be administered intermittently over a longer period of time, e.g., for several weeks, months or years. For example, the oligomers may be administered once every one, two, three, four, five, six, seven, eight, nine, ten, eleven or twelve months. In addition, the oligomers may be administered once every one, two, three, four or five years. Administration may be followed by, or concurrent with, administration of an antibiotic, steroid or other therapeutic agent. The treatment regimen may be adjusted (dose, frequency, route, etc.) as indicated, based on the results of immunoassays, other biochemical tests and physiological examination of the subject under treatment.

[0194] Nucleic acid molecules can be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres, as described herein and known in the art. In certain embodiments, microemulsification technology may be utilized to improve bioavailability of lipophilic (water insoluble) pharmaceutical agents. Examples include Trimetrine (Dordunoo, S. K., et al., Drug Development and Industrial Pharmacy, 17(12), 1685-1713, 1991 and REV 5901 (Sheen, P. C., et al., J Pharm Sci 80(7), 712-714, 1991). Among other benefits, microemulsification provides enhanced bioavailability by preferentially directing absorption to the lymphatic system instead of the circulatory system, which thereby bypasses the liver, and prevents destruction of the compounds in the hepatobiliary circulation.

[0195] In one aspect of invention, the formulations contain micelles formed from an oligomer as provided herein and at least one amphiphilic carrier, in which the micelles have an average diameter of less than about 100 nm. More preferred embodiments provide micelles having an average diameter less than about 50 nm, and even more preferred embodiments provide micelles having an average diameter less than about 30 nm, or even less than about 20 nm.

[0196] While all suitable amphiphilic carriers are contemplated, the presently preferred carriers are generally those that have Generally-Recognized-as-Safe (GRAS) status, and that can both solubilize the compound of the present invention and microemulsify it at a later stage when the solution comes into a contact with a complex water phase (such as one found in human gastro-intestinal tract). Usually, amphiphilic ingredients that satisfy these requirements have HLB (hydrophilic to lipophilic balance) values of 2-20, and their structures contain straight chain aliphatic radicals in the range of C-6 to C-20. Examples are polyethylene-glycolized fatty glycerides and polyethylene glycols.

[0197] Examples of amphiphilic carriers include saturated and monounsaturated polyethyleneglycolized fatty acid glycerides, such as those obtained from fully or partially hydrogenated various vegetable oils. Such oils may advantageously consist of tri-, di-, and mono-fatty acid glycerides and di- and mono-polyethyleneglycol esters of the corresponding

fatty acids, with a particularly preferred fatty acid composition including capric acid 4-10, capric acid 3-9, lauric acid 40-50, myristic acid 14-24, palmitic acid 4-14 and stearic acid 5-15%. Another useful class of amphiphilic carriers includes partially esterified sorbitan and/or sorbitol, with saturated or mono-unsaturated fatty acids (SPAN-series) or corresponding ethoxylated analogs (TWEEN-series).

[0198] Commercially available amphiphilic carriers may be particularly useful, including Gelucire-series, Labrafil, Labrasol, or Lauroglycol (all manufactured and distributed by Gattefossé Corporation, Saint Priest, France), PEG-monooleate, PEG-di-oleate, PEG-mono-laurate and di-laurate, Lecithin, Polysorbate 80, etc (produced and distributed by a number of companies in USA and worldwide).

[0199] In certain embodiments, the delivery may occur by use of liposomes, nanocapsules, microparticles, microspheres, lipid particles, vesicles, and the like, for the introduction of the compositions of the present invention into suitable host cells. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid particle, a liposome, a vesicle, a nanosphere, a nanoparticle or the like. The formulation and use of such delivery vehicles can be carried out using known and conventional techniques.

[0200] Hydrophilic polymers suitable for use in the present invention are those which are readily water-soluble, can be covalently attached to a vesicle-forming lipid, and which are tolerated in vivo without toxic effects (i.e., are biocompatible). Suitable polymers include polyethylene glycol (PEG), polylactic (also termed polylactide), polyglycolic acid (also termed polyglycolide), a polylactic-polyglycolic acid copolymer, and polyvinyl alcohol. In certain embodiments, polymers have a molecular weight of from about 100 or 120 daltons up to about 5,000 or 10,000 daltons, or from about 300 daltons to about 5,000 daltons. In other embodiments, the polymer is polyethyleneglycol having a molecular weight of from about 100 to about 5,000 daltons, or having a molecular weight of from about 300 to about 5,000 daltons. In certain embodiments, the polymer is polyethyleneglycol of 750 daltons (PEG(750)). Polymers may also be defined by the number of monomers therein; a preferred embodiment of the present invention utilizes polymers of at least about three monomers, such PEG polymers consisting of three monomers (approximately 150 daltons).

[0201] Other hydrophilic polymers which may be suitable for use in the present invention include polyvinylpyrrolidone, polymethoxazoline, polyethyloxazoline, polyhydroxypropyl methacrylamide, polymethacrylamide, polydimethylacrylamide, and derivatized celluloses such as hydroxymethylcellulose or hydroxyethylcellulose.

[0202] In certain embodiments, a formulation of the present invention comprises a biocompatible polymer selected from the group consisting of polyamides, polycarbonates, polyalkylenes, polymers of acrylic and methacrylic esters, polyvinyl polymers, polyglycolides, polysiloxanes, polyurethanes and co-polymers thereof, celluloses, polypropylene, polyethylenes, polystyrene, polymers of lactic acid and glycolic acid, polyanhydrides, poly(ortho)esters, poly(butic acid), poly(valeric acid), poly(lactide-co-caprolactone), polysaccharides, proteins, polyhyaluronic acids, polycyanoacrylates, and blends, mixtures, or copolymers thereof.

[0203] Cyclodextrins are cyclic oligosaccharides, consisting of 6, 7 or 8 glucose units, designated by the Greek letter α , β , or γ , respectively. The glucose units are linked by α -1,4-

glucosidic bonds. As a consequence of the chair conformation of the sugar units, all secondary hydroxyl groups (at C-2, C-3) are located on one side of the ring, while all the primary hydroxyl groups at C-6 are situated on the other side. As a result, the external faces are hydrophilic, making the cyclodextrins water-soluble. In contrast, the cavities of the cyclodextrins are hydrophobic, since they are lined by the hydrogen of atoms C-3 and C-5, and by ether-like oxygens. These matrices allow complexation with a variety of relatively hydrophobic compounds, including, for instance, steroid compounds such as 17 α -estradiol (see, e.g., van Uden et al. *Plant Cell Tiss. Org. Cult.* 38:1-3-113 (1994)). The complexation takes place by Van der Waals interactions and by hydrogen bond formation. For a general review of the chemistry of cyclodextrins, see, Wenz, *Agnew. Chem. Int. Ed. Engl.*, 33:803-822 (1994).

[0204] The physico-chemical properties of the cyclodextrin derivatives depend strongly on the kind and the degree of substitution. For example, their solubility in water ranges from insoluble (e.g., triacetyl-beta-cyclodextrin) to 147% soluble (w/v) (G-2-beta-cyclodextrin). In addition, they are soluble in many organic solvents. The properties of the cyclodextrins enable the control over solubility of various formulation components by increasing or decreasing their solubility.

[0205] Numerous cyclodextrins and methods for their preparation have been described. For example, Parmeter (I), et al. (U.S. Pat. No. 3,453,259) and Gramera, et al. (U.S. Pat. No. 3,459,731) described electroneutral cyclodextrins. Other derivatives include cyclodextrins with cationic properties [Parmeter (II), U.S. Pat. No. 3,453,257], insoluble crosslinked cyclodextrins (Solms, U.S. Pat. No. 3,420,788), and cyclodextrins with anionic properties [Parmeter (III), U.S. Pat. No. 3,426,011]. Among the cyclodextrin derivatives with anionic properties, carboxylic acids, phosphorous acids, phosphinous acids, phosphonic acids, phosphoric acids, thiophosphonic acids, thiosulphinic acids, and sulfonic acids have been appended to the parent cyclodextrin [see, Parmeter (III), *supra*]. Furthermore, sulfoalkyl ether cyclodextrin derivatives have been described by Stella, et al. (U.S. Pat. No. 5,134,127).

[0206] Liposomes consist of at least one lipid bilayer membrane enclosing an aqueous internal compartment. Liposomes may be characterized by membrane type and by size. Small unilamellar vesicles (SUVs) have a single membrane and typically range between 0.02 and 0.05 μ m in diameter; large unilamellar vesicles (LUVs) are typically larger than 0.05 μ m. Oligolamellar large vesicles and multilamellar vesicles have multiple, usually concentric, membrane layers and are typically larger than 0.1 μ m. Liposomes with several nonconcentric membranes, i.e., several smaller vesicles contained within a larger vesicle, are termed multivesicular vesicles.

[0207] One aspect of the present invention relates to formulations comprising liposomes containing an oligomer of the present invention, where the liposome membrane is formulated to provide a liposome with increased carrying capacity. Alternatively or in addition, the compound of the present invention may be contained within, or adsorbed onto, the liposome bilayer of the liposome. An oligomer of the present invention may be aggregated with a lipid surfactant and carried within the liposome's internal space; in these cases, the liposome membrane is formulated to resist the disruptive effects of the active agent-surfactant aggregate.

[0208] According to one embodiment of the present invention, the lipid bilayer of a liposome contains lipids derivatized with polyethylene glycol (PEG), such that the PEG chains extend from the inner surface of the lipid bilayer into the interior space encapsulated by the liposome, and extend from the exterior of the lipid bilayer into the surrounding environment.

[0209] Active agents contained within liposomes of the present invention are in solubilized form. Aggregates of surfactant and active agent (such as emulsions or micelles containing the active agent of interest) may be entrapped within the interior space of liposomes according to the present invention. A surfactant acts to disperse and solubilize the active agent, and may be selected from any suitable aliphatic, cycloaliphatic or aromatic surfactant, including but not limited to biocompatible lysophosphatidylcholines (LPGs) of varying chain lengths (for example, from about C14 to about C20). Polymer-derivatized lipids such as PEG-lipids may also be utilized for micelle formation as they will act to inhibit micelle/membrane fusion, and as the addition of a polymer to surfactant molecules decreases the CMC of the surfactant and aids in micelle formation. Preferred are surfactants with CMOs in the micromolar range; higher CMC surfactants may be utilized to prepare micelles entrapped within liposomes of the present invention.

[0210] Liposomes according to the present invention may be prepared by any of a variety of techniques that are known in the art. See, e.g., U.S. Pat. No. 4,235,871; Published PCT applications WO 96/14057; New RRC, *Liposomes: A practical approach*, IRL Press, Oxford (1990), pages 33-104; Lasic D D, *Liposomes from physics to applications*, Elsevier Science Publishers BV, Amsterdam, 1993. For example, liposomes of the present invention may be prepared by diffusing a lipid derivatized with a hydrophilic polymer into preformed liposomes, such as by exposing preformed liposomes to micelles composed of lipid-grafted polymers, at lipid concentrations corresponding to the final mole percent of derivatized lipid which is desired in the liposome. Liposomes containing a hydrophilic polymer can also be formed by homogenization, lipid-field hydration, or extrusion techniques, as are known in the art.

[0211] In another exemplary formulation procedure, the active agent is first dispersed by sonication in a lysophosphatidylcholine or other low CMC surfactant (including polymer grafted lipids) that readily solubilizes hydrophobic molecules. The resulting micellar suspension of active agent is then used to rehydrate a dried lipid sample that contains a suitable mole percent of polymer-grafted lipid, or cholesterol. The lipid and active agent suspension is then formed into liposomes using extrusion techniques as are known in the art, and the resulting liposomes separated from the unencapsulated solution by standard column separation.

[0212] In one aspect of the present invention, the liposomes are prepared to have substantially homogeneous sizes in a selected size range. One effective sizing method involves extruding an aqueous suspension of the liposomes through a series of polycarbonate membranes having a selected uniform pore size; the pore size of the membrane will correspond roughly with the largest sizes of liposomes produced by extrusion through that membrane. See e.g., U.S. Pat. No. 4,737,323 (Apr. 12, 1988). In certain embodiments, reagents such as DharmaFECT[®] and Lipofectamine[®] may be utilized to introduce polynucleotides or proteins into cells.

[0213] The release characteristics of a formulation of the present invention depend on the encapsulating material, the concentration of encapsulated drug, and the presence of release modifiers. For example, release can be manipulated to be pH dependent, for example, using a pH sensitive coating that releases only at a low pH, as in the stomach, or a higher pH, as in the intestine. An enteric coating can be used to prevent release from occurring until after passage through the stomach. Multiple coatings or mixtures of cyanamide encapsulated in different materials can be used to obtain an initial release in the stomach, followed by later release in the intestine. Release can also be manipulated by inclusion of salts or pore forming agents, which can increase water uptake or release of drug by diffusion from the capsule. Excipients which modify the solubility of the drug can also be used to control the release rate. Agents which enhance degradation of the matrix or release from the matrix can also be incorporated. They can be added to the drug, added as a separate phase (i.e., as particulates), or can be co-dissolved in the polymer phase depending on the compound. In most cases the amount should be between 0.1 and thirty percent (w/w polymer). Types of degradation enhancers include inorganic salts such as ammonium sulfate and ammonium chloride, organic acids such as citric acid, benzoic acid, and ascorbic acid, inorganic bases such as sodium carbonate, potassium carbonate, calcium carbonate, zinc carbonate, and zinc hydroxide, and organic bases such as protamine sulfate, spermine, choline, ethanolamine, diethanolamine, and triethanolamine and surfactants such as Tween® and Pluronic®. Pore forming agents which add microstructure to the matrices (i.e., water soluble compounds such as inorganic salts and sugars) are added as particulates. The range is typically between one and thirty percent (w/w polymer).

[0214] Uptake can also be manipulated by altering residence time of the particles in the gut. This can be achieved, for example, by coating the particle with, or selecting as the encapsulating material, a mucosal adhesive polymer. Examples include most polymers with free carboxyl groups, such as chitosan, celluloses, and especially polyacrylates (as used herein, polyacrylates refers to polymers including acrylate groups and modified acrylate groups such as cyanoacrylates and methacrylates).

[0215] An oligomer may be formulated to be contained within, or, adapted to release by a surgical or medical device or implant. In certain aspects, an implant may be coated or otherwise treated with an oligomer. For example, hydrogels, or other polymers, such as biocompatible and/or biodegradable polymers, may be used to coat an implant with the compositions of the present invention (i.e., the composition may be adapted for use with a medical device by using a hydrogel or other polymer). Polymers and copolymers for coating medical devices with an agent are well-known in the art. Examples of implants include, but are not limited to, stents, drug-eluting stents, sutures, prosthesis, vascular catheters, dialysis catheters, vascular grafts, prosthetic heart valves, cardiac pacemakers, implantable cardioverter defibrillators, IV needles, devices for bone setting and formation, such as pins, screws, plates, and other devices, and artificial tissue matrices for wound healing.

[0216] In addition to the methods provided herein, the oligomers for use according to the invention may be formulated for administration in any convenient way for use in human or veterinary medicine, by analogy with other pharmaceuticals. The antisense oligomers and their corresponding formula-

tions may be administered alone or in combination with other therapeutic strategies in the treatment of muscular dystrophy, such as myoblast transplantation, stem cell therapies, administration of aminoglycoside antibiotics, proteasome inhibitors, and up-regulation therapies (e.g., upregulation of utrophin, an autosomal parologue of dystrophin).

[0217] The routes of administration described are intended only as a guide since a skilled practitioner will be able to determine readily the optimum route of administration and any dosage for any particular animal and condition. Multiple approaches for introducing functional new genetic material into cells, both *in vitro* and *in vivo* have been attempted (Friedmann (1989) *Science*, 244:1275-1280). These approaches include integration of the gene to be expressed into modified retroviruses (Friedmann (1989) *supra*; Rosenberg (1991) *Cancer Research* 51(18), suppl.: 5074S-5079S); integration into non-retrovirus vectors (e.g., adeno-associated viral vectors) (Rosenfeld, et al. (1992) *Cell*, 68:143-155; Rosenfeld, et al. (1991) *Science*, 252:431-434); or delivery of a transgene linked to a heterologous promoter-enhancer element via liposomes (Friedmann (1989), *supra*; Brigham, et al. (1989) *Am. J. Med. Sci.*, 298:278-281; Nabel, et al. (1990) *Science*, 249:1285-1288; Hazinski, et al. (1991) *Am. J. Resp. Cell Molec. Biol.*, 4:206-209; and Wang and Huang (1987) *Proc. Natl. Acad. Sci. (USA)*, 84:7851-7855); coupled to ligand-specific, cation-based transport systems (Wu and Wu (1988) *J. Biol. Chem.*, 263:14621-14624) or the use of naked DNA, expression vectors (Nabel et al. (1990), *supra*); Wolff et al. (1990) *Science*, 247:1465-1468). Direct injection of transgenes into tissue produces only localized expression (Rosenfeld (1992) *supra*; Rosenfeld et al. (1991) *supra*; Brigham et al. (1989) *supra*; Nabel (1990) *supra*; and Hazinski et al. (1991) *supra*). The Brigham et al. group (Am. J. Med. Sci. (1989) 298:278-281 and Clinical Research (1991) 39 (abstract)) have reported *in vivo* transfection only of lungs of mice following either intravenous or intratracheal administration of a DNA liposome complex. An example of a review article of human gene therapy procedures is: Anderson, *Science* (1992) 256:808-813.

V. KITS

[0218] The invention also provides kits for treatment of a patient with a genetic disease which kit comprises at least an antisense molecule (e.g., one or more antisense oligonucleotides capable of specifically hybridizing to any one or more of exons 1-79 of the dystrophin gene; for example, Exon 51 as set forth in Tables 3 and 4 herein), packaged in a suitable container, together with instructions for its use. The kits may also contain peripheral reagents such as buffers, stabilizers, etc. Those of ordinary skill in the field should appreciate that applications of the above method has wide application for identifying antisense molecules suitable for use in the treatment of many other diseases.

VII. EXAMPLES

Materials and Methods

Patients

[0219] Eligible patients were between 7 and 13 years of age (inclusive), with out-of-frame deletions of the DMD gene that could be corrected by skipping exon 51. Patients were confirmed to have stable cardiac and pulmonary function and a stable dose of glucocorticoids for at least 24 weeks prior to

enrollment. Only patients who could walk between 200 and 400 meters ($\pm 10\%$) on the 6-Minute Walk Test (6MWT) at baseline were enrolled.

Study Design

[0220] This one-year trial was conducted in two phases: (1) treatment was double-blind through week 24 and (2) open-label thereafter. Primary endpoints were change in percent dystrophin fibers and ambulation as measured by the 6-Minute Walk Test (6MWT).

[0221] Study 201 was a single-site, randomized, double-blind, placebo-controlled, multiple-dose efficacy, safety and tolerability trial of eteplirsen. Twelve patients with DMD were randomized to one of three groups: eteplirsen 30 mg/kg/week (Cohort 1); eteplirsen 50 mg/kg/week (Cohort 2); or placebo/delayed eteplirsen (Cohort 3). All patients received weekly intravenous eteplirsen or placebo/delayed eteplirsen dosing. Placebo-treated patients crossed over to weekly eteplirsen 30 (n=2) or 50 mg/kg (n=2) at week 25. Efficacy and safety were assessed at scheduled visits, and an independent Data Safety Monitoring Board ensured the welfare of all patients. All patients had bicep biopsies at baseline. Follow-up biopsies were performed in the opposite arm (biceps) at week 12 for the 50 mg/kg group and two placebo-treated patients and at week 24 for the 30 mg/kg group and two placebo-treated patients.

[0222] Patients continued weekly dosing with 30 or 50 mg/kg eteplirsen under Study 202, a long-term, open-label extension study. All efficacy assessments continued to be performed during Study 202, including a third biopsy (in the left deltoid muscle) in all patients at week 48. Monitoring of adverse events continued throughout the study. A schematic of the study design is shown in FIG. 1.

Study Drug

[0223] Eteplirsen [sequence 5'-CTCCAACATCAAG-GAAGATGGCATTCTAG-3'] (SEQ ID NO:1) was supplied by Sarepta Therapeutics, Inc. in single-use vials of phosphate-buffered saline (100 mg/ml). Eteplirsen was reconstituted with 150 ml normal saline and infused over 60 minutes. Placebo, administered during the first 24 weeks of Study 201, was supplied as identical vials of phosphate-buffered saline and was administered in the same manner as eteplirsen.

Safety and Tolerability Monitoring

[0224] Safety was assessed by evaluation of adverse events, vital signs, physical examinations, electrocardiograms, echocardiograms, and clinical laboratory testing. In addition, kidney function was monitored via regular assessments of serum cystatin C and urine cystatin C and KIM-1.

Pharmacokinetic and Immune Assessments

[0225] Pharmacokinetic parameters of eteplirsen were established from plasma and urine taken after the twelfth dose using a validated and sensitive anion exchange high-performance liquid chromatography with fluorescence detection bioanalytical method. Single samples for analysis of plasma concentrations were taken at weeks 24, 25, and 36. Immune response to novel dystrophin protein was measured every six weeks through week 24 with ELISPOT following methods previously published.

Biochemical Efficacy Assessments

[0226] Pre- and post-treatment dystrophin expression studies were based on MANDYS106 [a gift from Glen Morris, MDA Monoclonal Antibody Library], a highly sensitive marker for dystrophin used in prior studies of eteplirsen and other exon skipping candidates. Three 10 μ m frozen sections, separated by at least 200 μ m, were stained with MANDYS106, followed by a secondary antibody (Alexa Fluor 594 goat antimouse antibody). Percent dystrophin-positive fibers were calculated by dividing the number of positive fibers by the total fibers counted. As normal muscle samples have 100% dystrophin-positive fibers, percent dystrophin-positive fibers is expressed as a percentage of normal. The same antibody-stained sections were used for dystrophin quantification using Bioquant image analysis software. The total dystrophin fluorescence signal intensity was reported as a percentage of normal.

[0227] Supportive measurements included expression of the components of the sarcoglycan complex (β, γ), neuronal NOS, and Western blot (with the anti-dystrophin antibody NCL-Dysl from Novacastra). RT-PCR analysis, for confirmation of exon skipping, was performed on 400 ng of total RNA using dystrophin-specific reverse primers as previously described.

Clinical Efficacy Assessments

[0228] The 6MWT was administered using the protocol established for patients with DMD by McDonald, et al. (Muscle Nerve, 2010; 42:966-74, herein incorporated by reference). Exploratory functional outcomes included the North Star Ambulatory Assessment, quantitative muscle testing, the 9-Hole Peg Test, pulmonary function testing (PFT), timed function tests, and assessment of quality of life.

Statistical Analysis

[0229] SAS version 9.3 (Cary, N.C.) was used for all statistical analyses. Mixed model with treatment as fixed effect, subject nested within treatment as random effect, with the baseline value and time since DMD diagnosis as covariates for the analysis of muscle biopsy data was used. Mixed model repeated measures (MMRM) with treatment, time, and treatment-by-time interaction terms as fixed effect, subject nested within treatment as random effect, and with the baseline value and time since DMD diagnosis as covariates for analysis of the 6MWT data was used. Safety and muscle biopsy analyses were performed on the intent-to-treat population; analysis of ambulation-related outcomes, including the 6MWT, used a modified intent-to-treat (mITT) population that excluded two patients in Cohort 1 who showed signs of disease progression and significant decline on the 6MWT within weeks of enrollment and could not perform measures of ambulation at week 24 or beyond.

Example 1

Subject Characteristics

[0230] Baseline characteristics of the 12 patients in this study are summarized in Table 2. Five different genotypes amenable to exon 51 skipping were represented in the study population. Mean distances on the 6-Minute Walk Test (6MWT) at baseline were similar to those in other studies of children with DMD, and as expected, were well below the 600 plus meters typically observed in age-matched healthy

children. Due to the stochastic nature of the sampling, the 30 mg/kg cohort was slightly older, heavier, and taller, relative to the other cohorts, and had a lower mean 6MWT distance at baseline. All patients received all infusions of study medication as planned and completed all assessments.

TABLE 2

Baseline Demography and Disease Characteristics			
Treatment Arm	Placebo/ Delayed Eteplirsen N = 4	Eteplirsen 30 mg/kg N = 4	Eteplirsen 50 mg/kg N = 4
<u>Mutation</u>			
45-50 n (%)	0	2 (50)	1 (25)
48-50 n (%)	0	1 (25)	0
49-50 n (%)	3 (75)	0	2 (50)
50 n (%)	1 (25)	0	0
52 n (%)	0	1 (25)	1 (25)
<u>Gender n (%)</u>			
Male	4 (100)	4 (100)	4 (100)
<u>Age, years</u>			
Mean	8.5	9.3	8.5
SD	1.73	0.50	1.29
Min, Max	7, 10	9, 10	7, 10
<u>Height, cm</u>			
Mean	119.3	130.5	121.3
SD	3.40	9.47	7.85
Min, Max	116, 124	117, 138	117, 133
<u>Weight, kg</u>			
Mean	30.6	34.8	29.0
SD	6.04	7.05	6.38
Min, Max	22.1, 36.2	24.8, 39.8	23.7, 38.3
<u>Race, n (%)</u>			
Asian	0	1 (25)	0
White	4 (100)	3 (75)	4 (100)
<u>6MWT*, meters</u>			
Mean	394.5	355.3	396.0
SD	42.25	74.78	26.61
Min, Max	364, 456	261, 442	365, 429

Example 2

Safety and Lack of Adverse Events

[0231] Eteplirsen was well tolerated with no treatment-related adverse events, serious adverse events, discontinuations or missed doses through 48 weeks of treatment. Moreover, no clinically significant changes were observed on physical examination or in vital signs. Electrocardiograms, echocardiograms, and PFTs remained stable, and chemistries showed no clinically significant changes in hematologic, renal, coagulation or liver functions. Mild and transient proteinuria was observed in a single placebo-treated subject.

Example 3

Pharmacokinetic Profile

[0232] Analysis of PK parameters at week 12 revealed rapid absorption. Plasma clearance averaged 339 ± 75.8 mL/hr/kg for 30 mg/kg and 319 ± 125 mL/hr/kg for 50 mg/kg. Half-life averaged 3.30 ± 0.341 hr for 30 mg/kg and 3.17 ± 0 .

249 hr for 50 mg/kg, with renal clearance accounting for approximately 65-70% of total systemic clearance.

Example 4

Efficacy

[0233] At week 48, eteplirsen produced robust increases in the number and intensity of dystrophin-positive fibers. As shown in FIG. 3, patients who received 30 or 50 mg/kg eteplirsen without interruption for 48 weeks showed a mean increase in the percentage of dystrophin-positive fibers to 47% of normal ($p \leq 0.001$), relative to baseline. Increases were similar when the 30 (52%; $p = 0.001$) and 50 (43%; $p \leq 0.008$) mg/kg cohorts were analyzed separately, suggesting that eteplirsen's effect on the production of novel dystrophin is independent of dose within this range of doses.

[0234] Biopsies were taken at staggered time points (see FIG. 2) to evaluate the impact of treatment duration on novel dystrophin production. At week 12, the 50 mg/kg cohort had undetectable levels of novel dystrophin. At week 24, the 30 mg/kg cohort demonstrated an increase in the percentage of dystrophin-positive fibers to 23% of normal ($p \leq 0.002$), and at week 48, after 24 weeks of treatment with 30 or 50 mg/kg eteplirsen, the 4 patients in the placebo/delayed eteplirsen cohort showed an increase to 38% of normal, relative to baseline ($p \leq 0.009$). Together these data suggest that treatment duration plays an important role in eteplirsen's ability to uniformly restore novel dystrophin production. Consistent with these findings, eteplirsen also significantly increased mean fluorescence signal intensity at week 48 in all three treatment groups (all p -values ≤ 0.023).

[0235] FIG. 4 illustrates eteplirsen's time-dependent effect on the percentage of dystrophin-positive fibers (Panel A), which was accompanied by restoration of β - and γ -sarcoglycan and nNOS μ at the sarcolemma (Panel B). Dystrophin expression and exon skipping were confirmed by Western blot and RT-PCR in all patients. RT-PCR results from a representative patient are shown in Panel C. These data confirmed the increase in functional dystrophin in the patients.

Example 5

Functional Outcomes

[0236] The progressive loss of walking ability is a universal hallmark of DMD, with most patients showing functional compromise by 7 or 8 years of age and becoming wheelchair dependent by 10 to 14 years of age. Consistent with this, boys assigned to the placebo/delayed eteplirsen cohort in this study showed a decline in walking ability after week 12 at a rate predicted by prior studies, culminating in a loss of approximately 60 meters by week 48 (FIG. 5). In marked contrast, eteplirsen-treated patients maintained a stable walking distance over the duration of the study, with a mean increase from baseline of about 7 meters by week 48. The difference between the eteplirsen-treated patients and those in the placebo/delayed eteplirsen cohort first became statistically significant at week 32 (39-meter difference; $p \leq 0.05$). Interestingly, patients in the placebo/delayed eteplirsen cohort appeared to stabilize after week 36, i.e., between 12 and 24 weeks after initiating treatment with eteplirsen at week 25. As previously noted, two boys who showed signs of rapid disease progression and significant decline on the 6MWT within weeks of enrollment and were unable to perform measures of ambulation at 24 weeks or beyond, were excluded from this

analysis. However, both remained on eteplirsen through week 48 with no treatment-related adverse events and maintained stable pulmonary and upper limb function as measured by PFT and the 9-Hole Peg Test, respectively.

[0237] Notably, patients receiving eteplirsen for 48 weeks, evaluable on the 6MWT (n=6), significantly (p≤0.001) improved on the 6MWT (67.3 m) compared to the placebo/delayed cohort.

Example 6

Immune Response

[0238] There were no differences between the eteplirsen- and placebo-treated patients in the number of interferon-γ-induced spot forming colonies to dystrophin peptide pools (extended over the entire protein) at any time point assessed, including week 24, indicating that the newly expressed dystrophin in the eteplirsen-treated patients did not elicit a T-cell response.

[0239] All publications and patent applications cited in this specification are herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference.

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SEQUENCE LISTING

[0272] With respect to the nucleic acid sequences provided in the application, persons skilled in the art will appreciate that depending on the use of the oligomers, Ts and Us are interchangeable.

TABLE 3

EXON	SEQ	ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
51	1	eteplirsen		CTC CAA CAT CAA GGA AGA TGG CAT
		H51A(+66 + 95)		TTC TAG
51	2	H51A(+66 + 90)		ACA UCA AGG AAG AUG GCA UUU CUA G
51	3	H51A(+61 + 90)		ACA UCA AGG AAG AUG GCA UUU CUA GUU UGG
51	4	Hu.DMD.exon51.25.001.2		GAG CAG GTA CCT CCA ACA TCA AGG AA
50	5	H50D(+07 - 18)		GGG AUC CAG UAU ACU UAC AGG CUC C
50	6	AVI-4038/5038		CTT ACA GGC TCC AAT AGT GGT CAG T
53	7	H53A27(+30 + 56)		CCT CCG GTT CTG AAG GTG TTC TTG TAC
53	8	H53A(+36 + 60)		GTT GCC TCC GGT TCT GAA GGT GTT C
45	9	H45A (-03 + 19)		CAA TGC CAT CCT GGA GTT CCT G

TABLE 4

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
10	H8A(-06 + 18)	GAU AGG UGG UAU CAA CAU CUG UAA
11	H8A (-04 + 18)	GAU AGG UGG UAU CAA CAU CUG
12	H8A(-07 + 18)	GAU AGG UGG UAU CAA CAU CUG UAA G
13	H8A(-06 + 14)	GGU GGU AUC AAC AUC UGU AA
14	H8A(-10 + 10)	GUA UCA ACA UCU GUA AGC AC
15	H7A(+45 + 67)	UGC AUG UUC CAG UCG UUG UGU GG
16	H7A(+02 + 26)	CAC UAU UCC AGU CAA AUA GGU CUG G
17	H7D(+15-10)	AUU UAC CAA CCU UCA GGA UCG AGU A
18	H7A(-18 + 03)	GGC CUA AAA CAC AUA CAC AUA
19	C6A(-10 + 10)	CAU UUU UGA CCU ACA UGU GG
20	C6A(-14 + 06)	UUU GAC CUA CAU GUG GAA AG
21	C6A(-14 + 12)	UAC AUU UUU GAC CUA CAU GUG GAA AG
22	C6A(-14 + 09)	AUU UUU GAC CUA CAU GGG AAA G
23	CH6A(+69 + 91)	UAC GAG UUG AUU GUC GGA CCC AG
24	C6D(+12 - 13)	GUG GUC UCC UUA CCU AUG ACU GUG G
25	C6D(+06 - 11)	GGU CUC CUU ACC UAU GA
26	H6D(+04 - 21)	UGU CUC AGU AAU CUU CUU ACC UAU
27	H6D(+18 - 04)	UCU UAC CUA UGA CUA UGG AUG AGA
28	H4A(+13 + 32)	GCA UGA ACU CUU GUG GAU CC

TABLE 4-continued

29	H4D(+04 - 16)	CCA GGG UAC UAC UUA CAU UA
30	H4D(-24 - 44)	AUC GUG UGU CAC AGC AUC CAG
31	H4A(+11 + 40)	UGU UCA GGG CAU GAA CUC UUG UGG AUC CUU
32	H3A(+30 + 60)	UAG GAG GCG CCU CCC AUC CUG UAG GUC ACU G
33	H3A(+35 + 65)	AGG UCU AGG AGG CGC CUC CCA UCC UGU AGG U
34	H3A(+30 + 54)	GCG CCU CCC AUC CUC UAG GUC ACU G
35	H3D(+46 - 21)	CUU CGA GGA GGU CUA GGA GGC GCC UC
36	H3A(+30 + 50)	CUC CCA UCC UGU AGG UCA CUG
37	H3D(+19 - 03)	UAC CAG UUU UUG CCC UGU CAG G
38	H3A(-06 + 20)	UCA AUA UGC UGC UUC CCA AAC UGA AA
39	H3A(+37 + 61)	CUA GGA GGC GCC UCC CAU CCU GUA G
40	H5A(+20 + 50)	UUA UGA UUU CCA UCU ACG AUG UCA GUA CUU C
41	H5D(+25 - 05)	CUU ACC UGC CAG UGG AGG AUU AUA UUC CAA A
42	H5D(+10 - 15)	CAU CAG GAU UCU UAC CUG CCA GUG G
43	H5A(+10 + 34)	CGA UGU CAG UAC UUC CAA UAU UCA C
44	H5D(-04 - 21)	ACC AUU CAU CAG GAU UCU
45	H5D(+16 - 02)	ACC UGC CAG UGG AGG AUU
46	H5A(-07 + 20)	CCA AUA UUC ACU AAA UCA ACC UGU UAA
47	H5D(+18 - 12)	CAG GAU UGU UAC CUG CCA GUG GAG GAU UAU
48	H5A(+05 + 35)	ACG AUG UCA GUA CUU CCA AUA UUC ACU AAA U
49	H5A(+15 + 45)	AUU UCC AUC UAC GAU GUC AGU ACU UCC AAU A
50	H10A(-05 + 16)	CAG GAG CUU CCA AAU GCU GCA
51	H10A(-05 + 24)	CUU GUC UUC AGG AGC UUC CAA AUG CUG CA
52	H10A(+98 + 119)	UCC UCA GCA GAA AGA AGC CAC G
53	H10A(+130 + 149)	UUA GAA AUC UCU CCU UGU GC
54	H10A(-33 - 14)	UAA AUU GGG UGU UAC ACA AU
55	H11D(+26 + 49)	CCC UGA GGC AUU CCC AUC UUG AAU
56	H11D(+11 - 09)	AGG ACU UAC UUG CUU UGU UU
57	H11A(+118 + 140)	CUU GAA UUU AGG AGA UUC AUC UG
58	H11A(+75 + 97)	CAU CUU CUG AUA AUU UUC CUG UU
59	H12A(+52 + 75)	UCU UCU GUU UUU GUU AGC CAG UCA
60	H12A(-10 + 10)	UCU AUG UAA ACU GAA AAU UU
61	H12A(+11 + 30)	UUC UGG AGA UCC AUU AAA AC
62	H13A(+77 + 100)	CAG CAG UUG CGU GAU CUC CAC UAG
63	H13A(+55 + 75)	UUC AUC AAC UAC CAC CAC CAU
64	H13D(+06 - 19)	CUA AGC AAA AUA AUC UGA CCU UAA G
65	H14A(+37 + 64)	CUU GUA AAA GAA CCC AGC GGU CUU CUG U
66	H14A(+14 + 35)	CAU CUA CAG AUG UUU GCC CAU C
67	H14A(+51 + 73)	GAA GGA UGU CUU GUA AAA GAA CC
68	H14D(-02 + 18)	ACC UGU UCU UCA GUA AGA CG
69	H14D(+14 - 10)	CAU GAC ACA CCU GUU CUU CAG UAA
70	H14A(+61 + 80)	CAU UUG AGA AGG AUG UCU UG
71	H14A(-12 + 12)	AUC UCC CAA UAC CUG GAG AAG AGA
72	H15A(-12 + 19)	GCC AUG CAC UAA AAA GGC ACU GCA AGA CAU U
73	H15A(+48 + 71)	UCU UUA AAG CCA GUU GUG UGA AUC
74	H15A(+08 + 28)	UUU CUG AAA GCC AUG CAC UAA
75	H15D(+17 - 08)	GUA CAU ACG GCC AGU UUU UGA AGA C
76	H16A(-12 + 19)	CUA GAU CCG CUU UUA AAA CCU GUU AAA ACA A
77	H16A(-06 + 25)	UCU UUU CUA GAU CCG CUU UUA AAA CCU GUU A
78	H16A(-06 + 19)	CUA GAU CCG CUU UUA AAA CCU GUU A
79	H16A(+87 + 109)	CCG UCU UCU GGG UCA CUG ACU UA
80	H16A(-07 + 19)	CUA GAU CCG CUU UUA AAA CCU GUU AA
81	H16A(-07 + 13)	CCG CUU UUA AAA CCU GUU AA
82	H16A(+12 + 37)	UGG AUU GCU UUU UCU UUU CUA GAU CC
83	H16A(+92 + 116)	CAU GCU UCC GUC UUC UGG GUC ACU G
84	H16A(+45 + 67)	G AUC UUG UUU GAG UGA AUA CAG U
85	H16A(+105 + 126)	GUU AUC CAG CCA UGC UUC CGU C
86	H16D(+05 - 20)	UGA UAA UUG GUA UCA CUA ACC UGU G
87	H16D(+12 - 11)	GUA UCA CUA ACC UGU GCU GUA C
88	H19A(+35 + 53)	CUG CUG GCA UCU UGC AGU U
89	H19A(+35 + 65)	GCC UGA GCU GAU CUG CUG GCA UCU UGC AGU U
90	H20A(+44 + 71)	CUG GCA GAA UUC GAU CCA CCG GCU GUU C
91	H20A(+147 + 168)	CAG CAG UAG UUG UCA UCU GCU C
92	H20A(+185 + 203)	UGA UGG GGU GGU GGG UUG G
93	H20A(-08 + 17)	AUC UGC AUU AAC ACC CUC UAG AAA GAA G
94	H20A(+30 + 53)	CCG GCU GUU CAG UUG UUC UGA GGC
95	H20A(-11 + 17)	AUC UGC AUU AAC ACC CUC UAG AAA GAA A
96	H20D(+08 - 20)	GAA GGA GAA GAG AUU CUU ACC UUA CAA A
97	H20A(+44 + 63)	AUU CGA UCC ACC GGC UGU UC
98	H20A(+149 + 168)	CAG CAG UAG UUG UCA UCU GC
99	H21A(-06 + 16)	GCC GGU UGA CUU CAU CCU GUG C
100	H21A(+85 + 106)	CUG CAU CCA GGA ACA UGG GUC C
101	H21A(+85 + 108)	GUC UGC AUC CAG GAA CAU GGG UC
102	H21A(+08 + 31)	GUU GAA GAU CUG AUA GCC GGU UGA
103	H21D(+18 - 07)	UAC UUA CUG UCU GUA GCU CUU UCU
104	H22A(+22 + 45)	CAC UCA UGG UCU CCU GAU AGC GCA
105	H22A(+125 + 146)	CUG CAA UUC CCC GAG UCU CUG C

TABLE 4-continued

106	H22A(+47 + 69)	ACU GCU GGA CCC AUG UCC UGA UG
107	H22A(+80 + 101)	CUA AGU UGA GGU AUG GAG AGU
108	H22D(+13 - 11)	UAU UCA CAG ACC UGC AAU UCC CC
109	H23A(+34 + 59)	ACA GUG GUG CUG AGA UAG UAU AGG CC
110	H23A(+18 + 39)	UAG GCC ACU UUG UUG CUC UUG C
111	H23A(+72 + 90)	UUC AGA GGG CGC UUU CUU C
112	H24A(+48 + 70)	GGG CAG GCC AUU CCU CCU UCA GA
113	H24A(-02 + 22)	UCU UCA GGG UUU GUA UGU GAU UCU
114	H25A(+9 + 36)	CUG GGC UGA AUU GUC UGA AUA UCA CUG
115	H25A(+131 + 156)	CUG UUG GCA CAU GUG AUC CCA CUG AG
116	H25D(+16 - 08)	GUC UAU ACC UGU UGG CAC AUG UGA
117	H26A(+132 + 156)	UGC UUU CUG UAA UUC AUC UGG AGU U
118	H26A(-07 + 19)	CCU CCU UUC UGG CAU AGA GCC UCC AC
119	H26A(+68 + 92)	UGU GUC AUC CAU UCG UGC AUC UCU G
120	H27A(+82 + 106)	UUA AGG CCU CUU GUG CUA CAG GUG G
121	H27A(-4 + 19)	GGG GCU CUU CUU UAG CUC UCU GA
122	H27D(+19 - 03)	GAC UUC CAA AGU CUU GCA UUU C
123	H28A(-05 + 19)	GCC AAC AUG CCC AAA CUU CCU AAG
124	H28A(+99 + 124)	CAG AGA UUU CCU CAG CUC CGC CAG GA
125	H28D(+16 - 05)	CUU ACA UCU AGC ACC UCA GAG
126	H29A(+57 + 81)	UCC GCC AUC UGU UAG GGU CUG UGC C
127	H29A(+18 + 42)	AUU UGG GUU AUC CUC UGA AUG UCG C
128	H29D(+17 - 05)	CAU ACC UCU UCA UGU AGU UCC C
129	H30A(+122 + 147)	CAU UUG AGC UGC GUC CAC CUU GUC UG
130	H30A(+25 + 50)	UCC UGG GCA GAC UGG AUG CUC UGU UC
131	H30D(+19 - 04)	UUG CCU GGG CUU CCU GAG GCA UU
132	H31D(+06 - 18)	UUC UGA AAU AAC AUA UAC CUG UGC
133	H31D(+03 - 22)	UAG UUU CUG AAA UAA CAU AUA CCU G
134	H31A(+05 + 25)	GAC UUG UCA AAU CAG AUU GGA
135	H31D(+04 - 20)	GUU UCU GAA AUA ACA UAU ACC UGU
136	H32D(+04 - 16)	CAC CAG AAA UAC AUA CCA CA
137	H32A(+151 + 170)	CAA UGA UUU AGC UGU GAC UG
138	H32A(+10 + 32)	CGA AAC UUC AUG GAG ACA UCU UG
139	H32A(+49 + 73)	CUU GUA GAC GCU GCU CAA AAU UGG C
140	H33D(+09 - 11)	CAU GCA CAC ACC UUU GCU CC
141	H33A(+53 + 76)	UCU GUA CAA UCU GAC GUC CAG UCU
142	H33A(+30 + 56)	GUC UUU AUC ACC AAU UCC ACU UCA GAC
143	H33A(+64 + 88)	CCG UCU GCU UUU UCU GUA CAA UCU G
144	H34A(+83 + 104)	UCC AUA UCU GUA GCU GCC AGC C
145	H34A(+143 + 165)	CCA GGC AAC UUC AGA AUC CAA AU
146	H34A(-20 + 10)	UUU CUG UUA CCU GAA AAG AAU UAU AAU GAA
147	H34A(+46 + 70)	CAU UCA UUU CCU UUC GCA UCU UAC G
148	H34A(+95 + 120)	UGA UCU CUU UGU CAA UUC CAU AUC UG
149	H34D(+10 - 20)	UUC AGU GAU AAU GGU UUU ACC UUU CCC CAG
150	H34A(+72 + 96)	CUG UAG CUG CCA GCC AAU CUG UCA AG
151	H35A(+141 + 161)	UCU UCU GCU CGG GAG GUG ACA
152	H35A(+116 + 135)	CCA GUU ACU AAU CAG AAG AC
153	H35A(+24 + 43)	UCU UCA GGU GCA CCU UCU GU
154	H36A(+26 + 50)	UGU GAU GUG GUC CAC AAU CUG GUC A
155	H36A(-02 + 18)	CCA UGU GUU UCU GGU AAU CC
156	H37A(+26 + 50)	CGU GUA GAG UCC ACC UUU GGG CGU A
157	H37A(+82 + 105)	UAC UAA UUU CCU GCA GUG GUC ACC
158	H37A(+134 + 157)	UUC UGU GUG AAA UGG CUG CAA AUC
159	H38A(-01 + 19)	CCU UCA AAG GAA UGG AGG CC
160	H38A(+59 + 83)	UGC UGA AAU UCA GCC UCC AGU GGU U
161	H38A(+88 + 112)	UGA AGU CUU CCU CUU UCA GAU UCA C
162	H39A(+62 + 85)	CUG GCU UUC UCU CAU CUG UGA UUC
163	H39A(+39 + 58)	GUU GUA AGU UGU CUC CUC UU
164	H39A(+102 + 121)	UUG UCU GUA ACA GCU GCU GU
165	H39D(+10 - 10)	GCU CUA AUA CCU UGA GAG CA
166	H40A(-05 + 17)	CUU UGA GAC CUC AAA UCC UGU U
167	H40A(+129 + 153)	CUU UAU UUU CCU UUC AUC UCU GGG C
168	H42A(-04 + 23)	AUC GUU UCU UCA CGG ACA GUG UGC UGG
169	H42A(+86 + 109)	GGG CUU GUG AGA CAU GAG UGA UUU
170	H42D(+19 - 02)	A CCU UCA GAG GAC UCC UCU UGC
171	H43D(+10-15)	UAU GUG UUA CCU ACC CUU GUC GGU C
172	H43A(+101 + 120)	GGA GAG AGC UUC CUG UAG CU
173	H43A(+78 + 100)	UCA CCC UUU CCA CAG CGC UUG CA
174	H44A(+85 + 104)	UUU GUG UCU UUC UGA GAA AC
175	H44D(+10 - 10)	AAA GAC UUA CCU UAA GAU AC
176	H44A(-06 + 14)	AUC UGU CAA AUC GCC UGC AG
177	H46D(+16 - 04)	UUA CCU UGA CUU GCU CAA GC
178	H46A(+90 + 109)	UCC AGG UUC AAG UGG GAU AC
179	H47A(+76 + 100)	GCU CUU CUG GGC UUA UGG GAG CAC U
180	H47D(+25 - 02)	ACC UUU AUC CAC UGG AGA UUU GUC UGC
181	H47A(-9 + 12)	UUC CAC CAG UAA CUG AAA CAG
182	H50A(+02 + 30)	CCA CUC AGA GCU CAG AUC UUC UAA CUU CC

TABLE 4-continued

183	H50A(+07 + 33)	CUU CCA CUC AGA GCU CAG AUC UUC UAA
184	H51A(-01 + 25)	ACC AGA GUA ACA GUC UGA GUA GGA GC
185	H51D(+16 - 07)	CUC AUA CCU UCU GCU UGA UGA UC
186	H51A(+111 + 134)	UUC UGU CCA AGC CCG GUU GAA AUC
187	H51A(+66 + 95)	CUC CAA CAU CAA GGA AGA UGG CAU UUC UAG
188	H51D(+08 - 17)	AUC AUU UUU UCU CAU ACC UUC UGC U
189	H51A/D(+08 - 17) & (-15 +)	AUC AUU UUU UCU CAU ACC UUC UGC UAG GAG CUA AAA
190	H51A(+175 + 195)	CAC CCA CCA UCA CCC UCU GUG
191	H51A(+199 + 220)	AUC AUC UCG UUG AUU UCC UCA A
192	H52A(-07 + 14)	UCC UGC AUU GUU GCC UGU AAG
193	H52A(+12 + 41)	UCC AAC UGG GGA CGC CUC UGU UCC AAA UCC
194	H52A(+17 + 37)	ACU GGG GAC GCC UCU GUU CCA
195	H52A(+93 + 112)	CCG UAA UGA UUG UUC UAG CC
196	H52D(+05 - 15)	UGU UAA AAA ACU UAC UUC GA
197	H53A(+45 + 69)	CAU UCA ACU GUU GCC UCC GGU UCU G
198	H53A(+39 + 62)	CUG UUG CCU CCG GUU CUG AAG GUG
199	H53A(+39 + 69)	CAU UCA ACU GUU GCC UCC GGU UCU GAA GGU G
200	H53D(+14 - 07)	UAC UAA CCU UGG UUU CUG UGA
201	H53A(+23 + 47)	CUG AAG GUG UUC UUG UAC UUC AUC C
202	H53A(+150 + 176)	UGU AUA GGG ACC CUC CUU CCA UGA CUC
203	H53D(+20 - 05)	CUA ACC UUG GUU UCU GUG AUU UUC U
204	H53D(+09 - 18)	GGU AUC UUU GAU ACU AAC CUU GGU UUC
205	H53A(-12 + 10)	AUU CUU UCA ACU AGA AUU AAA G
206	H53A(-07 + 18)	GAU UCU GAA UUC UUU CAA CUA GAA U
207	H53A(+07 + 26)	AUC CCA CUG AUU CUG AAU UC
208	H53A(+124 + 145)	UUG GCU CUG GCC UGU CCU AAG A
209	H46A(+86 + 115)	CUC UUU UCC AGG UUC AAG UGG GAU ACU AGC
210	H46A(+107 + 137)	CAA GCU UUU CUU UUA GUU GCU CUU UUC C
211	H46A(-10 + 20)	UAU UCU UUU GUU CUU CUA GCC UGG AGA AAG
212	H46A(+50 + 77)	CUG CUU CCU CCA ACC AUA AAA CAA AUU C
213	H45A(-06 + 20)	CCA AUG CCA UCC UGG AGU UCC UGU AA
214	H45A(+91 + 110)	UCC UGU AGA AUU CUG GCA UC
215	H45A(+125 + 151)	UGC AGA CCU CCU GCC ACC GCA GAU UCA
216	H45D(+16 - 04)	CUA CCU CUU UUU UCU GUC UG
217	H45A(+71 + 90)	UGU UUU UGA GGA UUG CUG AA

Description	Sequence	SEQ ID NO
H53A(+33 + 60)	GTTGCCTCCGGTTCTGAAGGTGTTCTTG	218
H53A(+23 + 47)	CTGAAGGTGTTCTGTACTTCATCC	219
H53A(+33 + 62)	CTGTTGCCTCCGGTTCTGAAGGTGTTCTTG	220
H53A(+33 + 65)	CAACTGTTGCCTCCGGTTCTGAAGGTGTTCTTG	221
H53A(+31 + 55)	CTCCGGTTCTGAAGGTGTTCTTGTA	222
H53A(+46 + 73)	ATTTCATTCAACTGTTGCCTCCGGTTCT	223
H53A(+22 + 46)	TGAAGGTGTTCTGTACTTCATCCC	224
H53A(+46 + 69)	CATTCAACTGTTGCCTCCGGTTCT	225
H53A(+40 + 61)	TGTTGCCTCCGGTTCTGAAGGT	226
H53A(+30 + 60)	GTTGCCTCCGGTTCTGAAGGTGTT	227
H53A(+30 + 57)	GCCTCCGGTTCTGAAGGTGTTCTGTAC	228
H53A(+30 + 56)	CCTCCGGTTCTGAAGGTGTTCTGTAC	229
H53A(+30 + 55)	CTCCGGTTCTGAAGGTGTTCTGTAC	230
H53A(+33 + 57)	GCCTCCGGTTCTGAAGGTGTTCTTG	231
H44A(-07 + 17)	CAGATCTGTCAAATCGCCTGCAGG	232
H44A(-07 + 20)	CAACAGATCTGTCAAATCGCCTGCAGG	233
H44A(-07 + 22)	CTAACAGATCTGTCAAATCGCCTGCAGG	234
H44A(+77 + 101)	GTGTCTTCTGAGAAACTGTTCAAC	235
H44A(+64 + 91)	GAGAAACTGTTCAAGCTTCTGTTAGCCAC	236
H44A(+62 + 89)	GAAACTGTTCAAGCTTCTGTTAGCCACTG	237
H44A(+62 + 85)	CTGTTCAAGCTTCTGTTAGCCACTG	238
H44A(-06 + 14)	ATCTGTCAAATCGCCTGCAG	239
H44A(+85 + 104)	TTTGTGTCCTTCTGAGAAC	240
H44A(+61 + 84)	TGTTCAAGCTTCTGTTAGCCACTG	241
H44A(-10 + 15)	GATCTGTCAAATCGCCTGCAGGTAA	242
H44A(+64 + 88)	AAACTGTTCAAGCTTCTGTTAGCCAC	243
H44A(+79 + 103)	TTGTTCTTCTGAGAAACTGTTCA	244
H44A(-06 + 20)	CAACAGATCTGTCAAATCGCCTGCAG	245

TABLE 4-continued

Name	Sequences	SEQ ID NO.
Oligomer Targeting Sequences (5' to 3'):		
Hu. DMD . Exon44 . 25 . 001	CTGCAGGTAAAAGCATATGGATCAA	250
Hu. DMD . Exon44 . 25 . 002	ATGCCCTGCAGGTAAAAGCATATGG	251
Hu. DMD . Exon44 . 25 . 003	GTCAAATGCCCTGCAGGTAAAAGCA	252
Hu. DMD . Exon44 . 25 . 005	CAACAGATCTGTCAAATGCCCTGCA	253
Hu. DMD . Exon44 . 25 . 006	TTTCTCAACAGATCTGTCAAATCGC	254
Hu. DMD . Exon44 . 25 . 007	CCATTCTCAACAGATCTGTCAAAT	255
Hu. DMD . Exon44 . 25 . 008	ATAATGAAAACGCCGCCATTCTCA	256
Hu. DMD . Exon44 . 25 . 009	AAATATCTTATATCATAATGAAAAA	257
Hu. DMD . Exon44 . 25 . 010	TGTTAGCCACTGATTAATATCTTT	258
Hu. DMD . Exon44 . 25 . 013	CCAATTCTCAGGAATTGTGTCCTT	259
Hu. DMD . Exon44 . 25 . 014	GTATTTAGCATGTTCCAATTCTCA	260
Hu. DMD . Exon44 . 25 . 015	CTTAAGATACCATTTGATTTAGCA	261
Hu. DMD . Exon44 . 25 . 016	CTTACCTTAAGATACCAATTGATT	262
Hu. DMD . Exon44 . 25 . 017	AAAGACTTACCTTAAGATACCAATT	263
Hu. DMD . Exon44 . 25 . 018	AAATCAAAGACTTACCTTAAGATAC	264
Hu. DMD . Exon44 . 25 . 019	AAAACAAATCAAAGACTTACCTTAA	265
Hu. DMD . Exon44 . 25 . 020	TCGAAAAAAACAAATCAAAGACTTAC	266
Hu. DMD . Exon45 . 25 . 001	CTGTAAGATACCAAAAGCCAAAAC	267
Hu. DMD . Exon45 . 25 . 002	CCTGTAAGATAACCAAAAGGCAAA	268
Hu. DMD . Exon45 . 25 . 002 . 2	AGTCCTGTAAGATACCAAAAGGC	269
Hu. DMD . Exon45 . 25 . 003	GAGTCCCTGTAAGATAACCAAAAGG	270
Hu. DMD . Exon45 . 25 . 003 . 2	CCTGAGTTCTGTAAGATACCAAA	271
Hu. DMD . Exon45 . 25 . 004	TCCTGGAGTTCTGTAAGATACCAAA	272
Hu. DMD . Exon45 . 25 . 004 . 2	GCCATCCTGGAGTCCCTGTAAGATA	273
Hu. DMD . Exon45 . 25 . 005	TGCCATCCTGGAGTCCCTGTAAGAT	274
Hu. DMD . Exon45 . 25 . 005 . 2	CCAATGCCATCCTGGAGTCCCTGTA	275
Hu. DMD . Exon45 . 25 . 006	CCAATGCCATCCTGGAGTCCCTGTA	276
Hu. DMD . Exon45 . 25 . 006 . 2	GCTGCCAATGCCATCCTGGAGTTC	277
Hu. DMD . Exon45 . 25 . 007	CGCTGCCAATGCCATCCTGGAGTT	278
Hu. DMD . Exon45 . 25 . 008	AACAGTTGCCGCTGCCAATGCCA	279
Hu. DMD . Exon45 . 25 . 008 . 2	CTGACAACTGTTGCCGCTGCCAA	280
Hu. DMD . Exon45 . 25 . 009	GTTGCATTCAATGTTCTGACAAACAG	281
Hu. DMD . Exon45 . 25 . 010	GCTGAATTATTCTTCCCCAGTTG	282
Hu. DMD . Exon45 . 25 . 010 . 2	ATTATTCCTCCCCAGTTGATTC	283
Hu. DMD . Exon45 . 25 . 011	GGCATCTGTTTGAGGATTGCTGA	284
Hu. DMD . Exon45 . 25 . 011 . 2	TTTGAGGATTGCTGAATTATTCTT	285
Hu. DMD . Exon45 . 25 . 012	AAATTTTCTGTAAGATACTGGCAT	286
Hu. DMD . Exon45 . 25 . 012 . 2	ATACTGGCATCTGTTTGAGGATT	287
Hu. DMD . Exon45 . 25 . 013	ACCGCAGATTCAAGGCTTCCCAATT	288
Hu. DMD . Exon45 . 25 . 014	CTGTTGCAAGACCTCCGCCACCGC	289
Hu. DMD . Exon45 . 25 . 014 . 2	AGATTCAAGCTTCCCAATTCTTCT	290
Hu. DMD . Exon45 . 25 . 015	CTCTTTTTCTGCTGACAGCTGTT	291
Hu. DMD . Exon45 . 25 . 015 . 2	ACCTCCCTGCCACCCAGATTCAAGC	292
Hu. DMD . Exon45 . 25 . 016	CCTACCTTTTCTGCTGACAG	293
Hu. DMD . Exon45 . 25 . 016 . 2	GACAGCTTTGCAAGACCTCCGCC	294
Hu. DMD . Exon45 . 25 . 017	GTCGCCCTACCTCTTTCTGCT	295
Hu. DMD . Exon45 . 25 . 018	GATCTGTCGCCCTACCTCTTTTC	296
Hu. DMD . Exon45 . 25 . 019	TATTAGATCTGTCGCCCTACCTTT	297
Hu. DMD . Exon45 . 25 . 020	ATTCTCATATTAGATCTGTCGCCCTAC	298
Hu. DMD . Exon45 . 20 . 001	AGATAACCAAAAGGCAAAAC	299
Hu. DMD . Exon45 . 20 . 002	AAAGATAACCAAAAGGCAAAA	300
Hu. DMD . Exon45 . 20 . 003	CCTGTAAGATAACCAAAAGG	301
Hu. DMD . Exon45 . 20 . 004	GAGTTCCCTGTAAGATAACCAA	302
Hu. DMD . Exon45 . 20 . 005	TCTGGAGTTCCCTGTAAGAT	303
Hu. DMD . Exon45 . 20 . 006	TGCCATCCTGGAGTCCCTGT	304
Hu. DMD . Exon45 . 20 . 007	CCCAATGCCATCCTGGAGTT	305
Hu. DMD . Exon45 . 20 . 008	CGCTGCCAATGCCATCCTG	306
Hu. DMD . Exon45 . 20 . 009	CTGACAAACAGTTGCCGCTG	307
Hu. DMD . Exon45 . 20 . 010	GTTCGATTCAATGTTCTGAC	308
Hu. DMD . Exon45 . 20 . 011	ATTATTCCTCCCCAGTTG	309
Hu. DMD . Exon45 . 20 . 012	TTTGAGGATTGCTGAATTAT	310
Hu. DMD . Exon45 . 20 . 013	ATACTGGCATCTGTTTGA	311
Hu. DMD . Exon45 . 20 . 014	AAATTTTCTGTAAGATACT	312
Hu. DMD . Exon45 . 20 . 015	AGATTCAAGCTTCCCAATT	313
Hu. DMD . Exon45 . 20 . 016	ACCTCCCTGCCACCCAGATT	314
Hu. DMD . Exon45 . 20 . 017	GACAGCTTTGCAAGACCTC	315
Hu. DMD . Exon45 . 20 . 018	CTCTTTTCTGCTGACAG	316
Hu. DMD . Exon45 . 20 . 019	CCTACCTTTTCTGCT	317

TABLE 4-continued

Hu. DMD. Exon45. 20. 020	GTGCCCTACCTTTTTTC	318
Hu. DMD. Exon45. 20. 021	GATCTGTCGCCCTACCTCTT	319
Hu. DMD. Exon45. 20. 022	TATTCAGATCTGTCGCCCTAC	320
Hu. DMD. Exon45. 20. 023	ATTCTTATTAGATCTGTCGC	321
Hu. DMD. Exon46. 25. 001	GGGGGATT'TGAGAAAATAAAATTAC	322
Hu. DMD. Exon46. 25. 002	ATTTGAGAAAATAAAATTACCTTGA	323
Hu. DMD. Exon46. 25. 002.2	CTAGCCTGGAGAAGAAGAATAAAA	324
Hu. DMD. Exon46. 25. 003	AGAAAATAAAATTACCTTGACTTGC	325
Hu. DMD. Exon46. 25. 003.2	TTCTTCTAGCCTGGAGAAGAAGA	326
Hu. DMD. Exon46. 25. 004	ATAAAATTACCTTGACTTGCTCAAG	327
Hu. DMD. Exon46. 25. 004.2	TTTTGTTCTTCTAGCCTGGAGAAG	328
Hu. DMD. Exon46. 25. 005	ATTACCTTGACTTGCTCAAGCTTT	329
Hu. DMD. Exon46. 25. 005.2	TATTCCTTTGTTCTTCTAGCCTGGA	330
Hu. DMD. Exon46. 25. 006	CTTGACTTGCTCAAGCTTTCTTT	331
Hu. DMD. Exon46. 25. 006.2	CAAGATATTCTTTGTTCTTCTAGC	332
Hu. DMD. Exon46. 25. 007	CTTTAGTTGCTGCTCTTCCAGG	333
Hu. DMD. Exon46. 25. 008	CCAGGTTCAAGTGGATACTAGCAA	334
Hu. DMD. Exon46. 25. 008.2	ATCTCTTGAAATTCTGACAAGATA	335
Hu. DMD. Exon46. 25. 009	AGCAATGTATCTGCTTCTCCAAC	336
Hu. DMD. Exon46. 25. 009.2	AACAAATTCTTAAATCTTTGA	337
Hu. DMD. Exon46. 25. 010	CCAACCATAAAACAAATTCTATTAA	338
Hu. DMD. Exon46. 25. 010.2	TTCTTCAACCATAAAACAAATTCA	339
Hu. DMD. Exon46. 25. 011	TTAAATCTTTGAAATTCTGACA	340
Hu. DMD. Exon46. 25. 012	TGACAAGATATTCTTTGTTCTCT	341
Hu. DMD. Exon46. 25. 012.2	TTCAAGTGGATACTAGCAATGTTA	342
Hu. DMD. Exon46. 25. 013	AGATATTCTTTGTTCTCTAGCCT	343
Hu. DMD. Exon46. 25. 013.2	CTGCTCTTCCAGGTTCAAGTGGG	344
Hu. DMD. Exon46. 25. 014	TTCTTTGTTCTTAGCTGGAGA	345
Hu. DMD. Exon46. 25. 014.2	CTTTCTTTAGTTGCTGCTCTTT	346
Hu. DMD. Exon46. 25. 015	TTGTTCTCTAGCCTGGAGAAGAA	347
Hu. DMD. Exon46. 25. 016	CTCTAGCCTGGAGAAGAAGAATA	348
Hu. DMD. Exon46. 25. 017	AGCCTGGAGAAGAAGAATAAAATT	349
Hu. DMD. Exon46. 25. 018	CTGGAGAAGAAGAATAAAATTGTT	350
Hu. DMD. Exon46. 20. 001	GAAGAAGAATAAAATTGTT	351
Hu. DMD. Exon46. 20. 002	GGAGAAAGAAGAATAAAATT	352
Hu. DMD. Exon46. 20. 003	AGCCTGGAGAAGAAGAATA	353
Hu. DMD. Exon46. 20. 004	CTTCTAGCCTGGAGAAGAA	354
Hu. DMD. Exon46. 20. 005	TTGTTCTCTAGCCTGGAGA	355
Hu. DMD. Exon46. 20. 006	TTCTTTGTTCTCTAGCCT	356
Hu. DMD. Exon46. 20. 007	TGACAAGATATTCTTTGTT	357
Hu. DMD. Exon46. 20. 008	ATCTCTTGAAATTCTGACA	358
Hu. DMD. Exon46. 20. 009	AACAAATTCTTAAATCTC	359
Hu. DMD. Exon46. 20. 010	TTCTTCAACCATAAAACAA	360
Hu. DMD. Exon46. 20. 011	AGCAATGTATCTGCTTCT	361
Hu. DMD. Exon46. 20. 012	TTCAAGTGGATACTAGCAA	362
Hu. DMD. Exon46. 20. 013	CTGCTCTTCCAGGTTCAA	363
Hu. DMD. Exon46. 20. 014	CTTTCTTTAGTTGCTGCT	364
Hu. DMD. Exon46. 20. 015	CTTGACTTGCTCAAGCTTT	365
Hu. DMD. Exon46. 20. 016	ATTACCTTGACTTGCTCAAG	366
Hu. DMD. Exon46. 20. 017	ATAAAATTACCTTGACTTGC	367
Hu. DMD. Exon46. 20. 018	AGAAAATAAAATTACCTTGA	368
Hu. DMD. Exon46. 20. 019	ATTTGAGAAAATAAAATTAC	369
Hu. DMD. Exon46. 20. 020	GGGGGATT'TGAGAAAATAAA	370
Hu. DMD. Exon47. 25. 001	CTGAAACAGACAATGCAACAACT	371
Hu. DMD. Exon47. 25. 002	AGTAACTGAAACAGACAAATGCAAC	372
Hu. DMD. Exon47. 25. 003	CCACCAGTAACGAAACAGACAAAT	373
Hu. DMD. Exon47. 25. 004	CTCTTCCACCAGTAACGAAACAGA	374
Hu. DMD. Exon47. 25. 005	GGCAACTCTTCCACCAGTAACGAA	375
Hu. DMD. Exon47. 25. 006	GCAGGGGCAACTCTTCCACCAGTAA	376
Hu. DMD. Exon47. 25. 007	CTGGCGAGGGGCAACTCTTCCACC	377
Hu. DMD. Exon47. 25. 008	TTTAAATTGTTGAGAATTCCCTGGC	378
Hu. DMD. Exon47. 25. 008.2	TTGTTTGAGAATTCCCTGGCGCAGG	379
Hu. DMD. Exon47. 25. 009	GCACGGGGCCTCCAGTTTCAATTAA	380
Hu. DMD. Exon47. 25. 009.2	TCCAGTTTCAATTAAATTGTTGAGA	381
Hu. DMD. Exon47. 25. 010	GCTTATGGGAGCACTTACAAGCACG	382
Hu. DMD. Exon47. 25. 010.2	TACAAGCACGGGTCTCCAGTTCA	383
Hu. DMD. Exon47. 25. 011	AGTTTATCTTGCTCTTCTGGGCTTA	384
Hu. DMD. Exon47. 25. 012	TCTGCTTGAGCTTATTTCAGTTT	385
Hu. DMD. Exon47. 25. 012.2	ATCTTGCTCTCTGGGCTTATGGGA	386
Hu. DMD. Exon47. 25. 013	CTTTATCCACTGGAGATTGTC	387
Hu. DMD. Exon47. 25. 013.2	CTTATTTCAAGTTTATCTTGCTCT	388
Hu. DMD. Exon47. 25. 014	CTAACCTTATCCACTGGAGATTG	389
Hu. DMD. Exon47. 25. 014.2	ATTTGCTTGAGCTTATTTCAGTT	390
Hu. DMD. Exon47. 25. 015	AATGTCAACCTTATCCACTGGAG	391
Hu. DMD. Exon47. 25. 016	TGTTTAATGTCTAACCTTATCAC	392
Hu. DMD. Exon47. 25. 017	AGAGATGGTTAACGTTAACCTTA	393
Hu. DMD. Exon47. 25. 018	ACCGAAGAGATGGTTAACGTTAAC	394

TABLE 4-continued

Hu. DMD. Exon47. 20. 001	ACAGACAAATGCAACAAACGT	395
Hu. DMD. Exon47. 20. 002	CTGAAACAGACAAATGCAAC	396
Hu. DMD. Exon47. 20. 003	AGTAACGTAAACAGACAAAT	397
Hu. DMD. Exon47. 20. 004	CCACCAGTAACGTAAACAGA	398
Hu. DMD. Exon47. 20. 005	CTCTTCCACCGAGTAACGTAA	399
Hu. DMD. Exon47. 20. 006	GGCAACTTTCACCGAGTAAC	400
Hu. DMD. Exon47. 20. 007	CTGGCGCAGGGGCAACTCTT	401
Hu. DMD. Exon47. 20. 008	TTGTTTGAGAATTCCCTGGC	402
Hu. DMD. Exon47. 20. 009	TCCAGTTTCATTAAATTGTT	403
Hu. DMD. Exon47. 20. 010	TACAAGCAGGGGCTCCAG	404
Hu. DMD. Exon47. 20. 011	GCTTATGGGAGCACTTACAA	405
Hu. DMD. Exon47. 20. 012	ATCTTGCTCTCTGGGCTTA	406
Hu. DMD. Exon47. 20. 013	CTTATTTCAAGTTTATCTT	407
Hu. DMD. Exon47. 20. 014	ATTGTCCTGCTTGAGCTTAT	408
Hu. DMD. Exon47. 20. 015	CTTTATCCACTGGAGATTG	409
Hu. DMD. Exon47. 20. 016	CTAACCTTATCCACTGGAG	410
Hu. DMD. Exon47. 20. 017	AAATGCTAACCTTTATCCAC	411
Hu. DMD. Exon47. 20. 018	TGGTTAATGCTAACCTTTA	412
Hu. DMD. Exon47. 20. 019	AGAGATGGTTAATGCTAAC	413
Hu. DMD. Exon47. 20. 020	ACCGAAGAGATGGTTAATGT	414
Hu. DMD. Exon48. 25. 001	CTGAAAGGAAAATACATTTAAAAA	415
Hu. DMD. Exon48. 25. 002	CCTGAAAGGAAAATACATTTAAA	416
Hu. DMD. Exon48. 25. 002.2	GAACACTGAAAGGAAAATACATTT	417
Hu. DMD. Exon48. 25. 003	GGAAACCTGAAAGGAAAATACATTT	418
Hu. DMD. Exon48. 25. 003.2	CTCTGGAAACCTGAAAGGAAAATAC	419
Hu. DMD. Exon48. 25. 004	GCTCTGGAAACCTGAAAGGAAAATA	420
Hu. DMD. Exon48. 25. 004.2	TAAGCTCTGAAACCTGAAAGGAA	421
Hu. DMD. Exon48. 25. 005	GTAAGCTCTGAAACCTGAAAGGAA	422
Hu. DMD. Exon48. 25. 005.2	TCAGGTAAAGCTCTGAAACCTGAA	423
Hu. DMD. Exon48. 25. 006	CTCAGGTAAAGCTCTGAAACCTGAA	424
Hu. DMD. Exon48. 25. 006.2	GTTTCTCAGGTAAAGCTCTGAAAC	425
Hu. DMD. Exon48. 25. 007	TGTTTCTCAGGTAAAGCTCTGAAAA	426
Hu. DMD. Exon48. 25. 007.2	AATTCTCCTTGTTCAGGTAAA	427
Hu. DMD. Exon48. 25. 008	TTTGAGCTTCATTTCTCTTGT	428
Hu. DMD. Exon48. 25. 008	TTTATTGAGCTTCATTTCTCTT	429
Hu. DMD. Exon48. 25. 009	AACTGCCAAGGTCTTTTTTGA	430
Hu. DMD. Exon48. 25. 010	AGGTCTTCAGCTTTTTCAAGCT	431
Hu. DMD. Exon48. 25. 010.2	TTCAAGCTTTTCAGCTGCCCC	432
Hu. DMD. Exon48. 25. 011	GATGATTTAACGTCTTCAGGTC	433
Hu. DMD. Exon48. 25. 011.2	CTGCTCTTCAGGTCTTCAGGTT	434
Hu. DMD. Exon48. 25. 012	AGGAGATAACACAGCAGCAGATGA	435
Hu. DMD. Exon48. 25. 012.2	CACCGAGATGATTAACTGCTCTCA	436
Hu. DMD. Exon48. 25. 013	ATTCCAACGTCTTAATAGGAG	437
Hu. DMD. Exon48. 25. 014	CTTGGTTTGGTTGGTTATAAATTTC	438
Hu. DMD. Exon48. 25. 014.2	CAACTGATTCTAATAGGAGATAAC	439
Hu. DMD. Exon48. 25. 015	CTTAACGTCAAATGGCTCTCTTG	440
Hu. DMD. Exon48. 25. 015.2	TTGGTTATAAAATTCCAACGTATTC	441
Hu. DMD. Exon48. 25. 016	CCTACCTTAACGTCAAATGGCTT	442
Hu. DMD. Exon48. 25. 016.2	TCCTCTGGTTGGTTGGTTATAA	443
Hu. DMD. Exon48. 25. 017	AGTCCCTAACCTAACGTCAAATGG	444
Hu. DMD. Exon48. 25. 018	CAAAAAGTCCCTAACCTAACGTCA	445
Hu. DMD. Exon48. 25. 019	TAAGCAAAAGTCCCTACCTTAA	446
Hu. DMD. Exon48. 25. 020	ATATTTAAAGCAAAAGTCCCTAC	447
Hu. DMD. Exon48. 20. 001	AGGAAAATACATTTAAAAA	448
Hu. DMD. Exon48. 20. 002	AAGGAAAATACATTTAAAAA	449
Hu. DMD. Exon48. 20. 003	CCTGAAAGGAAAATACATTT	450
Hu. DMD. Exon48. 20. 004	GGAAACCTGAAAGGAAAATA	451
Hu. DMD. Exon48. 20. 005	GCTCTGGAAACCTGAAAGGAA	452
Hu. DMD. Exon48. 20. 006	GTAAGCTCTGAAACCTGAA	453
Hu. DMD. Exon48. 20. 007	CTCAGGTAAAGCTCTGAAA	454
Hu. DMD. Exon48. 20. 008	AATTCTCCTTGTTCAG	455
Hu. DMD. Exon48. 20. 009	TTTTATTGAGCTTCATTT	456
Hu. DMD. Exon48. 20. 010	AAGCTGCCAAGGTCTTTTA	457
Hu. DMD. Exon48. 20. 011	TTCAAGCTTTTCAGGT	458
Hu. DMD. Exon48. 20. 012	CTGCTCTTCAGGTCTCAA	459
Hu. DMD. Exon48. 20. 013	CACCGAGATGATTAACTGCT	460
Hu. DMD. Exon48. 20. 014	AGGAGATAACACAGCAGCA	461
Hu. DMD. Exon48. 20. 015	CAACTGATTCTAATAGGAG	462
Hu. DMD. Exon48. 20. 016	TTGGTTATAAAATTCCAAC	463
Hu. DMD. Exon48. 20. 017	TCCTCTGGTTGGTTGGT	464
Hu. DMD. Exon48. 20. 018	CTTAACGTCAAATGGCTT	465
Hu. DMD. Exon48. 20. 019	CCTACCTTAACGTCAAATGG	466
Hu. DMD. Exon48. 20. 020	AGTCCCTAACCTAACGTCA	467
Hu. DMD. Exon48. 20. 021	CAAAAAGTCCCTACCTTAA	468
Hu. DMD. Exon48. 20. 022	TAAGCAAAAGTCCCTAC	469
Hu. DMD. Exon48. 20. 023	ATATTTAAAGCAAAAGTTC	470
Hu. DMD. Exon49. 25. 001	CTGGGGAAAAGAACCCATATAGTGC	471

TABLE 4-continued

Hu. DMD. Exon49. 25. 002	TCCTGGGAAAAGAACCCATATAGT	472
Hu. DMD. Exon49. 25. 002. 2	GTTCCCTGGGAAAAGAACCCATAT	473
Hu. DMD. Exon49. 25. 003	CACTTCTGGGAAAAGAACCCAT	474
Hu. DMD. Exon49. 25. 003. 2	TTTCAGTTCTGGGAAAAGAAC	475
Hu. DMD. Exon49. 25. 004	TATTCAGTTCTGGGAAAAGAA	476
Hu. DMD. Exon49. 25. 004. 2	TGCTATTTCAGTTCTGGGAAA	477
Hu. DMD. Exon49. 25. 005	ACTGCTATTTCAGTTCTGGGAA	478
Hu. DMD. Exon49. 25. 005. 2	TGAAC TGCTATTTCAGTTCTGG	479
Hu. DMD. Exon49. 25. 006	CTTGAAC TGCTATTTCAGTTCTG	480
Hu. DMD. Exon49. 25. 006. 2	TAGCTTGAACTGCTATTTCAGTT	481
Hu. DMD. Exon49. 25. 007	TTAGCTTGAACTGCTATTTCAGTT	482
Hu. DMD. Exon49. 25. 008	TTCCACATCGGGTGTAGTTGA	483
Hu. DMD. Exon49. 25. 009	TGCCCTTTAGACAAAATCTTCCA	484
Hu. DMD. Exon49. 25. 009. 2	TTAGACAAAATCTTCCACATCC	485
Hu. DMD. Exon49. 25. 010	GTTTTCTTGACAAATGCTGCC	486
Hu. DMD. Exon49. 25. 010. 2	GTACAAATGCTGCCCTTAGACAA	487
Hu. DMD. Exon49. 25. 011	CTTCACTGGCTGAGTGGCTGGTT	488
Hu. DMD. Exon49. 25. 011. 2	GGCTGGTTTTCTTGACAAATGC	489
Hu. DMD. Exon49. 25. 012	ATTACCTTCACTGGCTGAGTGGCTG	490
Hu. DMD. Exon49. 25. 013	GCTTCATTACCTTCACTGGCTGAGT	491
Hu. DMD. Exon49. 25. 014	AGTTGCTTCATTACCTTCACTGGC	492
Hu. DMD. Exon49. 25. 015	GCTAGAGTTGCTTCATTACCTTCA	493
Hu. DMD. Exon49. 25. 016	ATATTGCTAGAGTTGCTTCATTAC	494
Hu. DMD. Exon49. 20. 001	GAAAAGAACCCATATAGTGC	495
Hu. DMD. Exon49. 20. 002	GGAAAAGAACCCATATAGT	496
Hu. DMD. Exon49. 20. 003	TCTGGGAAAAGAACCCAT	497
Hu. DMD. Exon49. 20. 004	CAGTTCTGGGAAAAGAA	498
Hu. DMD. Exon49. 20. 005	TATTCAGTTCTGGGAA	499
Hu. DMD. Exon49. 20. 006	ACTGCTATTTCAGTTCTG	500
Hu. DMD. Exon49. 20. 007	CTTGAAC TGCTATTTCAGTT	501
Hu. DMD. Exon49. 20. 008	TTAGCTTGAACTGCTATTTCAGTT	502
Hu. DMD. Exon49. 20. 009	TTCCACATCGGGTGTAGTTAG	503
Hu. DMD. Exon49. 20. 010	TTTAGACAAAATCTTCCA	504
Hu. DMD. Exon49. 20. 011	GTACAAATGCTGCCCTTAG	505
Hu. DMD. Exon49. 20. 012	GGCTGGTTTTCTTGACAAAT	506
Hu. DMD. Exon49. 20. 013	CTTCACTGGCTGAGTGGCTG	507
Hu. DMD. Exon49. 20. 014	ATTACCTTCACTGGCTGAGT	508
Hu. DMD. Exon49. 20. 015	GCTTCATTACCTTCACTGGC	509
Hu. DMD. Exon49. 20. 016	AGTTGCTTCATTACCTTCA	510
Hu. DMD. Exon49. 20. 017	GCTAGAGTTGCTTCATTAC	511
Hu. DMD. Exon49. 20. 018	ATATTGCTAGAGTTGCTTC	512
Hu. DMD. Exon50. 25. 001	CTTTAACAGAAAAGCATACACATTA	513
Hu. DMD. Exon50. 25. 002	TCTCTTTAACAGAAAAGCATAC	514
Hu. DMD. Exon50. 25. 002. 2	TTCTCTTTAACAGAAAAGCATACA	515
Hu. DMD. Exon50. 25. 003	TAACCTCCTCTAACAGAAAAGCA	516
Hu. DMD. Exon50. 25. 003. 2	CTAACCTCCTCTAACAGAAAAGC	517
Hu. DMD. Exon50. 25. 004	TCTCTAACCTCCTCTAACAGAA	518
Hu. DMD. Exon50. 25. 004. 2	ATCTTCTAACCTCCTCTAACAGA	519
Hu. DMD. Exon50. 25. 005	TCAGATCTCTAACCTCCTCTTAA	520
Hu. DMD. Exon50. 25. 005. 2	CTCAGATCTCTAACCTCCTCTTAA	521
Hu. DMD. Exon50. 25. 006	AGAGCTCAGATCTCTAACCTCCTC	522
Hu. DMD. Exon50. 25. 006. 2	CAGAGCTCAGATCTCTAACCTCCT	523
NG-08-0731		
Hu. DMD. Exon50. 25. 007	CACTCAGAGCTCAGATCTCTACT	524
Hu. DMD. Exon50. 25. 007. 2	CCTTCCACTCAGAGCTCAGATCTTC	525
Hu. DMD. Exon50. 25. 008	GTAACAGGTTACCGCCTTCCACTC	526
Hu. DMD. Exon50. 25. 009	CTTGCCCTCAGCTCTGAAGTAA	527
Hu. DMD. Exon50. 25. 009. 2	CCCTCAGCTCTGAAGTAAACGGTT	528
Hu. DMD. Exon50. 25. 010	CCAGGAGCTAGGTGAGGCTGTTG	529
Hu. DMD. Exon50. 25. 010. 2	GGTCAGGCTGCTTGCCCTCAGCTC	530
Hu. DMD. Exon50. 25. 011	AGGCTCAAATAGTGGTCAGTCCAGG	531
Hu. DMD. Exon50. 25. 011. 2	TCAGTCCAGGAGCTAGGTGAGGCTG	532
Hu. DMD. Exon50. 25. 012	CTTACAGGCTCAAATAGTGGTCAGT	533
AV1-5038		
Hu. DMD. Exon50. 25. 013	GTATACTTACAGGCTCCAATAGTGG	534
Hu. DMD. Exon50. 25. 014	ATCCAGTATACTTACAGGCTCCAAT	535
Hu. DMD. Exon50. 25. 015	ATGGGATCCAGTATACTTACAGGCT	536
NG-08-0741		
Hu. DMD. Exon50. 25. 016	AGAGAATGGGATCCAGTATACTTAC	537
NG-08-0742		
Hu. DMD. Exon50. 20. 001	ACAGAAAAGCATAACACATTA	538
Hu. DMD. Exon50. 20. 002	TTAACAGAAAAGCATAACAC	539
Hu. DMD. Exon50. 20. 003	TCCTCTTTAACAGAAAAGCA	540
Hu. DMD. Exon50. 20. 004	TAACCTCCTCTAACAGAA	541
Hu. DMD. Exon50. 20. 005	TCTCTAACCTCCTCTTAA	542
Hu. DMD. Exon50. 20. 006	TCAGATCTCTAACCTCCTC	543
Hu. DMD. Exon50. 20. 007	CCTTCCACTCAGAGCTCAGA	544

TABLE 4-continued

Hu. DMD. Exon50.20.008	GTAACCGTTTACCGCCTTC	545
Hu. DMD. Exon50.20.009	CCCTCAGCTTGAAGTAAA	546
Hu. DMD. Exon50.20.010	GGTCAGGCTGCTTGCCTC	547
Hu. DMD. Exon50.20.011	TCAGTCAGGAGCTAGGTCA	548
Hu. DMD. Exon50.20.012	AGCTCCAATAGTGGTCACT	549
Hu. DMD. Exon50.20.013	CTTACAGGCTCAATAGTGG	550
Hu. DMD. Exon50.20.014	GTATACTTACAGGCTCAAT	551
Hu. DMD. Exon50.20.015	ATCCAGTATACTTACAGGCT	552
Hu. DMD. Exon50.20.016	ATGGGATCCAGTATACTTAC	553
Hu. DMD. Exon50.20.017	AGAGAATGGGATCCAGTATA	554
Hu. DMD. Exon51.25.001-44	CTAAAAATTTGGGTTTTGCAAA	555
Hu. DMD. Exon51.25.002-45	GCTAAAATTTGGGTTTTGCAAA	556
Hu. DMD. Exon51.25.002.2-46	TAGGAGCTAAAATTTGGGTTTT	557
Hu. DMD. Exon51.25.003	AGTAGGAGCTAAAATTTGGGTT	558
Hu. DMD. Exon51.25.003.2	TGAGTAGGAGCTAAAATTTGGG	559
Hu. DMD. Exon51.25.004	CTGAGTAGGAGCTAAAATTTGGG	560
Hu. DMD. Exon51.25.004.2	CACTCTGAGTAGGAGCTAAAATTT	561
Hu. DMD. Exon51.25.005	ACAGTCTGAGTAGGAGCTAAAATTT	562
Hu. DMD. Exon51.25.005.2	GACTAACAGTCTGAGTAGGAGCTAAA	563
Hu. DMD. Exon51.25.006	CAGAGTAACAGTCTGAGTAGGAGCT	564
Hu. DMD. Exon51.25.006.2	CACCAAGACTAACAGTCTGAGTAGGAG	565
Hu. DMD. Exon51.25.007	GTCACCAAGAGTAACAGTCTGAGTAG	566
Hu. DMD. Exon51.25.007.2	AACCCACAGGTTGTCAACCAAGAGTAA	567
Hu. DMD. Exon51.25.008	GTTGTGTCAACCAAGAGTAACTGCTG	568
Hu. DMD. Exon51.25.009	TGCCAGTTCCCTAGTAACCAACAGT	569
Hu. DMD. Exon51.25.010	ATTCTAGTTGGAGATGGCAGTTTC	570
Hu. DMD. Exon51.25.010.2	GGAGATGGCATTCTAGTTGGAG	571
Hu. DMD. Exon51.25.011	CATCAAGGAAGATGGCATTCTAGTT	572
Hu. DMD. Exon51.25.011.2	GAGCAGGTACCTCAAACATCAAGGAA	573
Hu. DMD. Exon51.25.012	ATCTGCCAGAGCAGGTACCTCAAAC	574
Hu. DMD. Exon51.25.013	AAAGTCTGTCCAAGCCCCGTTGAAAT	575
Hu. DMD. Exon51.25.013.2	CGGTTGAAATCTGCCAGAGCAGGTAC	576
Hu. DMD. Exon51.25.014	GAGAAAGCCAGTCGGTAAGTTCTGTC	577
Hu. DMD. Exon51.25.014.2	GTCGGTAAGTTCTGCCAAGCCCCG	578
Hu. DMD. Exon51.25.015	ATAACTTGATCAAGCAGAGAAAGCCA	579
Hu. DMD. Exon51.25.015.2	AACCGAGAAAAGCCAGTCGGTAAGT	580
Hu. DMD. Exon51.25.016	CACCCCTCTGTGATTTATAACTTGAT	581
Hu. DMD. Exon51.25.017	CAAGGTACCCACCATCACCTCTGT	582
Hu. DMD. Exon51.25.017.2	CATCACCCCTGTGATTTATAACT	583
Hu. DMD. Exon51.25.018	CTTCTGCTTGATGATCATCTGTTGA	584
Hu. DMD. Exon51.25.019	CCTCTGCTTGATGATCATCTGTTG	585
Hu. DMD. Exon51.25.019.2	ATCTCGTTGATATCTCAAGGTACCC	586
Hu. DMD. Exon51.25.020	TCATACTCTGCTTGATCATCT	587
Hu. DMD. Exon51.25.020.2	TCATTTTTCTCATACCTCTGCTTG	588
Hu. DMD. Exon51.25.021	TTTCTCATACCTCTGCTTGATGAT	589
Hu. DMD. Exon51.25.022	TTTATCATTTTCTCATACCTCT	590
Hu. DMD. Exon51.25.023	CCAACTTTATCATTTTCTCATAC	591
Hu. DMD. Exon51.20.001	ATATTTGGGTTTTGCAAA	592
Hu. DMD. Exon51.20.002	AAAATTTGGGTTTTG	593
Hu. DMD. Exon51.20.003	GACCTAAAATTTGGGTT	594
Hu. DMD. Exon51.20.004	AGTAGGAGCTAAAATTT	595
Hu. DMD. Exon51.20.005	GTCTGAGTAGGAGCTAAAAT	596
Hu. DMD. Exon51.20.006	TAACAGTCTGAGTAGGAGCT	597
Hu. DMD. Exon51.20.007	CAAGTAACAGTCTGAGTAG	598
Hu. DMD. Exon51.20.008	CACAGGTTGTCAACCAAGAG	599
Hu. DMD. Exon51.20.009	AGTTCCCTAGTAACCAAG	600
Hu. DMD. Exon51.20.010	TAGTTGGAGATGGCAGTT	601
Hu. DMD. Exon51.20.011	GGAGATGGCATTCTAGTT	602
Hu. DMD. Exon51.20.012	TACCTCAAACATCAAGGAAG	603
Hu. DMD. Exon51.20.013	ATCTGCCAGAGCAGGTACCT	604
Hu. DMD. Exon51.20.014	CCAAGCCGGTTGAAATCTG	605
Hu. DMD. Exon51.20.015	GTCGGTAAGTTCTGCCAAG	606
Hu. DMD. Exon51.20.016	AAGCAGAGAAAAGCCAGTCGG	607
Hu. DMD. Exon51.20.017	TTTTATAACTTGATCAAGCA	608
Hu. DMD. Exon51.20.018	CATCACCCCTGTGATTTA	609
Hu. DMD. Exon51.20.019	CTCAAGGTACCCACCATCA	610
Hu. DMD. Exon51.20.020	CATCTCGTTGATATCCTCAA	611
Hu. DMD. Exon51.20.021	CTTCTGCTTGATGATCATCT	612
Hu. DMD. Exon51.20.022	CATACCTCTGCTTGATGAT	613
Hu. DMD. Exon51.20.023	TTTCTCATACCTCTGCTG	614
Hu. DMD. Exon51.20.024	CATTTTTCTCATACCTCT	615
Hu. DMD. Exon51.20.025	TTTATCATTTTCTCATAC	616
Hu. DMD. Exon51.20.026	CAACTTTATCATTTTCT	617
Hu. DMD. Exon52.25.001	CTGTAAGAACAAATATCCCTAGTA	618
Hu. DMD. Exon52.25.002	TGCTGTAAGAACAAATATCCCTA	619
Hu. DMD. Exon52.25.002.2	GTTGCCTGTAAGAACAAATATCCCT	620
Hu. DMD. Exon52.25.003	ATTGTTGCCTGTAAGAACAAATATC	621

TABLE 4-continued

Hu. DMD. Exon52. 25. 003. 2	GCATTGTTGCCCTTAAGAACAAATA	622
Hu. DMD. Exon52. 25. 004	CCTGCATTGTTGCCCTGAAGAACAA	623
Hu. DMD. Exon52. 25. 004. 2	ATCCCTGCATTGTTGCCCTGAAGAAC	624
Hu. DMD. Exon52. 25. 005	CAAATCCTGCATTGTTGCCCTGAAG	625
Hu. DMD. Exon52. 25. 005. 2	TCCAATCCTGCATTGTTGCCCTGA	626
Hu. DMD. Exon52. 25. 006	TGTTCCAATCCTGCATTGTTGCC	627
Hu. DMD. Exon52. 25. 006. 2	TCTGTTCCAATCCTGCATTGTTGC	628
Hu. DMD. Exon52. 25. 007	AACTGGGGACGCCCTCTGTTCAAAT	629
Hu. DMD. Exon52. 25. 007. 2	GCTCTGTCTCAAATCCTGCATTGT	630
Hu. DMD. Exon52. 25. 008	CAGCGGTAATGAGTTCTTCAAATG	631
Hu. DMD. Exon52. 25. 008. 2	CTTCCAATGGGACGCCCTCTGTT	632
Hu. DMD. Exon52. 25. 009	CTTGTGTTCAAATTTGGGACGCG	633
Hu. DMD. Exon52. 25. 010	CTAGCCTCTTGATTGCTGGTCTTGT	634
Hu. DMD. Exon52. 25. 010. 2	TTTCAAATTTGGGACGGGTAAT	635
Hu. DMD. Exon52. 25. 011	TTCGATCCGTAATGATTGTTCTAGC	636
Hu. DMD. Exon52. 25. 011. 2	GATTGCTGGCTTGTGTTCAAATT	637
Hu. DMD. Exon52. 25. 012	CTTACTTCGATCCGTAATGATTGT	638
Hu. DMD. Exon52. 25. 012. 2	TTGTTCTAGCCTCTGATTGCTGGT	639
Hu. DMD. Exon52. 25. 013	AAAAACTTACTTCGATCCGTAATGA	640
Hu. DMD. Exon52. 25. 014	TGTTAAAAAACTTACTTCGATCCGT	641
Hu. DMD. Exon52. 25. 015	ATGCTTGTTAAAAAACTTACTTCGA	642
Hu. DMD. Exon52. 25. 016	GTCCCCATGCTTGTAAAAAACTTAC	643
Hu. DMD. Exon52. 20. 001	AGACAAATATCCCTTAGTA	644
Hu. DMD. Exon52. 20. 002	GTAAGAACAAATATCCCTTA	645
Hu. DMD. Exon52. 20. 003	TGCCGTGAAGAACAAATATC	646
Hu. DMD. Exon52. 20. 004	ATTGTTGCCTGTAAGAACAA	647
Hu. DMD. Exon52. 20. 005	CCTGCATTGCTGCTGTAAG	648
Hu. DMD. Exon52. 20. 006	CAAATCCTGCATTGTTGCC	649
Hu. DMD. Exon52. 20. 007	GCTCTGTCTCAAATCCTGC	650
Hu. DMD. Exon52. 20. 008	CTTCCAACTGGGACGCC	651
Hu. DMD. Exon52. 20. 009	CAGCGGTAATGAGTTCTTC	652
Hu. DMD. Exon52. 20. 010	TTTCAAATTTGGGACGCG	653
Hu. DMD. Exon52. 20. 011	GATTGCTGGCTTGTGTTTC	654
Hu. DMD. Exon52. 20. 012	TTGTTCTAGCCTCTGATTG	655
Hu. DMD. Exon52. 20. 013	TTCGATCCGTAATGATTGTT	656
Hu. DMD. Exon52. 20. 014	CTTACTTCGATCCGTAATGA	657
Hu. DMD. Exon52. 20. 015	AAAAACTTACTTCGATCCGT	658
Hu. DMD. Exon52. 20. 016	TGTTAAAAAACTTACTTCGA	659
Hu. DMD. Exon52. 20. 017	ATGCTTGTTAAAAAACTTAC	660
Hu. DMD. Exon52. 20. 018	GTCCCAGCTTGTAAAAAA	661
Hu. DMD. Exon53. 25. 001	CTAGAATAAAGGAAAAATAAT	662
Hu. DMD. Exon53. 25. 002	AACTAGAATAAAGGAAAATAAT	663
Hu. DMD. Exon53. 25. 002. 2	TTCAACTAGAATAAAGGAAAATA	664
Hu. DMD. Exon53. 25. 003	CTTCCAACTAGAATAAAGGAAA	665
Hu. DMD. Exon53. 25. 003. 2	ATTCTTCAACTAGAATAAAGGAA	666
Hu. DMD. Exon53. 25. 004	GAATTCTTCAACTAGAATAAAGG	667
Hu. DMD. Exon53. 25. 004. 2	TCTGAATTCTTCAACTAGAATAA	668
Hu. DMD. Exon53. 25. 005	ATTCTGAATTCTTCAACTAGAATA	669
Hu. DMD. Exon53. 25. 005. 2	CTGATTCTGAATTCTTCAACTAGA	670
Hu. DMD. Exon53. 25. 006	CACTGATTCTGAATTCTTCAACTA	671
Hu. DMD. Exon53. 25. 006. 2	TCCCACGTGATTCTGAATTCTTC	672
Hu. DMD. Exon53. 25. 007	CATCCCCACTGATTCTGAATTCTTC	673
Hu. DMD. Exon53. 25. 008	TACTTCATCCCACGTGATTCTGAATT	674
Hu. DMD. Exon53. 25. 009	CGTTCTGAAGGGTCTTGTACT	675
Hu. DMD. Exon53. 25. 009. 2	CTGTTGCCCTCCGGTCTGAAGGGT	676
Hu. DMD. Exon53. 25. 010	TTTCATTCAACTGTTGCCCTCGGTT	677
Hu. DMD. Exon53. 25. 010. 2	TAACATTTCACTGTTGCCCT	678
Hu. DMD. Exon53. 25. 011	TTGTGTTGAATCCTTAACTTCA	679
Hu. DMD. Exon53. 25. 012	TCTTCTCTAGCTTCCAGCATTG	680
Hu. DMD. Exon53. 25. 012. 2	CTTAGCTTCCAGCATTGTTGAA	681
Hu. DMD. Exon53. 25. 013	GTCCTAAGACCTGCTCAGCTTCTC	682
Hu. DMD. Exon53. 25. 013. 2	CTGCTCAGCTTCTCCCTAGCTTCC	683
Hu. DMD. Exon53. 25. 014	CTCAAGCTGGCTCTGGCTCT	684
Hu. DMD. Exon53. 25. 014. 2	GGCCGTGCTTAAGACCTGCTCAGCT	685
Hu. DMD. Exon53. 25. 015	TAGGGACCCCTCTCCATGACTCAA	686
Hu. DMD. Exon53. 25. 016	TTGGATTGCATCTACTGTATAAGG	687
Hu. DMD. Exon53. 25. 016. 2	ACCCCTCCTTCCCATGACTCAAGCTTG	688
Hu. DMD. Exon53. 25. 017	CTTGGTTCTGTGATTTCCTTG	689
Hu. DMD. Exon53. 25. 017. 2	ATCTACTGTATAAGGGACCTCCTTC	690
Hu. DMD. Exon53. 25. 018	CTAACCTGGTTCTGTGATTTC	691
Hu. DMD. Exon53. 25. 018. 2	TTTCTTTGGATTGCATCTACTGTA	692
Hu. DMD. Exon53. 25. 019	TGATACTAACCTGTTCTGTGAT	693
Hu. DMD. Exon53. 25. 020	ATCTTGATACTAACCTGTTCT	694
Hu. DMD. Exon53. 25. 021	AAGGTATTTGATACTAACCTTG	695
Hu. DMD. Exon53. 25. 022	TTAAAAAGGTATTTGATACTAAC	696
Hu. DMD. Exon53. 20. 001	ATAAAAGGAAAAATAATAT	697
Hu. DMD. Exon53. 20. 002	GAATAAAAGGAAAAATAATAT	698

TABLE 4-continued

Hu. DMD. Exon53. 20. 003	AACTAGAAATAAAGGAAAAA	699
Hu. DMD. Exon53. 20. 004	CTTCAACTAGAATAAAAGG	700
Hu. DMD. Exon53. 20. 005	GAATTCTTCAACTAGAATA	701
Hu. DMD. Exon53. 20. 006	ATTCTGAATTCTTCAACTA	702
Hu. DMD. Exon53. 20. 007	TACTTCATCCCACTGATTCT	703
Hu. DMD. Exon53. 20. 008	CTGAAGGTGTTCTTGTACT	704
Hu. DMD. Exon53. 20. 009	CTGTTGCCCTCGGTTCTGAA	705
Hu. DMD. Exon53. 20. 010	TAACATTTATTCAACTGTT	706
Hu. DMD. Exon53. 20. 011	TTGTGTTGAATCCTTAAACA	707
Hu. DMD. Exon53. 20. 012	CTTAGCTTCCAGCCATTGTG	708
Hu. DMD. Exon53. 20. 013	CTGCTCAGCTTCTCCCTAG	709
Hu. DMD. Exon53. 20. 014	GGCTGTCTTAAGACCTGCT	710
Hu. DMD. Exon53. 20. 015	CTCAAGCTTGGCTCTGGCCT	711
Hu. DMD. Exon53. 20. 016	ACCCCTCTTCCATGACTCAA	712
Hu. DMD. Exon53. 20. 017	ATCTACTGTATAAGGGACCT	713
Hu. DMD. Exon53. 20. 018	TTCTTTGGATTGCATCTA	714
Hu. DMD. Exon53. 20. 019	CTTGGTTCTGTGATTTCCT	715
Hu. DMD. Exon53. 20. 020	CTAACCTTGGTTCTGTGAT	716
Hu. DMD. Exon53. 20. 021	TGATACTAACCTTGGTTCT	717
Hu. DMD. Exon53. 20. 022	ATCTTGATACTAACCTTGG	718
Hu. DMD. Exon53. 20. 023	AAAGTATCTTGATACTAAC	719
Hu. DMD. Exon53. 20. 024	TTAAAAAGGTATCTTGATA	720
Hu. DMD. Exon54. 25. 001	CTATAGATTTTATGAGAAAGAGA	721
Hu. DMD. Exon54. 25. 002	AACTGCTAGATTTTATGAGAAA	722
Hu. DMD. Exon54. 25. 003	TGGCCAAGTGCATAGATTTTATG	723
Hu. DMD. Exon54. 25. 004	GTCTTGCCCAACTGCTATAGATT	724
Hu. DMD. Exon54. 25. 005	CGGAGGTCTTGGCCAAGTGCATA	725
Hu. DMD. Exon54. 25. 006	ACTGGCGGAGGTCTTGGCCAAGTG	726
Hu. DMD. Exon54. 25. 007	TTGTCTGCCACTGGCGGAGGTCTT	727
Hu. DMD. Exon54. 25. 008	AGTCATTGGCACATCTACATTGTT	728
Hu. DMD. Exon54. 25. 009	TTGCCACATCTACATTGCTG	729
Hu. DMD. Exon54. 25. 010	CCGGAGAAGTTCAAGGGCAAGTC	730
Hu. DMD. Exon54. 25. 010. 2	GTATCATCTGCAGAATAATCCCGA	731
Hu. DMD. Exon54. 25. 011	TAATCCCGAGAAGTTTCAGGGCCA	732
Hu. DMD. Exon54. 25. 012	TTATCATGTGGACTTTCTGGTATC	733
Hu. DMD. Exon54. 25. 012. 2	AGAGGCATTGATATTCTCTGTTATC	734
Hu. DMD. Exon54. 25. 013	ATGTGGACTTTCTGGTATCATCTG	735
Hu. DMD. Exon54. 25. 013	CTTTTATGAATGCTTCTCAAAGG	736
Hu. DMD. Exon54. 25. 013. 2	ATATTCTCTGTTATCATGTGGACTT	737
Hu. DMD. Exon54. 25. 014	CATACCTTTATGATATGCTTCTCCA	738
Hu. DMD. Exon54. 25. 014. 2	CTCCAAGGGCATTGATATTCTCG	739
Hu. DMD. Exon54. 25. 015	TAATTCTACACCTTTATGAATGCTT	740
Hu. DMD. Exon54. 25. 016	TAATGTAATTCTACACCTTTATGAA	741
Hu. DMD. Exon54. 25. 017	AGAAATAATGTAATTCTACACCTTT	742
Hu. DMD. Exon54. 25. 018	GTTTAGAAAATGTAATTCTAC	743
Hu. DMD. Exon54. 20. 001	GATTTTATGAGAAAGAGA	744
Hu. DMD. Exon54. 20. 002	CTATAGATTTTATGAGAAA	745
Hu. DMD. Exon54. 20. 003	AACTGCTATAGATTTTATG	746
Hu. DMD. Exon54. 20. 004	TGGCCAAGTGCATAGATTT	747
Hu. DMD. Exon54. 20. 005	GTCTTGCCCAACTGCTATA	748
Hu. DMD. Exon54. 20. 006	CGGAGGTCTTGGCCAAGTG	749
Hu. DMD. Exon54. 20. 007	TTGTCTGCCACTGGCGGAG	750
Hu. DMD. Exon54. 20. 008	TTGCCACATCTACATTG	751
Hu. DMD. Exon54. 20. 009	TTCAAGGGCAAGTCATTG	752
Hu. DMD. Exon54. 20. 010	TAATCCCGAGAAGTTTCAG	753
Hu. DMD. Exon54. 20. 011	GTATCATCTGCAGAATAATC	754
Hu. DMD. Exon54. 20. 012	ATGTGGACTTTCTGGTATC	755
Hu. DMD. Exon54. 20. 013	ATATTCTCTGTTATCATGTG	756
Hu. DMD. Exon54. 20. 014	CTCCAAGGGCATTGATATT	757
Hu. DMD. Exon54. 20. 015	CTTTTATGATGCTTCTCCA	758
Hu. DMD. Exon54. 20. 016	CATACCTTTATGATGCTT	759
Hu. DMD. Exon54. 20. 017	TAATTCTACACCTTTATGAA	760
Hu. DMD. Exon54. 20. 018	TAATGTAATTCTACACCTTT	761
Hu. DMD. Exon54. 20. 019	AGAAATAATGTAATTCTAC	762
Hu. DMD. Exon54. 20. 020	GTTTAGAAAATGTAATT	763
Hu. DMD. Exon55. 25. 001	CTGCAAAGGACCAATGTCAGATG	764
Hu. DMD. Exon55. 25. 002	TCACCCCTGCAAAGGACCAATGTT	765
Hu. DMD. Exon55. 25. 003	CTCACTCACCCCTGCAAAGGACCAAA	766
Hu. DMD. Exon55. 25. 004	TCTCGCTACTCACCCCTGCAAAGGA	767
Hu. DMD. Exon55. 25. 005	CAGCCTCTCGCTACTCACCCCTGCA	768
Hu. DMD. Exon55. 25. 006	CAAAGCAGCCTCTCGCTACTCACC	769
Hu. DMD. Exon55. 25. 007	TCTTCCAAGGCAGCCTCTCGCTCAC	770
Hu. DMD. Exon55. 25. 007. 2	TCTATGAGTTCTCCAAAGCAGCC	771
Hu. DMD. Exon55. 25. 008	GTTCAGTGAATCTATGAGTTCTTC	772
Hu. DMD. Exon55. 25. 008. 2	GAACTGTTGCAGTAATCTATGAGTT	773
Hu. DMD. Exon55. 25. 009	TTCCAGGTCCAGGGGAACTGTTGC	774
Hu. DMD. Exon55. 25. 010	GTAAGGCCAGGCAAGAAACTTTCCA	775

TABLE 4-continued

Hu. DMD. Exon55. 25. 010. 2	CCAGGCAAGAAACTTCCAGGTC	776
Hu. DMD. Exon55. 25. 011	TGGCAGTTGTTAGCTCTGTAAG	777
Hu. DMD. Exon55. 25. 011. 2	TTCACTCTGTAGCCAGGCAAGA	778
Hu. DMD. Exon55. 25. 012	GGTAGCATCTGTAGGACATTGGCA	779
Hu. DMD. Exon55. 25. 012. 2	GACATTGGCAGTTGTTTCAAGCTCT	780
Hu. DMD. Exon55. 25. 013	TCTAGGAGCCTTCTTACGGGTAG	781
Hu. DMD. Exon55. 25. 014	CTTTTACTCCCTGGAGCTTCTAG	782
Hu. DMD. Exon55. 25. 014. 2	GAGCCTTCCCTAACGGTAGCATCC	783
Hu. DMD. Exon55. 25. 015	TTGCCATTGTTTCACTGCTCTTT	784
Hu. DMD. Exon55. 25. 015. 2	CTTGGAGTCTCTAGGAGCTTCC	785
Hu. DMD. Exon55. 25. 016	CTTACTTGCCTGGTTCATCAGCT	786
Hu. DMD. Exon55. 25. 016. 2	CAGCTTTTACTCCCTGGAGTCT	787
Hu. DMD. Exon55. 25. 017	CTTGACTTACTTGCCATTGTTTCA	788
Hu. DMD. Exon55. 25. 018	AAATGCCTGACTTACTTGCCATTGT	789
Hu. DMD. Exon55. 25. 019	AGCGGAATGCCCTGACTTACTTGCC	790
Hu. DMD. Exon55. 25. 020	GCTAAAGCGGAATGCCCTGACTTAC	791
Hu. DMD. Exon55. 20. 001	AAGGACCAAATGTTCAAGATG	792
Hu. DMD. Exon55. 20. 002	CTGCAAAGGACCAAATGTTTC	793
Hu. DMD. Exon55. 20. 003	TCACCCCTGCAAAGGACAAA	794
Hu. DMD. Exon55. 20. 004	CTCACTCACCTGCAAAGGA	795
Hu. DMD. Exon55. 20. 005	TCTCGCTCACTCACCTGCA	796
Hu. DMD. Exon55. 20. 006	CAGCCTCTCGCTCACTCAC	797
Hu. DMD. Exon55. 20. 007	CAAAGCAGCCTCTGCTCAC	798
Hu. DMD. Exon55. 20. 008	TCTATGAGTTCTTCCAAAG	799
Hu. DMD. Exon55. 20. 009	GAACTGTTGCAGTAATCTAT	800
Hu. DMD. Exon55. 20. 010	TTCCAGGTCCAGGGGAACT	801
Hu. DMD. Exon55. 20. 011	CCAGGCAAGAAACTTTCCA	802
Hu. DMD. Exon55. 20. 012	TTCACTCTGTAGGCCAGG	803
Hu. DMD. Exon55. 20. 013	GACATTGGCAGTTGTTTCA	804
Hu. DMD. Exon55. 20. 014	GGTAGCATCCTGTAGGACAT	805
Hu. DMD. Exon55. 20. 015	GAGCCTTCTTACGGGTAG	806
Hu. DMD. Exon55. 20. 016	CTTGGAGTCTCTAGGAGCC	807
Hu. DMD. Exon55. 20. 017	CAGCTTTTACTCCCTGG	808
Hu. DMD. Exon55. 20. 018	TTGCCATTGTTTCACTGCT	809
Hu. DMD. Exon55. 20. 019	CTTACTTGCCTGGTTCAT	810
Hu. DMD. Exon55. 20. 020	CTTGACTTACTTGCCATTGT	811
Hu. DMD. Exon55. 20. 021	AAATGCCTGACTTACTTGCC	812
Hu. DMD. Exon55. 20. 022	AGCGGAATGCCCTGACTTAC	813
Hu. DMD. Exon55. 20. 023	GCTAAAGCGGAATGCCCTGA	814
H50A(+02 + 30) -AVI-5656	CCACTCAGAGCTAGATCTTAACTTCC	815
H50D(+07 - 18) -AVI-5915	GGGATCCAGTATACTTACAGGCTCC	816
H50A(+07 + 33)	CTTCACACTCAGAGCTCAGATCTCTAA	817
H51A(+61 + 90) -AVI-4657	ACATCAAGGAAGATGGCATTCTAGTTGG	818
H51A(+66 + 95) -AVI-4658	CTTCAAACATCAAGGAAGATGGCATTCTAG	819
H51A(+111 + 134)	TTCTGTCCAAGCCCGTTGAAATC	820
H51A(+175 + 195)	CACCCACCATCACCTCYGTG	821
H51A(+199 + 220)	ATCATCTCGTTGATATCCTCAA	822
H51A(+66 + 90)	ACATCAAGGAAGATGGCATTCTAG	823
H51A(-01 + 25)	ACCAGAGTAAACAGTCTGAGTAGGAGC	824
h51AON1	TCAAGGAAGATGGCATTCTTCT	825
h51AON2	CCTCTGTGATTTTATAACTTGAT	826
H51D(+08 - 17)	ATCATTTTTCTACACCTCTGCT	827
H51D(+16 - 07)	CTCATACCTCTGCTTGATGATC	828
haON#23	TGGCATTCTCTAGTTGG	829
haON#24	CCAGAGCAGGTACCTCCAAACATC	830
h44AON1	CGCCGCCATTCTCAAACAG	831
H45A(+71 + 90)	TGTTTTGAGGATTGCTGAA	832
h45AON1	GCTGAATTATTCTTCCCC	833
h45AON5	GCCCAATGCCATCTGG	834
H45A(-06 + 20)	CCAAATGCCATCTGGAGTCTCTGTA	835
H53A(+39 + 69)	CATTCAACTGTTGCCCTCCGGTTCTGAAGGTG	836
h53AON1	CTGTTGCCCTCCGGTTCTG	837
H53A(-12 + 10)	ATTCTTCAACTAGAATAAAAG	838
huEx45. 30. 66	GCCATCTGGAGTCTCTGTAAAGATACAAA	839
huEx45. 30. 71	CCAATGCCATCTGGAGTCTCTGTAAGATA	840
huEx45. 30. 79	GCCGCTGCCAATGCCATCTGGAGTCT	841
huEx45. 30. 83	GTTTGGCGCTGCCAATGCCATCTGGAGT	842
huEx45. 30. 88	CAACAGTTGCCGTGCCAATGCCATCT	843
huEx45. 30. 92	CTGACAACAGTTGCCGTGCCAATGCCA	844
huEx45. 30. 96	TGTTCTGACAACAGTTGCCGTGCCAAT	845
huEx45. 30. 99	CAATGTTCTGACAACAGTTGCCGTGCC	846
huEx45. 30. 103	CATTCAATGTTCTGACAACAGTTGCCGT	847
huEx45. 30. 120	TATTCTTCCCCAGTTGATTCAATGTTCT	848
huEx45. 30. 127	GCTGAATTATTCTTCCCCAGTTGCAATT	849
huEx45. 30. 132	GGATTGCTGAATTATTCTCCCCAGTTGC	850
huEx45. 30. 137	TTTGAGGATTGCTGAATTATTCTCCCCA	851
huEx53. 30. 84	GTACTTCATCCCACTGATTCTGAATTCTT	852

TABLE 4-continued

huEx53.30.88	TCTTGTACTTCATCCCACTGATTCTGAATT	853
huEx53.30.91	TGTTCTTGTACTTCATCCCACTGATTCTGA	854
huEx53.30.103	CGGTTCTGAAGGTGTTCTGTACTTCATCC	855
huEx53.30.106	CTCCGGTTCTGAAGGTGTTCTGTACTTC	856
huEx53.30.109	TGCCCTCCGGTTCTGAAGGTGTTCTGTACT	857
huEx53.30.112	TGTTGCCCTCCGGTTCTGAAGGTGTTCTGT	858
huEx53.30.115	AACTGTTGCCTCCGGTTCTGAAGGTGTTCT	859
huEx53.30.118	TTCAACTGTTGCCTCCGGTTCTGAAGGTG	860
h50A0N1		
h50A0N2		
Peptide Transporters (NH ₂ to COOH)*:		
rTAT	RRRQRRKKRKC	861
R9F2	RRRRRRRRFFC	862
(RAhxA) 4B	RAhxAhxAhxAhxAhxAhxA	863
(RAhxA) 4AhxB; (P007)	RAhxAhxAhxAhxAhxAhxAhxB	864
(AhxA) 4AhxB	AhxAhxAhxAhxAhxAhxAhxB	865
(RAhxA) 6B	RAhxAhxAhxAhxAhxAhxAhxB	866
(RAhxA) 8B	RAhxAhxAhxAhxAhxAhxAhxB	867
(RAhxA) 5AhxB	RAhxAhxAhxAhxAhxAhxAhxB	868
(RAhxAhxAhxAhxAhxB) 2AhxB; (CPO6062)	RAhxAhxAhxAhxAhxAhxAhxB	869
MSP	ASSLNIA	870
Cell Penetrating Peptide/Homing Peptide/PMO Conjugates (NH ₂ to COOH and 5' to 3')		
MSP-PMO	ASSLNIA-XB-	871
	GGCCAAACCTCGGCTTACCTGAAAT	875
CP06062-MSP-PMO	RXRRBRRXRRBR-XB-ASSLNIA-X-	872
	GGCCAAACCTCGGCTTACCTGAAAT	875
MSP-CP06062-PMO	ASSLNIA-X-RXRRBRRXRRBR-B-	873
	GGCCAAACCTCGGCTTACCTGAAAT	875
CP06062-PMO	RXRRBRRXRRBR-XB-	874
	GGCCAAACCTCGGCTTACCTGAAAT	875

*Ahx is 6-aminohexanoic acid and B is beta-alanine

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 891

<210> SEQ ID NO 1

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic (eteplirsen H51A(+66+95))

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ctccaacatc aaggaagatg gcatttctag 30

<210> SEQ ID NO 2

<211> LENGTH: 25

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic (H51A(+66+90))

<400> SEQUENCE: 2

acaugaagg aaggcattt ucuuag 25

<210> SEQ ID NO 3

<211> LENGTH: 30

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic (H51A(+61+90))

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gagcaggtac ctccaacatc aaggaa	26
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gggauccagu auacuuacag gcucc	25
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cttacaggct ccaatagtgg tcagt	25
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cctccgggttc tgaagggttt ctgtac	27
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gttgccctccg gttctgaagg tggtc	25
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<400> SEQUENCE: 10
gauagguggu auacaacaucu guaa                                24

<210> SEQ ID NO 11
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H8A (-03+18))

<400> SEQUENCE: 11
gauagguggu auacaacaucu g                                21

<210> SEQ ID NO 12
<211> LENGTH: 25
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gauagguggu auacaacaucu guaag                                25

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ggugguauc acaucuguaa                                20

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<223> OTHER INFORMATION: Synthetic (H8A(-10+10))

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guaucaacau cuguaagcac                                20

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<220> FEATURE:
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<400> SEQUENCE: 16

cacuauucca gucaaauagg ucugg 25

<210> SEQ ID NO 17
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H7D(+15-10))

<400> SEQUENCE: 17

auuuuaccaac cuucaggaua gagua 25

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<400> SEQUENCE: 18

ggccuaaaaac acauacacau a 21

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<223> OTHER INFORMATION: Synthetic (C6A(-10+10))

<400> SEQUENCE: 19

cauuuuuugac cuacaugugg 20

<210> SEQ ID NO 20
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 20

uuugaccuac auguggaaag 20

<210> SEQ ID NO 21
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<212> TYPE: RNA
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<220> FEATURE:
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<400> SEQUENCE: 21

uacauuuuug accuacaugu ggaaag 26

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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (C6A(-13+09))

<400> SEQUENCE: 22

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auuuuugacc uacaugggaa ag	22
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guggucuccu uaccuaugac ugugg	25
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ggucuccuuua ccuauga	17
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ugucucagua aucuucuuac cuau	24
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ucuuaccuau gacuauggau gaga	24
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gcaugaacuc uuguggaucc	20

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<210> SEQ ID NO 29
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 29

ccaggguacu acuuacauua                                20

<210> SEQ ID NO 30
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H4D(-24-44))

<400> SEQUENCE: 30

aucguguguc acagcaucca g                                21

<210> SEQ ID NO 31
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<212> TYPE: RNA
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<223> OTHER INFORMATION: Synthetic (H4A(+11+40))

<400> SEQUENCE: 31

uguucagggc augaacucuu guggauccuu                                30

<210> SEQ ID NO 32
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 32

uaggaggcgc cucccauccu guaggucacu g                                31

<210> SEQ ID NO 33
<211> LENGTH: 31
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H3A(+35+65))

<400> SEQUENCE: 33

aggcucuagga ggccucucca auccuguagg u                                31

<210> SEQ ID NO 34
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H3A(+30+54))

<400> SEQUENCE: 34

gcgcuuccca uccuguagg u cacug                                25

<210> SEQ ID NO 35
<211> LENGTH: 26
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H3D(+46-21))

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cuuucgaggag gucuaggagg cgccuc                                26

<210> SEQ ID NO 36
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H3A(+30+50))

<400> SEQUENCE: 36
cucccauccu guaggucacu g                                21

<210> SEQ ID NO 37
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H3D(+19-03))

<400> SEQUENCE: 37
uaccaguuuu ugcccuguca gg                                22

<210> SEQ ID NO 38
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H3A(-06+20))

<400> SEQUENCE: 38
ucaauaaugcu gcuuuccaaa cugaaa                                26

<210> SEQ ID NO 39
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H3A(+37+61))

<400> SEQUENCE: 39
cuaggaggcg ccuucccaucc uguag                                25

<210> SEQ ID NO 40
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H5A(+20+50))

<400> SEQUENCE: 40
uuaugauuuc caucuacgau gucaguacuu c                                31

<210> SEQ ID NO 41
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 41

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cuuaccugcc aguggaggau uauauuccaa a	31
<pre> <210> SEQ ID NO 42 <211> LENGTH: 25 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H5D(+10-15)) <400> SEQUENCE: 42 </pre>	
caucaggauu cuuaccugcc agugg	25
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cgaugucagu acuuuccaaau uucac	25
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accaaucauc aggauucu	18
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accugccagu ggaggauu	18
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ccaaauuuca cuaaaaaac cuguuuaa	27
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caggauuguu accugccagu ggaggauua	30

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<210> SEQ ID NO 48
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H5A(+05+35))

<400> SEQUENCE: 48

acgaaugucag uacuuccaaau auucacuaaa u           31

<210> SEQ ID NO 49
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H5A(+15+45))

<400> SEQUENCE: 49

auuuuccauu acgaaugucag uacuuccaaau a           31

<210> SEQ ID NO 50
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H10A(-05+16))

<400> SEQUENCE: 50

caggagcuuc caaaugcugc a           21

<210> SEQ ID NO 51
<211> LENGTH: 29
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H10A(-05+24))

<400> SEQUENCE: 51

cuugucuuca ggagcuucca aaugcugca           29

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H10A(+98+119))

<400> SEQUENCE: 52

uccucagcag aaagaagcca cg           22

<210> SEQ ID NO 53
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H10A(+130+149))

<400> SEQUENCE: 53

uuagaaaucu cuccuugugc           20

<210> SEQ ID NO 54
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H10A(-33-14))

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H11D(+26+49))

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ccugaggca uucccaucuu gaaau                                         24

<210> SEQ ID NO 56
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<223> OTHER INFORMATION: Synthetic (H11D(+11-09))

<400> SEQUENCE: 56
aggacuuuac ugcuuuguuu                                         20

<210> SEQ ID NO 57
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H11A(+118+140))

<400> SEQUENCE: 57
cuugaaauua ggagauucau cug                                         23

<210> SEQ ID NO 58
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H11A(+75+97))

<400> SEQUENCE: 58
caucuucuga uaauuuuccu guu                                         23

<210> SEQ ID NO 59
<211> LENGTH: 24
<212> TYPE: RNA
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<223> OTHER INFORMATION: Synthetic (H12A(+52+75))

<400> SEQUENCE: 59
ucuucuguuu uuguuagcca guca                                         24

<210> SEQ ID NO 60
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<400> SEQUENCE: 60

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cagcaguugc gugaucucca cuag	24
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uucaucaacu accaccacca u	21
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cuaagcaaaa uaaucugacc uuaag	25
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cuuguaaaag aacccttgggg ucuucugu	28
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caucuacaga uguuugccca uc	22

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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H14A(+51+73))

<400> SEQUENCE: 67

gaaggaauguc uuguaaaaga acc 23

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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H14D(-02+18))

<400> SEQUENCE: 68

accuguucuu caguaagacg 20

<210> SEQ ID NO 69
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H14D(+14-10))

<400> SEQUENCE: 69

caugacacac cuguucuuca guaa 24

<210> SEQ ID NO 70
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H14A(+61+80))

<400> SEQUENCE: 70

cauuugagaa ggaugucuug 20

<210> SEQ ID NO 71
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H14A(-12+12))

<400> SEQUENCE: 71

aucucccaau accuggagaa gaga 24

<210> SEQ ID NO 72
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H15A(-12+19))

<400> SEQUENCE: 72

gccaugcacu aaaaaggcac ugcaagacau u 31

<210> SEQ ID NO 73
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H15A(+48+71))

<400> SEQUENCE: 73
ucuuuaaagc caguugugug aauc                                24

<210> SEQ ID NO 74
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H15A(+08+28))

<400> SEQUENCE: 74
uuucugaaag ccaugcacua a                                21

<210> SEQ ID NO 75
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H15D(+17-08))

<400> SEQUENCE: 75
guacauacgg ccaguuuuug aagac                                25

<210> SEQ ID NO 76
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H16A(-12+19))

<400> SEQUENCE: 76
cuagauccgc uuuuaaaacc uguaaaaaca a                                31

<210> SEQ ID NO 77
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H16A(-06+25))

<400> SEQUENCE: 77
ucuuuucuag auccgcuuuu aaaaccuguu a                                31

<210> SEQ ID NO 78
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H16A(-06+19))

<400> SEQUENCE: 78
cuagauccgc uuuuaaaacc uguua                                25

<210> SEQ ID NO 79
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H16A(+87+109))

<400> SEQUENCE: 79

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ccgucuucug gguacugac uua	23
<pre> <210> SEQ ID NO 80 <211> LENGTH: 26 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H16A(-07+19)) <400> SEQUENCE: 80 </pre>	
cuagauccgc uuuuaaaacc uguuua	26
<pre> <210> SEQ ID NO 81 <211> LENGTH: 20 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H16A(-07+13)) <400> SEQUENCE: 81 </pre>	
ccgcuuuuuaa aaccuguuua	20
<pre> <210> SEQ ID NO 82 <211> LENGTH: 26 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H16A(+12+37)) <400> SEQUENCE: 82 </pre>	
uggauugcuu uuuuuuuuucu agaucc	26
<pre> <210> SEQ ID NO 83 <211> LENGTH: 25 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H16A(+92+116)) <400> SEQUENCE: 83 </pre>	
caugcuuccg ucuucugggu cacug	25
<pre> <210> SEQ ID NO 84 <211> LENGTH: 23 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H16A(+45+67)) <400> SEQUENCE: 84 </pre>	
gaucuuguuu gagugaaauac agu	23
<pre> <210> SEQ ID NO 85 <211> LENGTH: 22 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H16A(+105+126)) <400> SEQUENCE: 85 </pre>	
guuauccagc caugcuuccg uc	22

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<210> SEQ ID NO 86
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H16D(+05-20))

<400> SEQUENCE: 86

ugauaauugg uaucacuaac cugug                                25

<210> SEQ ID NO 87
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H16D(+12-11))

<400> SEQUENCE: 87

guaucacuaa ccugugcugu ac                                22

<210> SEQ ID NO 88
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H19A(+35+53))

<400> SEQUENCE: 88

cugcuggcau cuugcaguu                                19

<210> SEQ ID NO 89
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H19A(+35+65))

<400> SEQUENCE: 89

gccugagcug aucugcuggc aucuugcagu u                                31

<210> SEQ ID NO 90
<211> LENGTH: 28
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(+44+71))

<400> SEQUENCE: 90

cuggcagaau ucgauccacc ggcuguuuc                                28

<210> SEQ ID NO 91
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(+147+168))

<400> SEQUENCE: 91

cagcaguagu ugucaucugc uc                                22

<210> SEQ ID NO 92
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(+185+203))

<400> SEQUENCE: 92
ugauggggug guggguugg                                19

<210> SEQ ID NO 93
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(-08+17))

<400> SEQUENCE: 93
aucugcauua acacccucua gaaag                                25

<210> SEQ ID NO 94
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(+30+53))

<400> SEQUENCE: 94
ccggcuguuc aguuguucug aggc                                24

<210> SEQ ID NO 95
<211> LENGTH: 28
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(-11+17))

<400> SEQUENCE: 95
aucugcauua acacccucua gaaagaaa                                28

<210> SEQ ID NO 96
<211> LENGTH: 28
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20D(+08-20))

<400> SEQUENCE: 96
gaaggagaag agauucuuac cuuacaaa                                28

<210> SEQ ID NO 97
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(+44+63))

<400> SEQUENCE: 97
auucgaucca ccggcuguuc                                20

<210> SEQ ID NO 98
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H20A(+149+168))

<400> SEQUENCE: 98

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cagcaguagu ugucaucugc 20

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<210> SEQ ID NO 99
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H21A(-06+16))

<400> SEQUENCE: 99

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gccgguugac uucauccugu gc 22

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<210> SEQ ID NO 100
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H21A(+85+106))

<400> SEQUENCE: 100

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cugcauccag gaacaugggu cc 22

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<210> SEQ ID NO 101
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H21A(+85+108))

<400> SEQUENCE: 101

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gucugcaucc aggaacauugg guc 23

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<210> SEQ ID NO 102
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H21A(+08+31))

<400> SEQUENCE: 102

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guugaagauc ugauagccgg uuga 24

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<210> SEQ ID NO 103
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H21D(+18-07))

<400> SEQUENCE: 103

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uacuuacugu cuguagcucu uucu 24

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<210> SEQ ID NO 104
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H22A(+22+45))

<400> SEQUENCE: 104

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cacucauggu cuccugauag cgca 24

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<210> SEQ ID NO 105
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H22A(+125+146))

<400> SEQUENCE: 105
cugcaauucc ccgagucucu gc          22

<210> SEQ ID NO 106
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H22A(+47+69))

<400> SEQUENCE: 106
acugcuggac ccauguccug aug          23

<210> SEQ ID NO 107
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H22A(+80+101))

<400> SEQUENCE: 107
cuaaguugag guaaggagag u          21

<210> SEQ ID NO 108
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H22D(+13-11))

<400> SEQUENCE: 108
uauucacaga ccugcaauuc ccc          23

<210> SEQ ID NO 109
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H23A(+34+59))

<400> SEQUENCE: 109
acaguggugc ugagauagua uaggcc          26

<210> SEQ ID NO 110
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H23A(+18+39))

<400> SEQUENCE: 110
uaggccacuu uguugcucuu gc          22

<210> SEQ ID NO 111
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H23A(+72+90))

<400> SEQUENCE: 111
uucagagggc gcuuucuuc 19

<210> SEQ ID NO 112
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H24A(+48+70))

<400> SEQUENCE: 112
gggcaggcca uuccuccuuc aga 23

<210> SEQ ID NO 113
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H24A(-02+22))

<400> SEQUENCE: 113
ucuucagggu uuguauguga uucu 24

<210> SEQ ID NO 114
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H25A(+9+36))

<400> SEQUENCE: 114
cugggcugaa uugucugaaau aucacug 27

<210> SEQ ID NO 115
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H25A(+131+156))

<400> SEQUENCE: 115
cuguuuggcac augugaucc acugag 26

<210> SEQ ID NO 116
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H25D(+16-08))

<400> SEQUENCE: 116
gucuauaccu guuggcacau guga 24

<210> SEQ ID NO 117
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H26A(+132+156))

<400> SEQUENCE: 117

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ugcuuucugu aauucaucug gaguu 25

<210> SEQ ID NO 118
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H26A(-07+19))

<400> SEQUENCE: 118

ccuccuuuucu ggcauagacc uuccac 26

<210> SEQ ID NO 119
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H26A(+68+92))

<400> SEQUENCE: 119

ugugucaucc auucgugcau cucug 25

<210> SEQ ID NO 120
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H27A(+82+106))

<400> SEQUENCE: 120

uuaaggccuc uugugcuaca ggugg 25

<210> SEQ ID NO 121
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H27A(-4+19))

<400> SEQUENCE: 121

ggggcucuuc uuuagcucuc uga 23

<210> SEQ ID NO 122
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H27D(+19-03))

<400> SEQUENCE: 122

gacuuccaaa gucuugcauu uc 22

<210> SEQ ID NO 123
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H28A(-05+19))

<400> SEQUENCE: 123

gccaaacaaugc ccaaacuucc uaag 24

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<210> SEQ ID NO 124
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H28A(+99+124))

<400> SEQUENCE: 124

cagagauuuc cucagcuccg ccagga                                26

<210> SEQ ID NO 125
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H28D(+16-05))

<400> SEQUENCE: 125

cuuacaucua gcaccucaga g                                21

<210> SEQ ID NO 126
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H29A(+57+81))

<400> SEQUENCE: 126

uccgccaucu guuagggucu gugcc                                25

<210> SEQ ID NO 127
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H29A(+18+42))

<400> SEQUENCE: 127

auuuggguua uccucugaa gucgc                                25

<210> SEQ ID NO 128
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H29D(+17-05))

<400> SEQUENCE: 128

cauaccucuu cauguaguuc cc                                22

<210> SEQ ID NO 129
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H30A(+122+147))

<400> SEQUENCE: 129

cauuugagcu gcguccaccu ugucug                                26

<210> SEQ ID NO 130
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H30A(+25+50))

<400> SEQUENCE: 130

uccuggggcag acuggaaugcu cugwuc                                26

<210> SEQ ID NO 131
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H30D(+19-04))

<400> SEQUENCE: 131

uugccugggc uuccugaggc auu                                23

<210> SEQ ID NO 132
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H31D(+06-18))

<400> SEQUENCE: 132

uucugaaaua acauauuaccu gugc                                24

<210> SEQ ID NO 133
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H31D(+03-22))

<400> SEQUENCE: 133

uaguuucuga aauaacauau accug                                25

<210> SEQ ID NO 134
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H31A(+05+25))

<400> SEQUENCE: 134

gacuugucaa aucagauugg a                                21

<210> SEQ ID NO 135
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H31D(+04-20))

<400> SEQUENCE: 135

guuucugaaa uaacauauac cugu                                24

<210> SEQ ID NO 136
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H32D(+04-16))

<400> SEQUENCE: 136

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caccagaaau acauaccaca 20

<210> SEQ ID NO 137
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H32A(+151+170))

<400> SEQUENCE: 137

caaugauuuu gaugugacug 20

<210> SEQ ID NO 138
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H32A(+10+32))

<400> SEQUENCE: 138

cggaaacuuca uggagacaua uug 23

<210> SEQ ID NO 139
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H32A(+49+73))

<400> SEQUENCE: 139

cuuuguagacg cugcuuaaaa uuggc 25

<210> SEQ ID NO 140
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H33D(+09-11))

<400> SEQUENCE: 140

caugcacaca ccuuugcucc 20

<210> SEQ ID NO 141
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H33A(+53+76))

<400> SEQUENCE: 141

ucuguuacaaug cugacggucca gucu 24

<210> SEQ ID NO 142
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H33A(+30+56))

<400> SEQUENCE: 142

gucuuuuauca ccauuuccac uucagac 27

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<210> SEQ ID NO 143
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H33A(+64+88))

<400> SEQUENCE: 143
ccgucugcuu uuuucuguaca aucug 25

<210> SEQ ID NO 144
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H34A(+83+104))

<400> SEQUENCE: 144
uccauaucug uagcugccag cc 22

<210> SEQ ID NO 145
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H34A(+143+165))

<400> SEQUENCE: 145
ccaggcaacu ucagaaucca aau 23

<210> SEQ ID NO 146
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H34A(-20+10))

<400> SEQUENCE: 146
uuucuguuac cugaaaagaa uuuaauaugaa 30

<210> SEQ ID NO 147
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H34A(+46+70))

<400> SEQUENCE: 147
cauucauuuc cuuucgcauc uuacg 25

<210> SEQ ID NO 148
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H34A(+95+120))

<400> SEQUENCE: 148
ugaucucuuu gucaauucca uaucug 26

<210> SEQ ID NO 149
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H34D(+10-20))

<400> SEQUENCE: 149

uucagugaua uagguuuuac cuuuccccag                                30

<210> SEQ ID NO 150
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H34A(+72+96))

<400> SEQUENCE: 150

cuguagcugc cagccauucu gucaag                                26

<210> SEQ ID NO 151
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H35A(+141+161))

<400> SEQUENCE: 151

ucuucugcuc gggaggugac a                                21

<210> SEQ ID NO 152
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H35A(+116+135))

<400> SEQUENCE: 152

ccaguuacua uucagaagac                                20

<210> SEQ ID NO 153
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H35A(+24+43))

<400> SEQUENCE: 153

ucuucaggug caccuucugu                                20

<210> SEQ ID NO 154
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H36A(+26+50))

<400> SEQUENCE: 154

ugugaugugg uccacauucu gguca                                25

<210> SEQ ID NO 155
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H36A(-02+18))

<400> SEQUENCE: 155

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ccauguguuu cugguauucc	20
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cguguagagu ccaccuuugg gcgua	25
<pre> <210> SEQ ID NO 157 <211> LENGTH: 24 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H37A(+82+105)) <400> SEQUENCE: 157 </pre>	
uacuaauuuuc cugcaguggu cacc	24
<pre> <210> SEQ ID NO 158 <211> LENGTH: 24 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H37A(+134+157)) <400> SEQUENCE: 158 </pre>	
uucuguguga aauggcugca aauc	24
<pre> <210> SEQ ID NO 159 <211> LENGTH: 20 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H38A(-01+19)) <400> SEQUENCE: 159 </pre>	
ccucaaagg aauggaggcc	20
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ugcugaauuu cagccuccag ugguu	25
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ugaagucuuc cucuuucaga uucac	25

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<210> SEQ ID NO 162
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H39A(+62+85))

<400> SEQUENCE: 162
cuggcuuuucu cucaucugug auuc          24

<210> SEQ ID NO 163
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H39A(+39+58))

<400> SEQUENCE: 163
guuguaaguu gucuccucuu          20

<210> SEQ ID NO 164
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H39A(+102+121))

<400> SEQUENCE: 164
uugucuguaa cagcugcugu          20

<210> SEQ ID NO 165
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H39D(+10-10))

<400> SEQUENCE: 165
gcucuaauac cuuugagagca          20

<210> SEQ ID NO 166
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H40A(-05+17))

<400> SEQUENCE: 166
cuuugagacc ucaaaauccug uu          22

<210> SEQ ID NO 167
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H40A(+129+153))

<400> SEQUENCE: 167
cuuuauuuuc cuuucaucuc ugggc          25

<210> SEQ ID NO 168
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H42A(-04+23))

<400> SEQUENCE: 168

aucguuucuu cacggacagu gugcugg                                27

<210> SEQ ID NO 169
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H42A(+86+109))

<400> SEQUENCE: 169

gggcuuguga gacaugagug auuu                                24

<210> SEQ ID NO 170
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H42D(+19-02))

<400> SEQUENCE: 170

accuuucagag gacuccucuu gc                                22

<210> SEQ ID NO 171
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H43D(+10-15))

<400> SEQUENCE: 171

uauguguuac cuacccuugu cgguuc                                25

<210> SEQ ID NO 172
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H43A(+101+120))

<400> SEQUENCE: 172

ggagagagcu uccuguagcu                                20

<210> SEQ ID NO 173
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H43A(+78+100))

<400> SEQUENCE: 173

ucacccuuuc cacaggcguu gca                                23

<210> SEQ ID NO 174
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(+85+104))

<400> SEQUENCE: 174

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uuugugucuu ucugagaaac 20

<210> SEQ ID NO 175
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44D(+10-10))

<400> SEQUENCE: 175

aaagacuuac cuuaagauac 20

<210> SEQ ID NO 176
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(-06+14))

<400> SEQUENCE: 176

aucugucaa ucggcugcag 20

<210> SEQ ID NO 177
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H46D(+16-04))

<400> SEQUENCE: 177

uuaccuugac uugcucaagg 20

<210> SEQ ID NO 178
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H46A(+90+109))

<400> SEQUENCE: 178

uccagguuca agugggauac 20

<210> SEQ ID NO 179
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H47A(+76+100))

<400> SEQUENCE: 179

gcucuucugg gcuuuaggga gcacu 25

<210> SEQ ID NO 180
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H47D(+25-02))

<400> SEQUENCE: 180

accuuuaucc acuggagauu ugucugc 27

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<210> SEQ ID NO 181
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H47A(-9+12))

<400> SEQUENCE: 181
uuccaccagu aacugaaaca g 21

<210> SEQ ID NO 182
<211> LENGTH: 29
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H50A(+02+30))

<400> SEQUENCE: 182
ccacucagag cucagauuu cuaacuucc 29

<210> SEQ ID NO 183
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H50A(+07+33))

<400> SEQUENCE: 183
cuuccacuca gagcucagau cuucuua 27

<210> SEQ ID NO 184
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51A(-01+25))

<400> SEQUENCE: 184
accagaguua cagucugagu aggagc 26

<210> SEQ ID NO 185
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51D(+16-07))

<400> SEQUENCE: 185
cucauaccuu cugcuugaug auc 23

<210> SEQ ID NO 186
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51A(+111 +134))

<400> SEQUENCE: 186
uucuguccaa gccccguuga aauc 24

<210> SEQ ID NO 187
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51A(+66+95))

<400> SEQUENCE: 187
cuccaacauc aaggaagaaug gcauuucuag 30

<210> SEQ ID NO 188
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51D(+08-17))

<400> SEQUENCE: 188
aucauuuuuu cucauaccuu cugcu 25

<210> SEQ ID NO 189
<211> LENGTH: 36
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51A/D(+08-17) & (-15+))

<400> SEQUENCE: 189
aucauuuuuu cucauaccuu cugcuaggag cuaaaa 36

<210> SEQ ID NO 190
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51A(+175+195))

<400> SEQUENCE: 190
cacccaccau cacccucugu g 21

<210> SEQ ID NO 191
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H51A(+199+220))

<400> SEQUENCE: 191
aucaucucgu ugauauccuc aa 22

<210> SEQ ID NO 192
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H52A(-07+14))

<400> SEQUENCE: 192
uccugcauug uugccuguaa g 21

<210> SEQ ID NO 193
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H52A(+12+41))

<400> SEQUENCE: 193

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uccaacuggg gacgccug uuccaaaucc	30
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acuggggacg ccucuguuucc a	21
<pre> <210> SEQ ID NO 195 <211> LENGTH: 20 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H52A(+93+112)) <400> SEQUENCE: 195 ccguaaugau uguucuagcc </pre>	
ccguaaugau uguucuagcc	20
<pre> <210> SEQ ID NO 196 <211> LENGTH: 20 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H52D(+05-15)) <400> SEQUENCE: 196 uguuaaaaaaa cuuacuuucga </pre>	
uguuaaaaaaa cuuacuuucga	20
<pre> <210> SEQ ID NO 197 <211> LENGTH: 25 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H53A(+45+69)) <400> SEQUENCE: 197 cauuaacug uugccuccgg uucug </pre>	
cauuaacug uugccuccgg uucug	25
<pre> <210> SEQ ID NO 198 <211> LENGTH: 24 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H53A(+39+62)) <400> SEQUENCE: 198 cuguugccuc cgguucugaa ggug </pre>	
cuguugccuc cgguucugaa ggug	24
<pre> <210> SEQ ID NO 199 <211> LENGTH: 31 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H53A(+39+69)) <400> SEQUENCE: 199 cauuaacug uugccuccgg uucugaagg g </pre>	
cauuaacug uugccuccgg uucugaagg g	31

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<210> SEQ ID NO 200
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53D(+14-07))

<400> SEQUENCE: 200
uacuaaccuu gguuucugug a 21

<210> SEQ ID NO 201
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+23+47))

<400> SEQUENCE: 201
cugaaggugu ucuuuguacuu caucc 25

<210> SEQ ID NO 202
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+150+176))

<400> SEQUENCE: 202
uguaauaggga cccuccuuucc augacuc 27

<210> SEQ ID NO 203
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53D(+20-05))

<400> SEQUENCE: 203
cuaaccuugg uuuucugugau uuuucu 25

<210> SEQ ID NO 204
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53D(+09-18))

<400> SEQUENCE: 204
gguaucuuug auacuaaccu ugguuuc 27

<210> SEQ ID NO 205
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(-12+10))

<400> SEQUENCE: 205
auucuuucaa cuagaauaaa ag 22

<210> SEQ ID NO 206
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(-07+18))

<400> SEQUENCE: 206
gauucugaaau ucuuuucaacu agaaau 25

<210> SEQ ID NO 207
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+07+26))

<400> SEQUENCE: 207
aucccacuga uucugaaauuc 20

<210> SEQ ID NO 208
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+124+145))

<400> SEQUENCE: 208
uuggcucugg ccuguccuaa ga 22

<210> SEQ ID NO 209
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H46A(+86+115))

<400> SEQUENCE: 209
cucuuuuucca gguucaagug ggauacuagc 30

<210> SEQ ID NO 210
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H46A(+107+137))

<400> SEQUENCE: 210
caagcuuuuc uuuuaguugc ugcucuuuuc c 31

<210> SEQ ID NO 211
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H46A(-10+20))

<400> SEQUENCE: 211
uauucuuuug uucuuucuagc cuggagaaag 30

<210> SEQ ID NO 212
<211> LENGTH: 28
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H46A(+50+77))

<400> SEQUENCE: 212

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cugcuuccuc caaccauaaa acaaauuc	28
<pre> <210> SEQ ID NO 213 <211> LENGTH: 26 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H45A(-06+20)) <400> SEQUENCE: 213 </pre>	
ccaaugccau ccuggaguuc cuguaa	26
<pre> <210> SEQ ID NO 214 <211> LENGTH: 20 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H45A(+91 +110)) <400> SEQUENCE: 214 </pre>	
uccuguagaa uacuggcauc	20
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ugcagaccuc cugccaccgc agauuca	27
<pre> <210> SEQ ID NO 216 <211> LENGTH: 20 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H45D(+16 -04)) <400> SEQUENCE: 216 </pre>	
cuaccucuuu uuuucugucug	20
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uguuuuugag gauugcugaa	20
<pre> <210> SEQ ID NO 218 <211> LENGTH: 28 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (H53A(+33+60)) <400> SEQUENCE: 218 </pre>	
gttgcctccg gttctgaagg tgttcttg	28

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<210> SEQ ID NO 219
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+23+47))

<400> SEQUENCE: 219
ctgaagggtgt tcttgtactt catcc                                25

<210> SEQ ID NO 220
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+33+62))

<400> SEQUENCE: 220
ctgttgcctc cgggtctgaa ggtgttcttg                                30

<210> SEQ ID NO 221
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+33+65))

<400> SEQUENCE: 221
caactgttgc ctccgggttct gaagggtgttc ttg                                33

<210> SEQ ID NO 222
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+31+55))

<400> SEQUENCE: 222
ctccgggttct gaagggtgttc ttgta                                25

<210> SEQ ID NO 223
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+46+73))

<400> SEQUENCE: 223
attcattca actgttgcct ccgggttct                                28

<210> SEQ ID NO 224
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H53A(+22+46))

<400> SEQUENCE: 224
tgaagggttt ctgttacttc atccc                                25

<210> SEQ ID NO 225
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H53A(+46+69))  
  
<400> SEQUENCE: 225  
  
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<210> SEQ ID NO 226  
<211> LENGTH: 22  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H53A(+40+61))  
  
<400> SEQUENCE: 226  
  
tggcctcc gggtctgaag gt 22  
  
<210> SEQ ID NO 227  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H53A(+30+60))  
  
<400> SEQUENCE: 227  
  
gttcgcctccg gttctgaagg tgttc 25  
  
<210> SEQ ID NO 228  
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<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H53A(+30+57))  
  
<400> SEQUENCE: 228  
  
gcctccgggtt ctgaagggtgt tcttgta 28  
  
<210> SEQ ID NO 229  
<211> LENGTH: 27  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H53A(+30+56))  
  
<400> SEQUENCE: 229  
  
cctccgggttc tgaagggtgtt ctgtac 27  
  
<210> SEQ ID NO 230  
<211> LENGTH: 26  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H53A(+30+55))  
  
<400> SEQUENCE: 230  
  
ctccgggtct gaagggtgtc ttgtac 26  
  
<210> SEQ ID NO 231  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H53A(+33+57))  
  
<400> SEQUENCE: 231
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gcctccggtt ctgaagggtgt tcttg	25
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24	
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27	
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29	
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25	
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28	
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28	

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<210> SEQ ID NO 238
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(+62+85))

<400> SEQUENCE: 238

ctgttcagct tctgttagcc actg                                24

<210> SEQ ID NO 239
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(-06+14))

<400> SEQUENCE: 239

atctgtcaaa tcgcctgcag                                20

<210> SEQ ID NO 240
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(+85+104))

<400> SEQUENCE: 240

tttgtgtctt tctgagaaac                                20

<210> SEQ ID NO 241
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(+61+84))

<400> SEQUENCE: 241

tgttcagctt ctgttagcca ctga                                24

<210> SEQ ID NO 242
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(-10+15))

<400> SEQUENCE: 242

gatctgtcaa atgcgcgtca ggtaa                                25

<210> SEQ ID NO 243
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (H44A(+64+88))

<400> SEQUENCE: 243

aaactgttca gcttctgtta gccac                                25

<210> SEQ ID NO 244
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Synthetic (H44A(+79+103))  
  
<400> SEQUENCE: 244  
  
tttgttcttt ctgagaaact gttca 25  
  
<210> SEQ ID NO 245  
<211> LENGTH: 26  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H44A(-06+20))  
  
<400> SEQUENCE: 245  
  
caacagatct gtcaaatcgc ctgcag 26  
  
<210> SEQ ID NO 246  
<211> LENGTH: 26  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H44A(-09+17))  
  
<400> SEQUENCE: 246  
  
cagatctgtc aaatcgccctg caggta 26  
  
<210> SEQ ID NO 247  
<211> LENGTH: 27  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H44A(+59+85))  
  
<400> SEQUENCE: 247  
  
ctgttcagct tctgttagcc actgatt 27  
  
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<211> LENGTH: 31  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H44A(+59+89))  
  
<400> SEQUENCE: 248  
  
gaaaactgttc agttctgtt agccactgat t 31  
  
<210> SEQ ID NO 249  
<211> LENGTH: 26  
<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (H44A(+65+90))  
  
<400> SEQUENCE: 249  
  
agaaaactgtt cagttctgt tagcc 26  
  
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<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.001)  
  
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atcgccctgca ggtaaaagca tatgg	25
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gtcaaatcgc ctgcaggtaa aagca	25
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caacagatct gtcaaatcgc ctgca	25
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tttctcaaca gatctgtcaa atcgc	25
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ccatttctca acagatctgt caaat	25
 <pre><210> SEQ ID NO 256 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.008) <400> SEQUENCE: 256</pre>	
ataatgaaaa cgccgccatt tctca	25

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<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.009)

<400> SEQUENCE: 257
aaatatctt atatcataat gaaaa 25

<210> SEQ ID NO 258
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.010)

<400> SEQUENCE: 258
tgttagccac tgattaaata tcttt 25

<210> SEQ ID NO 259
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.013)

<400> SEQUENCE: 259
ccaattctca ggaatttgcg tcttt 25

<210> SEQ ID NO 260
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.014)

<400> SEQUENCE: 260
gtattttagca tgttcccaat tctca 25

<210> SEQ ID NO 261
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.015)

<400> SEQUENCE: 261
cttaagatac catttgtatt tagca 25

<210> SEQ ID NO 262
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.016)

<400> SEQUENCE: 262
cttaccttaa gataccattt gtatt 25

<210> SEQ ID NO 263
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.017)  
  
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<210> SEQ ID NO 264  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.018)  
  
<400> SEQUENCE: 264  
  
aaatcaaaga cttaccttaa gatac 25  
  
<210> SEQ ID NO 265  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.019)  
  
<400> SEQUENCE: 265  
  
aaaacaaatc aaagacttac cttaa 25  
  
<210> SEQ ID NO 266  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon44.25.020)  
  
<400> SEQUENCE: 266  
  
tcgaaaaaac aaatcaaaga cttac 25  
  
<210> SEQ ID NO 267  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.001)  
  
<400> SEQUENCE: 267  
  
ctgtaaagata ccaaaaaggc aaaac 25  
  
<210> SEQ ID NO 268  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.002)  
  
<400> SEQUENCE: 268  
  
cctgtaaagat accaaaaagg caaaa 25  
  
<210> SEQ ID NO 269  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.002.2)  
  
<400> SEQUENCE: 269
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agttcctgta agataccaaa aaggc	25
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gagttcctgt aagataccaa aaagg	25
 <pre><210> SEQ ID NO 271 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.003.2)</pre>	
<400> SEQUENCE: 271	
cctggagttc ctgtaagata cccaa	25
 <pre><210> SEQ ID NO 272 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.004)</pre>	
<400> SEQUENCE: 272	
tcctggagtt cctgtaagat accaa	25
 <pre><210> SEQ ID NO 273 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.004.2)</pre>	
<400> SEQUENCE: 273	
gccccatcctgg agttcctgta agata	25
 <pre><210> SEQ ID NO 274 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.005)</pre>	
<400> SEQUENCE: 274	
tgcctatcctg gagttcctgt aagat	25
 <pre><210> SEQ ID NO 275 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.005.2)</pre>	
<400> SEQUENCE: 275	
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<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.006)

<400> SEQUENCE: 276
ccaaatgcca tcctggagtt cctgt 25

<210> SEQ ID NO 277
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.006.2)

<400> SEQUENCE: 277
gctgccccaa gccatcctgg agttc 25

<210> SEQ ID NO 278
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.007)

<400> SEQUENCE: 278
cgctgccccaa tgccatcctg gagtt 25

<210> SEQ ID NO 279
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.008)

<400> SEQUENCE: 279
aacagtttgc cgctgccccaa tgcca 25

<210> SEQ ID NO 280
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.008.2)

<400> SEQUENCE: 280
ctgacaacag tttgccgtg cccaa 25

<210> SEQ ID NO 281
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.009)

<400> SEQUENCE: 281
gttgcattca atgttctgac aacag 25

<210> SEQ ID NO 282
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.010)  
  
<400> SEQUENCE: 282  
  
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<210> SEQ ID NO 283  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.010.2)  
  
<400> SEQUENCE: 283  
  
attattttctt ccccagttgc attca 25  
  
<210> SEQ ID NO 284  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.011)  
  
<400> SEQUENCE: 284  
  
ggcatctgtt tttgaggatt gctga 25  
  
<210> SEQ ID NO 285  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.011.2)  
  
<400> SEQUENCE: 285  
  
tttgaggatt gctgaattat ttctt 25  
  
<210> SEQ ID NO 286  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.012)  
  
<400> SEQUENCE: 286  
  
aatttttcct gtagaatact ggcatt 25  
  
<210> SEQ ID NO 287  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.012.2)  
  
<400> SEQUENCE: 287  
  
atactggcat ctgttttga ggatt 25  
  
<210> SEQ ID NO 288  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.013)  
  
<400> SEQUENCE: 288
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accgcagatt caggcttccc aattt	25
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ctgtttgcag acctcctgcc accgc	25
 <pre><210> SEQ ID NO 290 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.014.2)</pre>	
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agattcaggc ttcccaattt ttccct	25
 <pre><210> SEQ ID NO 291 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.015)</pre>	
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ctcttttttc tgtctgacag ctgtt	25
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acctcctgcc accgcagatt cagggc	25
 <pre><210> SEQ ID NO 293 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.016)</pre>	
<400> SEQUENCE: 293	
cctacactttt ttttctgtct gacag	25
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<400> SEQUENCE: 294	
gacagctgtt tgcagacctc ctgcc	25

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<210> SEQ ID NO 295
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.017)

<400> SEQUENCE: 295

gtcgccctac ctctttttc tgtct 25

<210> SEQ ID NO 296
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.018)

<400> SEQUENCE: 296

gatctgtcgc cctacctttt 25

<210> SEQ ID NO 297
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.019)

<400> SEQUENCE: 297

tattagatct gtcgcctac ctctt 25

<210> SEQ ID NO 298
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.25.020)

<400> SEQUENCE: 298

attccttata gatctgtcgc cctac 25

<210> SEQ ID NO 299
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.001)

<400> SEQUENCE: 299

agataccaaa aaggcaaaac 20

<210> SEQ ID NO 300
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.002)

<400> SEQUENCE: 300

aagataccaa aaggcaaaa 20

<210> SEQ ID NO 301
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.003)  
  
<400> SEQUENCE: 301  
  
cctgtaagat accaaaaagg 20  
  
<210> SEQ ID NO 302  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.004)  
  
<400> SEQUENCE: 302  
  
gagttcctgt aagataccaa 20  
  
<210> SEQ ID NO 303  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.005)  
  
<400> SEQUENCE: 303  
  
tcctggagtt cctgtaagat 20  
  
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<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.006)  
  
<400> SEQUENCE: 304  
  
tgccatcctg gagttcctgt 20  
  
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<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.007)  
  
<400> SEQUENCE: 305  
  
cccaatgcca tcctggagtt 20  
  
<210> SEQ ID NO 306  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.008)  
  
<400> SEQUENCE: 306  
  
cgctgccccaa tgccatcctg 20  
  
<210> SEQ ID NO 307  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.009)  
  
<400> SEQUENCE: 307
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ctgacaacag tttgccgtg	20
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gttgcattca atgttctgac	20
 <pre><210> SEQ ID NO 309 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.011) <400> SEQUENCE: 309</pre>	
attatttctt ccccagttgc	20
 <pre><210> SEQ ID NO 310 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.012) <400> SEQUENCE: 310</pre>	
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 <pre><210> SEQ ID NO 311 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.013) <400> SEQUENCE: 311</pre>	
atactggcat ctgtttttga	20
 <pre><210> SEQ ID NO 312 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.014) <400> SEQUENCE: 312</pre>	
aatttttcctt gtagaatact	20
 <pre><210> SEQ ID NO 313 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.015) <400> SEQUENCE: 313</pre>	
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<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.016)

<400> SEQUENCE: 314
acccctcgcc accgcagatt 20

<210> SEQ ID NO 315
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.017)

<400> SEQUENCE: 315
gacagctgtt tgcagacctc 20

<210> SEQ ID NO 316
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.018)

<400> SEQUENCE: 316
ctctttttc tgtctgacag 20

<210> SEQ ID NO 317
<211> LENGTH: 20
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.019)

<400> SEQUENCE: 317
cctacacctt ttttctgtct 20

<210> SEQ ID NO 318
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.020)

<400> SEQUENCE: 318
gtcgccctac ctctttttc 20

<210> SEQ ID NO 319
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.021)

<400> SEQUENCE: 319
gatctgtcgc cctacacctt 20

<210> SEQ ID NO 320
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.022)  
  
<400> SEQUENCE: 320  
  
tattagatct gtcgcccctac 20  
  
<210> SEQ ID NO 321  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon45.20.023)  
  
<400> SEQUENCE: 321  
  
atccctatta gatctgtcgc 20  
  
<210> SEQ ID NO 322  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.001)  
  
<400> SEQUENCE: 322  
  
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<210> SEQ ID NO 323  
<211> LENGTH: 25  
<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.002)  
  
<400> SEQUENCE: 323  
  
atttgagaaa ataaaattac ctgta 25  
  
<210> SEQ ID NO 324  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.002.2)  
  
<400> SEQUENCE: 324  
  
ctagcctgga gaaagaagaa taaaa 25  
  
<210> SEQ ID NO 325  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.003)  
  
<400> SEQUENCE: 325  
  
agaaaataaa attaccttga ctgac 25  
  
<210> SEQ ID NO 326  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.003.2)  
  
<400> SEQUENCE: 326
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ttcttcttagc ctggagaaag aagaa	25
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ataaaattac cttgacttgc tcaag	25
 <pre><210> SEQ ID NO 328 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.004.2)</pre>	
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ttttgttctt ctagcctgga gaaag	25
 <pre><210> SEQ ID NO 329 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.005)</pre>	
<400> SEQUENCE: 329	
attaccttga cttgctcaag ctttt	25
 <pre><210> SEQ ID NO 330 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.005.2)</pre>	
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tattcttttg ttcttcttagc ctgga	25
 <pre><210> SEQ ID NO 331 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.006)</pre>	
<400> SEQUENCE: 331	
cttgacttgc tcaagctttt ctttt	25
 <pre><210> SEQ ID NO 332 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.006.2)</pre>	
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caagatattc ttttgttctt ctagc	25

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<210> SEQ ID NO 333
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.007)

<400> SEQUENCE: 333
cttttagttg ctgctttt ccagg 25

<210> SEQ ID NO 334
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.008)

<400> SEQUENCE: 334
ccaggttcaa gtgggatact agcaa 25

<210> SEQ ID NO 335
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.008.2)

<400> SEQUENCE: 335
atctcttga aattctgaca agata 25

<210> SEQ ID NO 336
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.009)

<400> SEQUENCE: 336
agcaatgtta tctgcttcct ccaac 25

<210> SEQ ID NO 337
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.009.2)

<400> SEQUENCE: 337
aacaaattca tttaaatctc tttga 25

<210> SEQ ID NO 338
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.010)

<400> SEQUENCE: 338
ccaaaccataa aacaaattca tttaa 25

<210> SEQ ID NO 339
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.010.2)

<400> SEQUENCE: 339

ttcctccaaac cataaaacaa attca

25

<210> SEQ ID NO 340
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.011)

<400> SEQUENCE: 340

ttaaatctc tttgaaattc tgaca

25

<210> SEQ ID NO 341
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.012)

<400> SEQUENCE: 341

tgacaagata ttctttgtt cttct

25

<210> SEQ ID NO 342
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.012.2)

<400> SEQUENCE: 342

ttcaagtggg atactagcaa tgtta

25

<210> SEQ ID NO 343
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.013)

<400> SEQUENCE: 343

agatattctt ttgttcttctt agcct

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<210> SEQ ID NO 344
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.013.2)

<400> SEQUENCE: 344

ctgctctttt ccaggttcaa gtggg

25

<210> SEQ ID NO 345
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.014)

<400> SEQUENCE: 345

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ttctttgtt cttctagect ggaga	25
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cttttctttt agttgctgct ctttt	25
 <pre><210> SEQ ID NO 347 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.015)</pre>	
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tggttcttct agcctggaga aagaa	25
 <pre><210> SEQ ID NO 348 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.016)</pre>	
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cttcttagcct ggagaaaagaa gaata	25
 <pre><210> SEQ ID NO 349 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.017)</pre>	
<400> SEQUENCE: 349	
agcctggaga aagaagaata aaatt	25
 <pre><210> SEQ ID NO 350 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.25.018)</pre>	
<400> SEQUENCE: 350	
ctggagaaaag aagaataaaaa ttgtt	25
 <pre><210> SEQ ID NO 351 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.001)</pre>	
<400> SEQUENCE: 351	
gaaagaagaa taaaattgtt	20

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<210> SEQ ID NO 352
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.002)
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<400> SEQUENCE: 352
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ggagaaaagaa gaataaaatt 20
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<210> SEQ ID NO 353
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.003)
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<400> SEQUENCE: 353
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agcctggaga aagaagaata 20
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<210> SEQ ID NO 354
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.004)
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<400> SEQUENCE: 354
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cttcttagcct ggagaaaagaa 20
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<210> SEQ ID NO 355
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.005)
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<400> SEQUENCE: 355
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ttgttcttct agcctggaga 20
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<210> SEQ ID NO 356
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.006)
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<400> SEQUENCE: 356
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ttcttttgtt cttcttagcct 20
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<210> SEQ ID NO 357
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.007)
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<400> SEQUENCE: 357
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tgacaagata ttcttttgtt 20
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<210> SEQ ID NO 358
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.008)  
  
<400> SEQUENCE: 358  
  
atctctttga aattctgaca 20  
  
<210> SEQ ID NO 359  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.009)  
  
<400> SEQUENCE: 359  
  
aacaattca tttaaatctc 20  
  
<210> SEQ ID NO 360  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.010)  
  
<400> SEQUENCE: 360  
  
ttcctccaaac cataaaaacaa 20  
  
<210> SEQ ID NO 361  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.011)  
  
<400> SEQUENCE: 361  
  
agcaatgtta tctgcttct 20  
  
<210> SEQ ID NO 362  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.012)  
  
<400> SEQUENCE: 362  
  
ttcaagtggg atactagcaa 20  
  
<210> SEQ ID NO 363  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.013)  
  
<400> SEQUENCE: 363  
  
ctgctctttt ccaggttcaa 20  
  
<210> SEQ ID NO 364  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.014)  
  
<400> SEQUENCE: 364
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ctttttttt agttgctgct	20
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cttgacttgc tcaagctttt	20
 <pre><210> SEQ ID NO 366 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.016) <400> SEQUENCE: 366</pre>	
attaccttga cttgctcaag	20
 <pre><210> SEQ ID NO 367 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.017) <400> SEQUENCE: 367</pre>	
ataaaattac cttgacttgc	20
 <pre><210> SEQ ID NO 368 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.018) <400> SEQUENCE: 368</pre>	
agaaaataaa attaccttga	20
 <pre><210> SEQ ID NO 369 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.019) <400> SEQUENCE: 369</pre>	
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 <pre><210> SEQ ID NO 370 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon46.20.020) <400> SEQUENCE: 370</pre>	
ggggggatttg agaaaataaa	20

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<210> SEQ ID NO 371
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.001)

<400> SEQUENCE: 371
ctgaaacaga caaatgcaac aacgt 25

<210> SEQ ID NO 372
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.002)

<400> SEQUENCE: 372
agtaactgaa acagacaaat gcaac 25

<210> SEQ ID NO 373
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.003)

<400> SEQUENCE: 373
ccaccaggtaa ctgaaacaga caaat 25

<210> SEQ ID NO 374
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.004)

<400> SEQUENCE: 374
ctttccacc agtaactgaa acaga 25

<210> SEQ ID NO 375
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.005)

<400> SEQUENCE: 375
ggcaacttccacc ccaccaggtaa ctgaa 25

<210> SEQ ID NO 376
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.006)

<400> SEQUENCE: 376
gcaggggcaaa ctttccacc agtaa 25

<210> SEQ ID NO 377
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.007)  
  
<400> SEQUENCE: 377  
  
ctggcgcgagg ggcaactctt ccacc 25  
  
<210> SEQ ID NO 378  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.008)  
  
<400> SEQUENCE: 378  
  
ttaattgtt tgagaattcc ctggc 25  
  
<210> SEQ ID NO 379  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.008.2)  
  
<400> SEQUENCE: 379  
  
ttgtttgaga attccctggc gcagg 25  
  
<210> SEQ ID NO 380  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.009)  
  
<400> SEQUENCE: 380  
  
gcacgggtcc tccagtttca tttaa 25  
  
<210> SEQ ID NO 381  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.009.2)  
  
<400> SEQUENCE: 381  
  
tccagtttca tttaattgtt tgaga 25  
  
<210> SEQ ID NO 382  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.010)  
  
<400> SEQUENCE: 382  
  
gcttatggga gcacttacaa gcacg 25  
  
<210> SEQ ID NO 383  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.010.2)  
  
<400> SEQUENCE: 383
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tacaaggcag ggtcctccag tttca	25
 <pre><210> SEQ ID NO 384 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.011) <400> SEQUENCE: 384</pre>	
agtttatctt gctcttctgg gctta	25
 <pre><210> SEQ ID NO 385 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.012) <400> SEQUENCE: 385</pre>	
tctgctttag cttatttca agttt	25
 <pre><210> SEQ ID NO 386 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.012.2) <400> SEQUENCE: 386</pre>	
atcttgctct tctgggctta tggga	25
 <pre><210> SEQ ID NO 387 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.013) <400> SEQUENCE: 387</pre>	
ctttatccac tggagatttgc tctgc	25
 <pre><210> SEQ ID NO 388 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.013.2) <400> SEQUENCE: 388</pre>	
cttattttca agtttatctt gctct	25
 <pre><210> SEQ ID NO 389 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.014) <400> SEQUENCE: 389</pre>	
ctaaccttta tccactggag atttg	25

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<210> SEQ ID NO 390
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.014.2)

<400> SEQUENCE: 390

atttgtctgc ttgagttat tttca 25

<210> SEQ ID NO 391
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.015)

<400> SEQUENCE: 391

aatgtctaac ctttatccac tggag 25

<210> SEQ ID NO 392
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.016)

<400> SEQUENCE: 392

tggtaatgt ctaaccctta tccac 25

<210> SEQ ID NO 393
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.017)

<400> SEQUENCE: 393

agagatggtt aatgtctaac ctta 25

<210> SEQ ID NO 394
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.25.018)

<400> SEQUENCE: 394

acggaagaga tggtaatgt ctaac 25

<210> SEQ ID NO 395
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.001)

<400> SEQUENCE: 395

acagacaaat gcaacaacgt 20

<210> SEQ ID NO 396
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.002)

<400> SEQUENCE: 396

ctgaaacaga caaatgcaac

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<210> SEQ ID NO 397
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.003)

<400> SEQUENCE: 397

agtaactgaa acagacaaat

20

<210> SEQ ID NO 398
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.004)

<400> SEQUENCE: 398

ccaccagtaa ctgaaacaga

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<210> SEQ ID NO 399
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.005)

<400> SEQUENCE: 399

ctttccacc agtaactgaa

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<400> SEQUENCE: 400

ggcaacttcc accagtaa

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<210> SEQ ID NO 401
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 401

ctggcgccagg ggcaacttcc

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<210> SEQ ID NO 402
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 402

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<220> FEATURE:
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<400> SEQUENCE: 409
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.016)
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<400> SEQUENCE: 410
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<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.017)
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<400> SEQUENCE: 411
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<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.018)
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<400> SEQUENCE: 412
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<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.019)
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<400> SEQUENCE: 413
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<210> SEQ ID NO 414
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon47.20.020)
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<400> SEQUENCE: 414
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acggaagaga tggtaatgt 20
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.001)  
  
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<210> SEQ ID NO 416  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.002)  
  
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<210> SEQ ID NO 417  
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<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.002.2)  
  
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gaaacacctgaa agggaaaatac atttt 25  
  
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<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.003)  
  
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<210> SEQ ID NO 419  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.003.2)  
  
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ctctggaaac ctgaaaggaa aatac 25  
  
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<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.004)  
  
<400> SEQUENCE: 420  
  
gctctggaaa cctgaaagga aaata 25  
  
<210> SEQ ID NO 421  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.004.2)  
  
<400> SEQUENCE: 421
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taaagctctg gaaacctgaa aggaa	25
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tcaggtaaag ctctggaaac ctgaa	25
 <pre><210> SEQ ID NO 424 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.006)</pre>	
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ctcaggtaaa gctctggaaa cctga	25
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<210> SEQ ID NO 428
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.008)

<400> SEQUENCE: 428

tttgagctc aatttctcct ttttt 25

<210> SEQ ID NO 429
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.008)

<400> SEQUENCE: 429

ttttatgttga gcttcaattt ctccct 25

<210> SEQ ID NO 430
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.009)

<400> SEQUENCE: 430

aagctgcccc aaggctttta ttttga 25

<210> SEQ ID NO 431
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.010)

<400> SEQUENCE: 431

aggctttcaa gcttttttc aagct 25

<210> SEQ ID NO 432
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.010.2)

<400> SEQUENCE: 432

ttcaagcttt ttttcaagct gcccc 25

<210> SEQ ID NO 433
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.011)

<400> SEQUENCE: 433

gatgatttaa ctgctttca aggtc 25

<210> SEQ ID NO 434
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.011.2)

<400> SEQUENCE: 434

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25

<210> SEQ ID NO 435
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.012)

<400> SEQUENCE: 435

aggagataac cacagcagca gatga

25

<210> SEQ ID NO 436
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.012.2)

<400> SEQUENCE: 436

cagcagatga tttaactgct cttca

25

<210> SEQ ID NO 437
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.013)

<400> SEQUENCE: 437

atttccaact gattcctaat aggag

25

<210> SEQ ID NO 438
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.014)

<400> SEQUENCE: 438

cttggtttgg ttgggtataa atttc

25

<210> SEQ ID NO 439
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.014.2)

<400> SEQUENCE: 439

caactgattc ctaataggag ataac

25

<210> SEQ ID NO 440
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.015)

<400> SEQUENCE: 440

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cctacacctaa cgtcaaatgg tcctt	25
 <pre><210> SEQ ID NO 443 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.016.2)</pre>	
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tccttcttgg tttgggttgg tataa	25
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agttccctac cttaacgtca aatgg	25
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caaaaagttc cctacacctaa cgtca	25
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<210> SEQ ID NO 447
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.25.020)

<400> SEQUENCE: 447

atatttaaag caaaaagttc cctac 25

<210> SEQ ID NO 448
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.001)

<400> SEQUENCE: 448

aggaaaatac attttaaaaa 20

<210> SEQ ID NO 449
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.002)

<400> SEQUENCE: 449

aaggaaaata cattttaaaaa 20

<210> SEQ ID NO 450
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.003)

<400> SEQUENCE: 450

cctgaaagga aaatacacattt 20

<210> SEQ ID NO 451
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.004)

<400> SEQUENCE: 451

gaaaacctga aaggaaaata 20

<210> SEQ ID NO 452
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.005)

<400> SEQUENCE: 452

gctctggaaa cctgaaagga 20

<210> SEQ ID NO 453
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.006)

<400> SEQUENCE: 453

gtaaaagctctt gggaaacctgaa

20

<210> SEQ ID NO 454
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.007)

<400> SEQUENCE: 454

ctcaggtaaa gctctggaaa

20

<210> SEQ ID NO 455
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.008)

<400> SEQUENCE: 455

aatttctcctt tgtttctcag

20

<210> SEQ ID NO 456
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.009)

<400> SEQUENCE: 456

ttttatgttga gcttcaattt

20

<210> SEQ ID NO 457
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.010)

<400> SEQUENCE: 457

aagctgccccca aggtctttta

20

<210> SEQ ID NO 458
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.011)

<400> SEQUENCE: 458

ttcaagctttt ttttcaagct

20

<210> SEQ ID NO 459
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.012)

<400> SEQUENCE: 459

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aggagataac cacagcagca	20
 <pre><210> SEQ ID NO 462 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.015) <400> SEQUENCE: 462</pre>	
caactgattc ctaataggag	20
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ttggttataa atttccaaact	20
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tccttcttgg tttgggttgg	20
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<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.019)

<400> SEQUENCE: 466
cctacacctaa cgtcaaatgg                                20

<210> SEQ ID NO 467
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.020)

<400> SEQUENCE: 467
agttccctac cttAACgtca                                20

<210> SEQ ID NO 468
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.021)

<400> SEQUENCE: 468
caaaaagttc cctacacctaa                                20

<210> SEQ ID NO 469
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.022)

<400> SEQUENCE: 469
taaAGcaaaa agttccctac                                20

<210> SEQ ID NO 470
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon48.20.023)

<400> SEQUENCE: 470
atatttaaag caaaaagttc                                20

<210> SEQ ID NO 471
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.001)

<400> SEQUENCE: 471
ctggggaaaaa gaacccatat agtgc                                25

<210> SEQ ID NO 472
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.002)  
  
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<210> SEQ ID NO 473  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.002.2)  
  
<400> SEQUENCE: 473  
  
gttcctggg gaaaagaacc catat 25  
  
<210> SEQ ID NO 474  
<211> LENGTH: 25  
<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.003)  
  
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<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.003.2)  
  
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tttcagttc ctggggaaaa gaacc 25  
  
<210> SEQ ID NO 476  
<211> LENGTH: 25  
<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.004)  
  
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tatttcagtt tcctgggaa aagaa 25  
  
<210> SEQ ID NO 477  
<211> LENGTH: 25  
<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.004.2)  
  
<400> SEQUENCE: 477  
  
tgctatttca gtttcctggg gaaaa 25  
  
<210> SEQ ID NO 478  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.25.005)  
  
<400> SEQUENCE: 478
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<210> SEQ ID NO 493
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<400> SEQUENCE: 493

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<210> SEQ ID NO 494
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<400> SEQUENCE: 494

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<210> SEQ ID NO 495
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gaaaagaacc catatagtgc

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<210> SEQ ID NO 496
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ggaaaaagaa cccatatagt

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<400> SEQUENCE: 504

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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.20.013)

<400> SEQUENCE: 507

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<400> SEQUENCE: 508

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 509

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.20.016)

<400> SEQUENCE: 510

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<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon49.20.017)

<400> SEQUENCE: 511

gctagagggtt gcttcattac

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<400> SEQUENCE: 512

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<210> SEQ ID NO 513
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<212> TYPE: DNA
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<400> SEQUENCE: 513

ctttaacaga aaagcataca catta

25

<210> SEQ ID NO 514
<211> LENGTH: 25
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.002)

<400> SEQUENCE: 514

tcctctttaa cagaaaagca tacac

25

<210> SEQ ID NO 515
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.002.2)

<400> SEQUENCE: 515

ttcctcttta acagaaaagc ataca

25

<210> SEQ ID NO 516
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.003)

<400> SEQUENCE: 516

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.006.2 NG-08-0731)

<400> SEQUENCE: 523

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<210> SEQ ID NO 524
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.007)

<400> SEQUENCE: 524

cactcagagc tcagatcttc tact 24

<210> SEQ ID NO 525
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.007.2)

<400> SEQUENCE: 525

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<210> SEQ ID NO 526
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<400> SEQUENCE: 526

gttaaacgggtt taccgccttc cactc 25

<210> SEQ ID NO 527
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.009)

<400> SEQUENCE: 527

ctttgcctc agctcttcaa gtaaa 25

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.009.2)

<400> SEQUENCE: 528

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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.010)  
  
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<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.010.2)  
  
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<212> TYPE: DNA  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.011)  
  
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<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.011.2)  
  
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<212> TYPE: DNA  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.012 AVI-5038)  
  
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<210> SEQ ID NO 534  
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<212> TYPE: DNA  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.013)  
  
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<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.25.014)  
  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.20.005)

<400> SEQUENCE: 542

tcttcttaact tcctctttaa 20

<210> SEQ ID NO 543
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.20.006)

<400> SEQUENCE: 543

tcagatcttc taacttcctc 20

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.20.007)

<400> SEQUENCE: 544

ccttccactc agagctcaga 20

<210> SEQ ID NO 545
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.20.008)

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<210> SEQ ID NO 546
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.20.013)  
  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.20.014)  
  
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<212> TYPE: DNA  
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<220> FEATURE:  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon50.20.016)  
  
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tgagtaggag ctaaaaatattt ttgggg	25
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<210> SEQ ID NO 561
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.004.2)

<400> SEQUENCE: 561

cagtctgagt aggagctaaa atatt 25

<210> SEQ ID NO 562
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.005)

<400> SEQUENCE: 562

acagtctgag taggagctaa aatatt 26

<210> SEQ ID NO 563
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.005.2)

<400> SEQUENCE: 563

gagtaacagt ctgagtagga gctaaa 26

<210> SEQ ID NO 564
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.006)

<400> SEQUENCE: 564

cagagtaaca gtctgagtag gagct 25

<210> SEQ ID NO 565
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.006.2)

<400> SEQUENCE: 565

caccagagta acagtctgag taggag 26

<210> SEQ ID NO 566
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.007)

<400> SEQUENCE: 566

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<210> SEQ ID NO 567
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.007.2)

<400> SEQUENCE: 567

aaccacaggt tgtgtcacca gagtaa

26

<210> SEQ ID NO 568
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.008)

<400> SEQUENCE: 568

gttgtgtcac cagagtaaca gtctg

25

<210> SEQ ID NO 569
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.009)

<400> SEQUENCE: 569

tggcagtttc cttagtaacc acaggt

26

<210> SEQ ID NO 570
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.010)

<400> SEQUENCE: 570

atttctagtt tggagatggc agtttc

26

<210> SEQ ID NO 571
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.010.2)

<400> SEQUENCE: 571

ggaagatggc atttctagtt tggag

25

<210> SEQ ID NO 572
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.011)

<400> SEQUENCE: 572

catcaaggaa gatggcattt cttagtt

26

<210> SEQ ID NO 573
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<212> TYPE: DNA
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<400> SEQUENCE: 573

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gagcaggtac ctccaacatc aaggaa 26

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<211> LENGTH: 25
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.012)
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<400> SEQUENCE: 574

atctgccaga gcaggtacct ccaac 25

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<210> SEQ ID NO 575
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.013)
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<400> SEQUENCE: 575

aagttctgtc caagcccggt tgaat 26

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<210> SEQ ID NO 576
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 576

cggttgaaat ctgccagac aggtac 26

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<210> SEQ ID NO 577
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.014)
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<400> SEQUENCE: 577

gagaaagcca gtcggtaagt tctgtc 26

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<210> SEQ ID NO 578
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.014.2)
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<400> SEQUENCE: 578

gtcggttaagt tctgtccaag cccgg 25

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<210> SEQ ID NO 579
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.015)
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<400> SEQUENCE: 579

ataacttgat caagcagaga aagcca 26

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<210> SEQ ID NO 580
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.015.2)

<400> SEQUENCE: 580

aagcagagaa agccagtcgg taagt

25

<210> SEQ ID NO 581
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.016)

<400> SEQUENCE: 581

caccctctgt gattttataa cttgat

26

<210> SEQ ID NO 582
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.017)

<400> SEQUENCE: 582

caaggtcacc caccatcacc ctctgt

26

<210> SEQ ID NO 583
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.017.2)

<400> SEQUENCE: 583

catcacccctc tgtgatttta taact

25

<210> SEQ ID NO 584
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.018)

<400> SEQUENCE: 584

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26

<210> SEQ ID NO 585
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.019)

<400> SEQUENCE: 585

cttctgctt gatgatcatc tcgttg

26

<210> SEQ ID NO 586
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.019.2)

<400> SEQUENCE: 586

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26

<210> SEQ ID NO 587
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.020)

<400> SEQUENCE: 587

tcatcaccc tcgttgatga tcatct

26

<210> SEQ ID NO 588
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.020.2)

<400> SEQUENCE: 588

tcatattttc tcataccctc tgcttg

26

<210> SEQ ID NO 589
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.021)

<400> SEQUENCE: 589

ttttctcata ccttctgttt gatgtat

26

<210> SEQ ID NO 590
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.022)

<400> SEQUENCE: 590

ttttatcatt ttttctcata ccttct

26

<210> SEQ ID NO 591
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.25.023)

<400> SEQUENCE: 591

ccaaatttta tcatattttc tcatac

26

<210> SEQ ID NO 592
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.001)

<400> SEQUENCE: 592

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 <pre><210> SEQ ID NO 594 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.003) <400> SEQUENCE: 594</pre>	
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 <pre><210> SEQ ID NO 595 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.004) <400> SEQUENCE: 595</pre>	
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 <pre><210> SEQ ID NO 596 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.005) <400> SEQUENCE: 596</pre>	
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 <pre><210> SEQ ID NO 598 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.007) <400> SEQUENCE: 598</pre>	
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<210> SEQ ID NO 599
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.008)

<400> SEQUENCE: 599

cacaggttgt gtcaccagag

20

<210> SEQ ID NO 600
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.009)

<400> SEQUENCE: 600

agtttcctta gtaaccacag

20

<210> SEQ ID NO 601
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.010)

<400> SEQUENCE: 601

tagtttggag atggcagtt

20

<210> SEQ ID NO 602
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.011)

<400> SEQUENCE: 602

ggaagatggc atttctagtt

20

<210> SEQ ID NO 603
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.012)

<400> SEQUENCE: 603

tacctccaac atcaaggaag

20

<210> SEQ ID NO 604
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.013)

<400> SEQUENCE: 604

atctgccaga gcaggtacct

20

<210> SEQ ID NO 605
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.014)  
  
<400> SEQUENCE: 605  
  
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<210> SEQ ID NO 606  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.015)  
  
<400> SEQUENCE: 606  
  
gtcggttaagt tctgtccaag 20  
  
<210> SEQ ID NO 607  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.016)  
  
<400> SEQUENCE: 607  
  
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<210> SEQ ID NO 608  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.017)  
  
<400> SEQUENCE: 608  
  
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<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.018)  
  
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<210> SEQ ID NO 610  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.019)  
  
<400> SEQUENCE: 610  
  
ctcaagggtca cccaccatca 20  
  
<210> SEQ ID NO 611  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.020)  
  
<400> SEQUENCE: 611
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cataccttct gcttgatgat	20
 <pre><210> SEQ ID NO 614 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon51.20.023) <400> SEQUENCE: 614</pre>	
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.001)

<400> SEQUENCE: 618
ctgttaagaac aaatatccct tagta                                25

<210> SEQ ID NO 619
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.002)

<400> SEQUENCE: 619
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<210> SEQ ID NO 620
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.002.2)

<400> SEQUENCE: 620
gttgccctgtta agaacaataa tccct                                25

<210> SEQ ID NO 621
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.003)

<400> SEQUENCE: 621
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<210> SEQ ID NO 622
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.003.2)

<400> SEQUENCE: 622
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<210> SEQ ID NO 623
<211> LENGTH: 25
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.004)

<400> SEQUENCE: 623
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<210> SEQ ID NO 624
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.004.2)

<400> SEQUENCE: 624

atcctgcatt gttgcgtta agaac

25

<210> SEQ ID NO 625
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.005)

<400> SEQUENCE: 625

caaatcctgc attgttgctt gtaag

25

<210> SEQ ID NO 626
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.005.2)

<400> SEQUENCE: 626

tccaaatcct gcattgttgc ctgtt

25

<210> SEQ ID NO 627
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.006)

<400> SEQUENCE: 627

tgttccaaat cctgcattgtt tgcct

25

<210> SEQ ID NO 628
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.006.2)

<400> SEQUENCE: 628

tctgttccaa atcctgcatt gttgc

25

<210> SEQ ID NO 629
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.007)

<400> SEQUENCE: 629

aactggggac gcctctgttc caaat

25

<210> SEQ ID NO 630
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.007.2)

<400> SEQUENCE: 630

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 <pre><210> SEQ ID NO 631 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.008)</pre>	
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 <pre><210> SEQ ID NO 632 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.008.2)</pre>	
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cttccaactg gggacgcctc tgttc	25
 <pre><210> SEQ ID NO 633 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.009)</pre>	
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ttttcaatt ttgggcagcg gtaat	25
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.25.011.2)

<400> SEQUENCE: 637
gattgctggc cttgttttc aaatt 25

<210> SEQ ID NO 638
<211> LENGTH: 25
<212> TYPE: DNA
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<400> SEQUENCE: 638
cattacttcga tccgtaatga ttgtt 25

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<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 640
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<400> SEQUENCE: 641
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<210> SEQ ID NO 642
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<212> TYPE: DNA  
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<210> SEQ ID NO 646  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.20.003)  
  
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<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
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<210> SEQ ID NO 656
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<400> SEQUENCE: 656

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<213> ORGANISM: Artificial Sequence
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cttacttcga tccgtaatga 20

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.20.015)

<400> SEQUENCE: 658

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<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 659

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<220> FEATURE:
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<400> SEQUENCE: 660

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<210> SEQ ID NO 661
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon52.20.018)

<400> SEQUENCE: 661

gtcccatgct tgttaaaaaa 20

<210> SEQ ID NO 662
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.001)  
  
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<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.002)  
  
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<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.002.2)  
  
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<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.003)  
  
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<212> TYPE: DNA  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.003.2)  
  
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<211> LENGTH: 25  
<212> TYPE: DNA  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.004)  
  
<400> SEQUENCE: 667  
  
gaatttttc aactagaata aaagg 25  
  
<210> SEQ ID NO 668  
<211> LENGTH: 25  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.004.2)  
  
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 <pre><210> SEQ ID NO 671 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.006)</pre>	
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 <pre><210> SEQ ID NO 673 <211> LENGTH: 25 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.007)</pre>	
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<400> SEQUENCE: 675
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<210> SEQ ID NO 676
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.009.2)

<400> SEQUENCE: 676
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<210> SEQ ID NO 677
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.010)

<400> SEQUENCE: 677
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<210> SEQ ID NO 678
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.010.2)

<400> SEQUENCE: 678
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<210> SEQ ID NO 679
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.011)

<400> SEQUENCE: 679
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.012)

<400> SEQUENCE: 680
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<210> SEQ ID NO 681
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 681

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25

<210> SEQ ID NO 682
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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25

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<400> SEQUENCE: 683

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25

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.014)

<400> SEQUENCE: 684

ctcaagcttg gctctggct gtcct

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<210> SEQ ID NO 685
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.014.2)

<400> SEQUENCE: 685

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25

<210> SEQ ID NO 686
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.015)

<400> SEQUENCE: 686

tagggaccct cttccatga ctcaa

25

<210> SEQ ID NO 687
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.016)

<400> SEQUENCE: 687

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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.020)

<400> SEQUENCE: 694
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<210> SEQ ID NO 695
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.021)

<400> SEQUENCE: 695
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<210> SEQ ID NO 696
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.25.022)

<400> SEQUENCE: 696
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<210> SEQ ID NO 697
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<400> SEQUENCE: 697
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<210> SEQ ID NO 698
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.002)

<400> SEQUENCE: 698
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<210> SEQ ID NO 699
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.003)

<400> SEQUENCE: 699
aactagaata aaaggaaaaaa 20

<210> SEQ ID NO 700
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.004)  
  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.005)  
  
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gaattcttcc aactagaata 20  
  
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<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.006)  
  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.008)  
  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.009)  
  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.010)  
  
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<400> SEQUENCE: 713
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<210> SEQ ID NO 714
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<400> SEQUENCE: 714
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<210> SEQ ID NO 715
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.019)

<400> SEQUENCE: 715
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<210> SEQ ID NO 716
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon53.20.020)

<400> SEQUENCE: 716
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<210> SEQ ID NO 717
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<210> SEQ ID NO 718
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<220> FEATURE:  
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<220> FEATURE:  
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<212> TYPE: DNA  
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<220> FEATURE:  
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<220> FEATURE:  
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<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.004)  
  
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<212> TYPE: DNA  
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<220> FEATURE:  
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<400> SEQUENCE: 732

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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.011)

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<210> SEQ ID NO 734
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<400> SEQUENCE: 734

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<211> LENGTH: 25
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<400> SEQUENCE: 735

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<400> SEQUENCE: 736

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.013.2)

<400> SEQUENCE: 737

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.014)

<400> SEQUENCE: 738

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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 739

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25

<210> SEQ ID NO 740
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.015)

<400> SEQUENCE: 740

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25

<210> SEQ ID NO 741
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.016)

<400> SEQUENCE: 741

taatgttaatt catacccttt atgaa

25

<210> SEQ ID NO 742
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.017)

<400> SEQUENCE: 742

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25

<210> SEQ ID NO 743
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.25.018)

<400> SEQUENCE: 743

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25

<210> SEQ ID NO 744
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 <pre><210> SEQ ID NO 747 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.004) <400> SEQUENCE: 747</pre>	
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 <pre><210> SEQ ID NO 748 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.005) <400> SEQUENCE: 748</pre>	
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 <pre><210> SEQ ID NO 749 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.006) <400> SEQUENCE: 749</pre>	
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 <pre><210> SEQ ID NO 750 <211> LENGTH: 20 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.007) <400> SEQUENCE: 750</pre>	
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<210> SEQ ID NO 751
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.008)

<400> SEQUENCE: 751

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<210> SEQ ID NO 752
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.009)

<400> SEQUENCE: 752

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<210> SEQ ID NO 753
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<400> SEQUENCE: 753

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<210> SEQ ID NO 754
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.011)

<400> SEQUENCE: 754

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<210> SEQ ID NO 755
<211> LENGTH: 20
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.012)

<400> SEQUENCE: 755

atgtggactt ttctggtata 20

<210> SEQ ID NO 756
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.013)

<400> SEQUENCE: 756

atattctctg ttatcatgtg 20

<210> SEQ ID NO 757
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.014)  
  
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<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.015)  
  
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<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.016)  
  
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<210> SEQ ID NO 760  
<211> LENGTH: 20  
<212> TYPE: DNA  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.017)  
  
<400> SEQUENCE: 760  
  
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<210> SEQ ID NO 761  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.018)  
  
<400> SEQUENCE: 761  
  
taatgttaatt catacctttt 20  
  
<210> SEQ ID NO 762  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.019)  
  
<400> SEQUENCE: 762  
  
agaaataatg taattcatac 20  
  
<210> SEQ ID NO 763  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon54.20.020)  
  
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gttttagaaa taatgttaatt	20
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tcaccctgca aaggaccaaa tgttc	25
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ctcaactcacc ctgcaaaggaa ccaaa	25
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.007)

<400> SEQUENCE: 770
tcttccaaag cagcctctcg ctcac 25

<210> SEQ ID NO 771
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.007.2)

<400> SEQUENCE: 771
tctatgagtt tcttccaaag cagcc 25

<210> SEQ ID NO 772
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.008)

<400> SEQUENCE: 772
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<210> SEQ ID NO 773
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.008.2)

<400> SEQUENCE: 773
gaactgttgc agtaatctat gagtt 25

<210> SEQ ID NO 774
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.009)

<400> SEQUENCE: 774
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.010)

<400> SEQUENCE: 775
gtaagccagg caagaaactt ttcca 25

<210> SEQ ID NO 776
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.010.2)

<400> SEQUENCE: 776

ccaggcaaga aactttcca ggtcc

25

<210> SEQ ID NO 777
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.011)

<400> SEQUENCE: 777

tggcagttgt ttcagttct gtaag

25

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.011.2)

<400> SEQUENCE: 778

ttcagcttct gtaagccagg caaga

25

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.012)

<400> SEQUENCE: 779

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25

<210> SEQ ID NO 780
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.012.2)

<400> SEQUENCE: 780

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25

<210> SEQ ID NO 781
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.013)

<400> SEQUENCE: 781

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25

<210> SEQ ID NO 782
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.014)

<400> SEQUENCE: 782

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.018)

<400> SEQUENCE: 789
aaatgcctga cttacttgcc attgt 25

<210> SEQ ID NO 790
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.019)

<400> SEQUENCE: 790
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<210> SEQ ID NO 791
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.25.020)

<400> SEQUENCE: 791
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<210> SEQ ID NO 792
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<220> FEATURE:
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<400> SEQUENCE: 792
aaggacaaa tgttcagatg 20

<210> SEQ ID NO 793
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.20.002)

<400> SEQUENCE: 793
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<210> SEQ ID NO 794
<211> LENGTH: 20
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.20.003)

<400> SEQUENCE: 794
tcaccctgca aaggacaaa 20

<210> SEQ ID NO 795
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.20.004)  
  
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<210> SEQ ID NO 796  
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<212> TYPE: DNA  
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<223> OTHER INFORMATION: Synthetic (Hu.DMD.Exon55.20.005)  
  
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<400> SEQUENCE: 827

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<220> FEATURE:  
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<220> FEATURE:  
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<400> SEQUENCE: 851

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<223> OTHER INFORMATION: Synthetic (huEx53.30.84)  
  
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<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (huEx53.30.88)  
  
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<223> OTHER INFORMATION: Synthetic (huEx53.30.91)  
  
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<223> OTHER INFORMATION: Synthetic (huEx53.30.109)  
  
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<211> LENGTH: 30  
<212> TYPE: DNA  
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<220> FEATURE:  
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<223> OTHER INFORMATION: Xaa is beta-alanine  
  
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<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: Xaa is beta-alanine

<400> SEQUENCE: 865

Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Xaa
1 5 10

<210> SEQ ID NO 866
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RAhx) 6B)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: Xaa is beta-alanine

<400> SEQUENCE: 866

Arg Xaa Arg Xaa Arg Xaa Arg Xaa Arg Xaa Arg Xaa Xaa
1 5 10

<210> SEQ ID NO 867
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RAhx) 8B)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)

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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (15)..(15)
<223> OTHER INFORMATION: Xaa is beta-alanine

<400> SEQUENCE: 867

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Arg Xaa Xaa
1 5 10 15

```

```

<210> SEQ ID NO 868
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RAhxR)5AhxB)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (16)..(16)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (17)..(17)
<223> OTHER INFORMATION: Xaa is beta-alanine

<400> SEQUENCE: 868

```

```

Arg Xaa Arg Xaa
1 5 10 15

```

Xaa

```

<210> SEQ ID NO 869
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RAhxRRBR)2AhxB; (CPO6062))
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is beta-alanine

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<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (8)..(8)  
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (11)..(11)  
<223> OTHER INFORMATION: Xaa is beta-alanine  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (13)..(13)  
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid (Ahx)  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (14)..(14)  
<223> OTHER INFORMATION: Xaa is beta-alanine  
  
<400> SEQUENCE: 869
```

Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Xaa Xaa
1 5 10

```
<210> SEQ ID NO 870  
<211> LENGTH: 7  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (MSP)
```

```
<400> SEQUENCE: 870
```

Ala Ser Ser Leu Asn Ile Ala
1 5

```
<210> SEQ ID NO 871  
<211> LENGTH: 9  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (MSP-PMO)  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (8)..(9)  
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid  
  
<400> SEQUENCE: 871
```

Ala Ser Ser Leu Asn Ile Ala Xaa Xaa
1 5

```
<210> SEQ ID NO 872  
<211> LENGTH: 22  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic (CP06062-MSP-PMO)  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (2)..(2)  
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (5)..(5)  
<223> OTHER INFORMATION: Xaa is beta-alanine  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (8)..(8)  
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid  
<220> FEATURE:  
<221> NAME/KEY: misc_feature  
<222> LOCATION: (11)..(11)  
<223> OTHER INFORMATION: Xaa is beta-alanine  
<220> FEATURE:
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```

<221> NAME/KEY: misc_feature
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: Xaa is beta-alanine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (22)..(22)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid

<400> SEQUENCE: 872

```

```

Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Xaa Ala Ser
1           5           10          15

Ser Leu Asn Ile Ala Xaa
20

```

```

<210> SEQ ID NO 873
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (MSP-CP06062-PMO)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: Xaa is beta-alanine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (16)..(16)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (19)..(19)
<223> OTHER INFORMATION: Xaa is beta-alanine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (21)..(21)
<223> OTHER INFORMATION: Xaa is beta-alanine

<400> SEQUENCE: 873

```

```

Ala Ser Ser Leu Asn Ile Ala Xaa Arg Xaa Arg Arg Xaa
1           5           10          15

Arg Arg Xaa Arg Xaa
20

```

```

<210> SEQ ID NO 874
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (CP06062-PMO)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is beta-alanine
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Xaa is beta-alanine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: Xaa is beta-alanine

```

<400> SEQUENCE: 874

```

Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Xaa Xaa
1           5           10

```

```

<210> SEQ ID NO 875
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (PMO)

```

<400> SEQUENCE: 875

```

ggccaaacct cggcttacct gaaat           25

```

```

<210> SEQ ID NO 876
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (rTAT)

```

<400> SEQUENCE: 876

```

Arg Arg Arg Gln Arg Arg Lys Lys Arg
1           5

```

```

<210> SEQ ID NO 877
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (Tat)

```

<400> SEQUENCE: 877

```

Arg Lys Lys Arg Arg Gln Arg Arg Arg
1           5

```

```

<210> SEQ ID NO 878
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R9F2)

```

<400> SEQUENCE: 878

```

Arg Arg Arg Arg Arg Arg Arg Arg Arg Phe Phe
1           5           10

```

```

<210> SEQ ID NO 879
<211> LENGTH: 11
<212> TYPE: PRT

```

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R5F2R4)

<400> SEQUENCE: 879

Arg Arg Arg Arg Arg Phe Phe Arg Arg Arg Arg
1 5 10

<210> SEQ ID NO 880
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R4)

<400> SEQUENCE: 880

Arg Arg Arg Arg

1

<210> SEQ ID NO 881
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R5)

<400> SEQUENCE: 881

Arg Arg Arg Arg Arg

1 5

<210> SEQ ID NO 882
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R6)

<400> SEQUENCE: 882

Arg Arg Arg Arg Arg Arg

1 5

<210> SEQ ID NO 883
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R7)

<400> SEQUENCE: 883

Arg Arg Arg Arg Arg Arg Arg

1 5

<210> SEQ ID NO 884
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R8)

<400> SEQUENCE: 884

Arg Arg Arg Arg Arg Arg Arg Arg

1 5

<210> SEQ ID NO 885

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```

<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic (R9)

<400> SEQUENCE: 885

Arg Arg Arg Arg Arg Arg Arg Arg Arg
1 5

<210> SEQ ID NO 886
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RX)8)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (16)..(16)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid

<400> SEQUENCE: 886

Arg Xaa Arg Xaa Arg Xaa Arg Xaa Arg Xaa Arg Xaa Arg Xaa
1 5 10 15

<210> SEQ ID NO 887
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RAhxR)4; (P007) )
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (5)..(5)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
<220> FEATURE:

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<221> NAME/KEY: misc_feature
 <222> LOCATION: (11)..(11)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid

<400> SEQUENCE: 887

Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg
 1 5 10

<210> SEQ ID NO 888
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic ((RAhxR)5; (CP04057))
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (2)..(2)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (5)..(5)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (8)..(8)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (11)..(11)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (14)..(14)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid

<400> SEQUENCE: 888

Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg
 1 5 10 15

<210> SEQ ID NO 889
 <211> LENGTH: 12
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic ((RAhxRRBR)2; (CP06062))
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (2)..(2)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (5)..(5)
 <223> OTHER INFORMATION: Xaa is beta-alanine
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (8)..(8)
 <223> OTHER INFORMATION: Xaa is 6-aminohexanoic acid
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (11)..(11)
 <223> OTHER INFORMATION: Xaa is beta-alanine

<400> SEQUENCE: 889

Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg Arg Xaa Arg
 1 5 10

<210> SEQ ID NO 890
 <211> LENGTH: 14
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RAR)4F2)

<400> SEQUENCE: 890

Arg Ala Arg Arg Ala Arg Arg Ala Arg Arg Ala Arg Phe Phe
1           5           10

<210> SEQ ID NO 891
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic ((RGR)4F2))

<400> SEQUENCE: 891

Arg Gly Arg Arg Gly Arg Arg Gly Arg Arg Gly Arg Phe Phe
1           5           10

```

1. A method of treating Duchenne muscular dystrophy or Becker muscular dystrophy in a human subject comprising administering about 30 mg/kg to about 50 mg/kg of a composition comprising an antisense oligonucleotide of 20 to 50 nucleotides in length comprising at least 10 consecutive nucleotides complementary to a target region in an exon of the human dystrophin gene, wherein the antisense oligonucleotide specifically hybridizes to the target region inducing exon skipping, thereby treating Duchenne muscular dystrophy or Becker muscular dystrophy in the subject.

2. The method of claim 1, wherein treatment increases the number of dystrophin-positive fibers to at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% of normal in the subject.

3. The method of claim 2, wherein the number of dystrophin-positive fibers is increased to between 20-60% of normal in the human subject.

4. The method of claim 2, wherein the number of dystrophin-positive fibers is increased to between 30-50% of normal in the human subject.

5. The method of claim 1, wherein about 30 mg/kg of the composition is administered to the human subject.

6. The method of claim 1, wherein about 50 mg/kg of the composition is administered to the human subject.

7. The method of claim 1, wherein treatment improves or maintains a stable walking distance in a 6 minute walk test from a 20% deficit in the subject relative to a healthy peer.

8. The method of claim 1, wherein the antisense oligonucleotide is substantially uncharged.

9. The method of claim 1, wherein the antisense oligonucleotide comprises morpholino subunits linked by phosphorus-containing intersubunit linkages joining a morpholino nitrogen of one subunit to a 5' exocyclic carbon of an adjacent subunit.

10. The method of claim 1, wherein the antisense oligonucleotide comprises morpholino subunits linked by substantially uncharged phosphorus-containing intersubunit link-

ages joining a morpholino nitrogen of one subunit to a 5' exocyclic carbon of an adjacent subunit.

11. The method of claim 1, wherein the antisense oligonucleotide comprises morpholino subunits and phosphorodiamide intersubunit linkages.

12. The method of claim 1, wherein the antisense oligonucleotide is chemically linked to one or more moieties or conjugates that enhance the activity, cellular distribution, or cellular uptake of the antisense oligonucleotide.

13. The method of claim 12, wherein the antisense oligonucleotide is conjugated to an arginine-rich peptide.

14. The method of claim 1, wherein the antisense oligonucleotide is 30 to 50 nucleotides in length.

15. The method of claim 1, wherein the antisense oligonucleotide is 20 to 30 nucleotides in length.

16. The method of claim 1, wherein the exon in the human dystrophin gene is selected from the group consisting of exon 51, exon 50, exon 53, exon 45, exon 46, exon 44, exon 52, exon 55 and exon 8.

17. The method of claim 1, wherein the antisense oligonucleotide is selected from the group consisting of SEQ ID NOS: 1-9.

18. The method of claim 1, wherein the antisense oligonucleotide is SEQ ID NO: 1.

19. The method of claim 1, wherein the antisense oligonucleotide is any one or a combination of the nucleotide sequences set forth in Tables 3 and 4, wherein uracil bases in the antisense oligonucleotide are optionally thymine bases.

20. The method of claim 1, wherein the composition further comprises phosphate-buffered saline.

21. The method of claim 1, wherein the composition is administered by systemic administration.

22. The method of claim 1, wherein the composition is administered once weekly by infusion.

23. The method of claim 1, further comprising administering a steroid to the human subject.

* * * * *