the region R23 is a region that consists of a base sequence of 20 bases in the upstream direction from the 3' end of the 55th exon and a base sequence of 400 bases in the downstream direction from the 5' end of the 55th intron in the human dystrophin pre-mRNA, or

the region R24 is a region that consists of a base sequence of 400 bases in the upstream direction from the 3' end of the 55th intron and a base sequence of 50 bases in the downstream direction from the 5' end of the 56th exon in the human dystrophin pre-mRNA.

[0034]

In an alternative embodiment, R1 to R24 which are examples of the target region Rn of the present invention are, but not limited to, as follows:

(A1) Region R1

The region R1 is a region indicated by the range of -20 bases to +400 bases when the boundary between the 3' end of exon 44 and the 5' end of intron 44 is defined as basing point 0, a base sequence region on the 5' side (upstream) from the basing point is indicated by "−+" (minus), and a base sequence region on the 3' side (downstream) therefrom is indicated by "+−" ~~(minus)~~. In this respect, the region indicated by the range of -20 bases to -1 base belongs to exon 44, and the region indicated by the range of +1 base to +400 bases belongs to intron 44.

(A2) Region R2

75% or higher, 80% or higher, 85% or higher, 90% or higher, or 95% or higher.

Herein, the ten numerically consecutive exons may be the 45th to the 54th exons, or the 46th to the 55th exons.

[0073]

(C10) Eleven numerically consecutive exons ~~selected from the group consisting~~ of the 45th exon to the 55th exon in human dystrophin pre-mRNA are skipped with the efficiency of 5% or higher, 10% or higher, 15% or higher, 20% or higher, 25% or higher, 30% or higher, 35% or higher, 40% or higher, 45% or higher, 50% or higher, 55% or higher, 60% or higher, 65% or higher, 70% or higher, 75% or higher, 80% or higher, 85% or higher, 90% or higher, or 95% or higher.

Herein, the eleven numerically consecutive exons may be the 45th to the 55th exons.

[0074]

The antisense oligomer of the present invention may be 10 to 60 bases long, 10 to 55 bases long, 10 to 50 bases long, 10 to 45 bases long, 10 to 40 bases long, 10 to 35 bases long, 10 to 30 bases long, 10 to 25 bases long, 15 to 60 bases long, 15 to 55 bases long, 15 to 50 bases long, 15 to 45 bases long, 15 to 40 bases long, 15 to 35 bases long, 15 to 30 bases long, 15 to 25 bases long, 16 to 60 bases long, 16 to 55 bases long, 16 to 50 bases long, 16 to 45 bases long, 16 to 40 bases long, 16

DAZAP1, hnRNP I, Fox-1, Fox-2, hnRNP H1, hnRNP H2, hnRNP H3, hnRNP L, Sam68, and SRp40.

[0130]

As used herein, the splice site is the boundary between an exon and an intron. The splice site can be predicted from the 5' end of the intron starting at GU, AU, or the like, and the 3' end of the intron ending at AG, AC, or the like.

[0131]

As used herein, the branch site is a sequence within an intronthat initiates an attack on a 5' splice site during splicing reaction and forms a covalent bond. The branch site sequence refers to a base sequence in an intron containing the branch site.

[0132]

Examples of the splicing silencer sequence, the branch site sequence, or the splice site sequence which is the target (hereinafter, referred to as a "suppressor sequence") of the suppressor antisense oligomer of the present invention include base sequences given below (SEQ ID NOs: 370 to 384 and 390). The positions of the splicing silencer~~suppressor~~ sequence, the branch site sequence, and the splice site sequence can be detected using software such as SpliceAid (Francesco Piva et al., Bioinformatics, 25 (9), 1211-1213, 2009), SpliceAid-2 (Francesco Piva et al., Human Mutation, 33 (1), 81-85, 2012), SpliceAid-F (Matteo Giulietti et al., Nucleic Acids Res., 41, D125-

antisense oligomer consisting of any one base sequence selected from the group consisting of SEQ ID NOs: 1 to 111, 113 to 177, 179, 180, 182, 183, 185 to 193, 195 to 198, 200 to 223, and 225 to 232, more preferably an antisense oligomer consisting of any one base sequence selected from the group consisting of SEQ ID NOs: 1, 5, 6, 7, 8, 10, 11, 14, 26, 27, 28, 29, 35, 38, 39, 40, 41, 43, 45, 46, 47, 50, 51, 52, 53, 54, 55, 58, 59, 63, 64, 65, 66, 67, 68, 74, 75, 76, 77, 78, 80, 82, 86, 92, 97, 98, 100, 102, 113, 119, 121, 122, 124, 125, 126, 128, 130, 131, 132, 139, 142, 144, 146, 147, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 225, 228, 231, and 232, and further preferably an antisense oligomer consisting of any one base sequence selected from the group consisting of SEQ ID NOs: 1, 5, 11, 27, 28, 35, 40, 41, 43, 45, 46, 47, 50, 51, 52, 54, 55, 59, 63, 64, 65, 66, 68, 74, 75, 76, 77, 78, 102, 113, 119, 128, 131, 132, 139, 142, 161, 162, 163, 225, and 228.

The suppressor antisense oligomer contained in the pharmaceutical composition of the present invention or the pharmaceutical combination of the present invention can be any suppressor antisense oligomer of the present invention and is, but not particularly limited to, preferably a suppressor antisense oligomer consisting of any one base sequence selected from the group consisting of SEQ ID NOs: 257 to 275, more preferably a suppressor antisense oligomer consisting of any one base sequence selected from the group consisting of SEQ ID NO: 1,

The pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention in the form of an aqueous solution may comprise the suppressor antisense oligomer of the present invention in a concentration of 2.5 to 500 mg/mL, 5 to 450 mg/mL, 10 to 400 mg/mL, 15 to 350 mg/mL, 20 to 300 mg/mL, 20 to 250 mg/mL, 20 to 200 mg/mL, 20 to 150 mg/mL, 20 to 100 mg/mL, 20 to 50 mg/mL, 20 to 40 mg/mL, 20 to 30 mg/mL, 23 to 27 mg/mL, 24 to 26 mg/mL, or 25 mg/mL. Alternatively, the pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention may comprise the suppressor antisense oligomer of the present invention in a concentration of 10 to 100 mg/mL, 15 to 95 mg/mL, 20 to 80 mg/mL, 25 to 75 mg/mL, 30 to 70 mg/mL, 35 to 65 mg/mL, 40 to 60 mg/mL, 45 to 55 mg/mL, 47 to 53 mg/mL, 48 to 52 mg/mL, 49 to 51 mg/mL, or 50 mg/mL.

[0180]

The pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention may be in a dry form. In this case, in order to prepare the pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention in an aqueous solution form, for example, 125 mg or 250 mg of the antisense oligomer of the present invention in a dry form may be mixed with 0.5 mL to 100 mL of water (which corresponds to the antisense oligomer of the present invention in a concentration of

1.25 mg/mL to 250 mg/mL or 2.5 mg/mL to 500 mg/mL), preferably with 1 mL to 50 mL of water (which corresponds to the antisense oligomer of the present invention in a concentration of 2.5 mg/mL to 125 mg/mL or 5 mg/mL to 250 mg/mL), more preferably with 5 mL to 10 mL of water (which correspond to the antisense oligomer of the present invention in a concentration of 12.5 mg/mL to 25 mg/mL or 25 mg/mL to 50 mg/mL) and used.

[0181]

When the pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention is in a dry form, in order to prepare the pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention in an aqueous solution form, for example, 125 mg or 250 mg of the suppressor antisense oligomer of the present invention in a dry form may be mixed with 0.5 mL to 100 mL of water (which corresponds to the suppressor antisense oligomer of the present invention in a concentration of 1.25 mg/mL to 250 mg/mL or 2.5 mg/mL to 500 mg/mL), preferably with 1 mL to 50 mL of water (which corresponds to the suppressor antisense oligomer of the present invention in a concentration of 2.5 mg/mL to 125 mg/mL or 5 mg/mL to 250 mg/mL), more preferably with 5 mL to 10 mL of water (which correspond to the suppressor antisense oligomer of the present invention in a concentration of 12.5 mg/mL to 25 mg/mL or 25 mg/mL to 50 mg/mL) and used.

[0182]

The concentrations of the antisense oligomer of the present invention and the suppressor antisense oligomer of the present invention contained in the pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention may be the respective concentrations of the antisense oligomer of the present invention and the suppressor antisense oligomer of the present invention or may be the total concentration of the antisense oligomer of the present invention and the suppressor antisense oligomer of the present invention.

[0183]

In addition to the antisense oligomer of the present invention and/or the suppressor antisense oligomer of the present invention and the carrier described above, pharmaceutically acceptable additives may also be optionally formulated in the pharmaceutical composition of the present invention and/or the pharmaceutical combination of the present invention. Examples of such additives are emulsification aids (*e.g.*, fatty acids having 6 to 22 carbon atoms and their pharmaceutically acceptable salts, albumin and dextran), stabilizers (*e.g.*, cholesterol, phosphatidic acid, mannitol, and sorbitol), isotonizing agents (*e.g.*, sodium chloride, glucose, maltose, lactose, sucrose, and trehalose), and pH controlling agents (*e.g.*, hydrochloric acid, sulfuric

consisting of SEQ ID NOs: 331 to 335, and has a length within ±0.5% of the length of the any one base sequence selected.

[0201]

Thus, a further embodiment of the suppressor antisense oligomer for human SGCG is a suppressor antisense oligomer for human SGCG consisting of any one base sequence selected from the group consisting of (M1) and (M2-1) to (M2-16), or a pharmaceutically acceptable salt thereof, or hydrate thereof. The suppressor antisense oligomer for human SGCG is included in the present invention. ~~The suppressor antisense oligomer for human SGCG is included in the present invention.~~ The suppressor antisense oligomer for human SGCG is capable of enhancing the efficiency of multi-skipping from SGCG pre-mRNA.

[0202]

The antisense oligomer for human Notch3 that induces multi-exon skipping from human Notch3 pre-mRNA targets, for example, a region in the vicinity of an acceptor of intron 3, i.e., the range of -400 to +50 bases with the 3' end of intron 3 defined as a basing point, and is, for example, an antisense oligomer for human Notch3 consisting of

(N1) any one base sequence selected from the group consisting of SEQ ID NOs: 309 to 330, or