Claims

[Claim 1]

A combination of antisense oligomers or pharmaceutically acceptable salts thereof, or hydrates thereof which cause simultaneous skipping of any two or more numerically consecutive exons selected from the group consisting of the 45th exon to the 55th exon in human dystrophin pre-mRNA,

the combination comprising:

(i) a first antisense oligomer or a pharmaceutically acceptable salt thereof, or a hydrate thereof, comprising:

a first unit oligomer comprising a base sequence complementary to a base sequence consisting of a base sequence of 11 bases in the upstream direction from the 3' end of the 44th intron and a base sequence of 69 bases in the downstream direction from the 5' end of the 45th exon in the human dystrophin pre-mRNA, or a partial base sequence thereof; and

a second unit oligomer comprising a base sequence complementary to a base sequence of from the 52nd to 75th bases in the upstream direction from the 3' end of the 44th intron in the human dystrophin pre-mRNA, or a partial base sequence thereof; and

(ii) a second antisense oligomer or a pharmaceutically acceptable salt thereof, or a hydrate

thereof, comprising a base sequence complementary to a base sequence consisting of a base sequence of 33 bases in the upstream direction from the 3' end of the 54th intron and a base sequence of 53 bases in the downstream direction from the 5' end of the 55th exon in the human dystrophin pre-mRNA, or a partial base sequence thereof.

[Claim 2]

The combination according to claim 1, wherein

the first unit oligomer comprises a base sequence complementary to consecutive 15 to 30 bases of a base sequence consisting of a base sequence of 11 bases in the upstream direction from the 3' end of the 44th intron and a base sequence of 69 bases in the downstream direction from the 5' end of the 45th exon in the human dystrophin pre-mRNA,

the second unit oligomer comprises a base sequence complementary to consecutive 1 to 10 bases of a base sequence of from the 52nd to 75th bases in the upstream direction from the 3' end of the 44th intron in the human dystrophin pre-mRNA, and

the second antisense oligomer comprises a base sequence complementary to consecutive 15 to 30 bases of a base sequence consisting of a base sequence of 33 bases in the upstream direction from the 3' end of the 54th intron and a base sequence of 53 bases in the downstream direction from the 5' end of the 55th exon in the human dystrophin pre-mRNA.

[Claim 3]

The combination according to claim 1 or 2, wherein

the first unit oligomer comprises a base sequence complementary to:

(a) any one base sequence selected from the group consisting of SEQ ID NOs: 211 to 906;

(b) a base sequence that hybridizes under stringent conditions to a base sequence complementary to any one base sequence selected from the group consisting of SEQ ID NOs: 211 to 906;

(c) a base sequence that has at least 85% identity with any one base sequence selected from the group consisting of SEQ ID NOs: 211 to 906, and has a length within ±15% of the length of the any one base sequence selected; or

(d) a partial base sequence of any one base sequence selected from the group consisting of the base sequences (a), (b), and (c), and/or

the second unit oligomer comprises a base sequence complementary to:

(a) any one base sequence selected from the group consisting of SEQ ID NOs: 1 to 105;

(b) a base sequence that hybridizes under stringent conditions to a base sequence complementary to any one base sequence selected from the group consisting of SEQ ID NOs: 1 to 105;

(c) a base sequence that has at least 85% identity with any one base sequence selected from the group consisting of SEQ ID NOs: 1 to 105, and has a length within ±15% of the length of the any one base sequence selected; or

(d) a partial base sequence of any one base sequence selected from the group consisting of the base sequences (a), (b), and (c).

[Claim 4]

The combination according to any one of claims 1 to 3, wherein

the second antisense oligomer comprises a base sequence complementary to:

(a) any one base sequence selected from the group consisting of SEQ ID NOs: 3507 to 4298;

(b) a base sequence that hybridizes under stringent conditions to a base sequence complementary to any one base sequence selected from the group consisting of SEQ ID NOs: 3507 to 4298;

(c) a base sequence that has at least 85% identity with any one base sequence selected from the group consisting of SEQ ID NOs: 3507 to 4298, and has a length within ±15% of the length of the any one base sequence selected; or

(d) a partial base sequence of any one base sequence selected from the group consisting of the base sequences (a), (b), and (c).

[Claim 5]

The combination according to any one of claims 1 to 4, wherein the first antisense oligomer comprises the first unit oligomer and the second unit oligomer from the 5' ends in this order, the first unit oligomer comprises any one base sequence selected from SEQ ID NOs: 907 to 1602, the second unit oligomer comprises any one base sequence selected from SEQ ID NOs: 106 to 210, and the second antisense oligomer comprises any one base sequence selected from SEQ ID NOs: 4299 to 5090.

[Claim 6]

The combination according to any one of claims 1 to 5, wherein the first unit oligomer comprises any one base sequence selected from the group consisting of SEQ ID NOs: 1180, 1190, 1201, 1212, 1222, 1224, and 1239.

[Claim 7]

The combination according to any one of claims 1 to 6, wherein the second unit oligomer comprises any one base sequence selected from the group consisting of SEQ ID NOs: 114, 124, 151, 201, 203, and 205.

[Claim 8]

The combination according to claim 6 or 7, wherein

the first antisense oligomer comprises the first unit oligomer and the second unit oligomer from the 5' ends in this order, and

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, and the second unit oligomer comprises a base sequence of SEQ ID NO: 151,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, and the second unit oligomer comprises a base sequence of SEQ ID NO: 201,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, and the second unit oligomer comprises a base sequence of SEQ ID NO: 203,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, and the second unit oligomer comprises a base sequence of SEQ ID NO: 205,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1239, and the second unit oligomer comprises a base sequence of SEQ ID NO: 114,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1224, and the second unit oligomer comprises a base sequence of SEQ ID NO: 124,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1180, and the second unit oligomer comprises a base sequence of SEQ ID NO: 151,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1190, and the second unit oligomer comprises a base sequence of SEQ ID NO: 151,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1212, and the second unit oligomer comprises a base sequence of SEQ ID NO: 151, or

the first unit oligomer comprises a base sequence of SEQ ID NO: 1222, and the second unit oligomer comprises a base sequence of SEQ ID NO: 151.

[Claim 9]

The combination according to any one of claims 1 to 8, wherein the second antisense oligomer comprises a base sequence selected from the group consisting of SEQ ID NOs: 4698, 4702, 4752, 4923, 4926, 4936, 4950, and 4977.

[Claim 10]

The combination according to any one of claims 1 to 9, wherein

the first antisense oligomer comprises the first unit oligomer and the second unit oligomer from the 5' ends in this order, and

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 201, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 203, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 205, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1239, the second unit oligomer comprises a base sequence of SEQ ID NO: 114, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1224, the second unit oligomer comprises a base sequence of SEQ ID NO: 124, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1180, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1190, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1212, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1222, the second unit oligomer comprises a

base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4698,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4702,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4752,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4923,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4926,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4936,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4977, or

the first unit oligomer comprises a base sequence of SEQ ID NO: 1180, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4977.

[Claim 11]

The combination according to any one of claims 5 to 10, wherein the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, and the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950.

[Claim 12]

The combination according to any one of claims 1 to 11, further comprising:

(iii) a third antisense oligomer or a pharmaceutically acceptable salt thereof, or a hydrate thereof, comprising a base sequence complementary to a base sequence consisting of a base sequence of 23 bases in the upstream direction from the 3' end of the 45th exon and a base sequence of 73 bases in the downstream direction from the 5' end of the 45th intron in the human dystrophin pre-mRNA, or a partial base sequence thereof.

[Claim 13]

The combination according to claim 12, wherein the third antisense oligomer comprises a base sequence complementary to consecutive 15 to 30 bases of a base sequence consisting of a base sequence of 23 bases in the upstream direction from the 3' end of the 45th exon and a base sequence of 73 bases in the downstream direction from the 5' end of the 45th intron in the human dystrophin pre-mRNA.

[Claim 14]

The combination according to claim 12 or 13, wherein

the third antisense oligomer comprises a base sequence complementary to:

(a) any one base sequence selected from the group consisting of SEQ ID NOs: 1603 to 2554;

(b) a base sequence that hybridizes under stringent conditions to a base sequence complementary to any one base sequence selected from the group consisting of SEQ ID NOs: 1603 to 2554;

(c) a base sequence that has at least 85% identity with any one base sequence selected from the group consisting of SEQ ID NOs: 1603 to 2554, and has a length within ±15% of the length of the any one base sequence selected; or

(d) a partial base sequence of any one base sequence selected from the group consisting of the base sequences (a), (b), and (c).

[Claim 15]

The combination according to (14), wherein the third antisense oligomer comprises a base sequence complementary to:

(a) any one base sequence selected from the group consisting of SEQ ID NOs: 1611 to 1654, 1664 to 1707, 1718 to 1761, 1773 to 1816, 1829 to 1872, 1886 to 1929, 1944 to 1987, 2003 to 2046, 2063 to 2106, 2124 to 2167, 2186 to 2229, 2249 to 2292, 2313 to 2356, 2378 to 2421, 2444 to 2487, and 2511 to 2554;

(b) a base sequence that hybridizes under stringent conditions to a base sequence complementary to any one base sequence selected from the group consisting of SEQ ID NOs: 1611 to 1654, 1664 to 1707, 1718 to 1761, 1773 to 1816, 1829 to 1872, 1886 to 1929, 1944 to 1987, 2003 to 2046, 2063 to 2106, 2124 to 2167, 2186 to 2229, 2249 to 2292, 2313 to 2356, 2378 to 2421, 2444 to 2487, and 2511 to 2554;

(c) a base sequence that has at least 85% identity with any one base sequence selected from the group consisting of SEQ ID NOs: 1611 to 1654, 1664 to 1707, 1718 to 1761, 1773 to 1816, 1829 to 1872, 1886 to 1929, 1944 to 1987, 2003 to 2046, 2063 to 2106, 2124 to 2167, 2186 to 2229, 2249 to 2292, 2313 to 2356, 2378 to 2421, 2444 to 2487, and 2511 to 2554, and has a length within ±15% of the length of the any one base sequence selected; or

(d) a partial base sequence of any one base sequence selected from the group consisting of the base sequences (a), (b), and (c).

[Claim 16]

The combination according to claim 15, wherein the third antisense oligomer comprises a base sequence complementary to:

(a) any one base sequence selected from the group consisting of SEQ ID NOs: 1617 to 1654, 1670 to 1707, 1724 to 1761, 1779 to 1816, 1835 to 1872, 1892 to 1929, 1950 to 1987, 2009 to 2046, 2069 to 2106, 2130 to 2167, 2192 to 2229, 2255 to 2292, 2319 to 2356, 2384 to 2421, 2450 to 2487, and 2517 to 2554;

(b) a base sequence that hybridizes under stringent conditions to a base sequence complementary to any one base sequence selected from the group consisting of SEQ ID NOs: 1617 to 1654, 1670 to 1707, 1724 to 1761, 1779 to 1816, 1835 to 1872, 1892 to 1929, 1950 to 1987, 2009 to 2046, 2069 to 2106, 2130 to 2167, 2192 to 2229, 2255 to 2292, 2319 to 2356, 2384 to 2421, 2450 to 2487, and 2517 to 2554;

(c) a base sequence that has at least 85% identity with any one base sequence selected from the group consisting of SEQ ID NOs: 1617 to 1654, 1670 to 1707, 1724 to 1761, 1779 to 1816, 1835 to 1872, 1892 to 1929, 1950 to 1987, 2009 to 2046, 2069 to 2106, 2130 to 2167, 2192 to 2229, 2255 to 2292, 2319 to 2356, 2384 to 2421,

2450 to 2487, and 2517 to 2554, and has a length within ±15% of the length of the any one base sequence selected; or

(d) a partial base sequence of any one base sequence selected from the group consisting of the base sequences (a), (b), and (c).

[Claim 17]

The combination according to any one of claims 1 to 14, wherein the third antisense oligomer comprises a base sequence selected from the group consisting of SEQ ID NOs: 3060, 3065, 3077, 3082, 3087, 3090, 3096, 3108, 3119, and 3320.

[Claim 18]

The combination according to any one of claims 12 to 17, wherein the first antisense oligomer comprises the first unit oligomer and the second unit oligomer from the 5' ends in this order, the first unit oligomer comprises any one base sequence selected from SEQ ID NOs: 907 to 1602, the second unit oligomer comprises any one base sequence selected from SEQ ID NOs: 106 to 210, the second antisense oligomer comprises any one base sequence selected from SEQ ID NOs: 4299 to 5090, and the third antisense oligomer comprises any one base sequence selected from SEQ ID NOs: 2555 to 3506.

[Claim 19]

The combination according to any one of claims 1 to 18, wherein

the first antisense oligomer comprises the first unit oligomer and the second unit oligomer from the 5' ends in this order, and

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 201, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 203, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 205, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1239, the second unit oligomer comprises a base sequence of SEQ ID NO: 114, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1224, the second unit oligomer comprises a base sequence of SEQ ID NO: 124, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1180, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1190, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1212, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense

oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1222, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3060,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3065,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3077,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3087,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3090,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3096,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3108,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense

oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3119,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3320,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4698, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4702, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4752, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4923, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4926, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4936, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4977, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082,

the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense

oligomer comprises a base sequence of SEQ ID NO: 4977, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3096, or

the first unit oligomer comprises a base sequence of SEQ ID NO: 1180, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4977, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3096.

[Claim 20]

The combination according to claim 18 or 19, wherein the first unit oligomer comprises a base sequence of SEQ ID NO: 1201, the second unit oligomer comprises a base sequence of SEQ ID NO: 151, the second antisense oligomer comprises a base sequence of SEQ ID NO: 4950, and the third antisense oligomer comprises a base sequence of SEQ ID NO: 3082, 3090, or 3096.

[Claim 21]

The combination according to any one of claims 1 to 20, the combination causing skipping of all exons from the 45th exon to the 55th exon in the human dystrophin pre-mRNA.

[Claim 22]

The combination according to any one of claims 1 to 11, wherein the first and second antisense oligomers are oligonucleotides, or the combination according to any one

of claims 12 to 21, wherein the first to third antisense oligomers are oligonucleotides.

[Claim 23]

The combination according to claim 22, wherein a sugar moiety and/or a phosphate-binding region of at least one base constituting the oligonucleotide is modified.

[Claim 24]

The combination according to claim 22 or 23, wherein the sugar moiety of at least one base constituting the oligonucleotide is a ribose in which a 2'-OH group is replaced by any one group selected from the group consisting of -OR, -R, -R'OR, -SH, -SR, $-NH_2$, -NHR, $-NR_2$, $-N_3$, -CN, -F, -Cl, -Br, and -I (wherein R is an alkyl or an aryl and R' is an alkylene).

[Claim 25]

The combination according to any one of claims 22 to 24, wherein the phosphate-binding region of at least one base constituting the oligonucleotide is any one selected from the group consisting of a phosphorothioate bond, a phosphorodithioate bond, an alkylphosphonate bond, a phosphoramidate bond, and a boranophosphate bond.

[Claim 26]

The combination according to any one of claims 1 to 11, wherein the first and second antisense oligomers are morpholino oligomers, or the combination according to any

one of claims 12 to 21, wherein the first to third antisense oligomers are oligonucleotides.

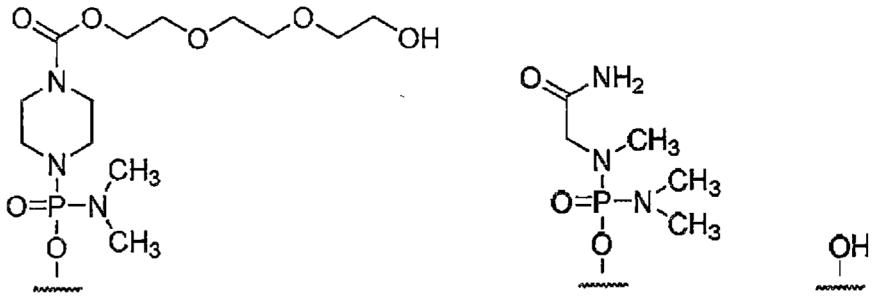
[Claim 27]

The combination according to claim 26, wherein the first to third antisense oligomers are phosphorodiamidate morpholino oligomers.

[Claim 28]

The combination according to claim 26 or 27, wherein the 5' end of each of the first to third antisense oligomers is a group represented by any one of the following chemical formulae (1) to (3):

[Chem. 1]



(1) (2) (3)

[Claim 29]

(a) A pharmaceutical composition comprising the first and second antisense oligomers according to any one of claims 1 to 28, or pharmaceutically acceptable salts thereof, or hydrates thereof, or

(b) a pharmaceutical combination comprising (i) a pharmaceutical composition comprising the first antisense oligomer according to any one of claims 1 to 28, or a

pharmaceutically acceptable salt thereof, or a hydrate thereof, and (ii) a pharmaceutical composition comprising the second antisense oligomer according to any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, or a hydrate thereof.

[Claim 30]

(a) A pharmaceutical composition comprising the first to third antisense oligomers according to any one of claims 12 to 28, or pharmaceutically acceptable salts thereof, or hydrates thereof, or

(b) a pharmaceutical combination comprising (i) a pharmaceutical composition comprising the first antisense oligomer according to any one of claims 12 to 28, or a pharmaceutically acceptable salt thereof, or a hydrate thereof, (ii) a pharmaceutical composition comprising the second antisense oligomer according to any one of claims 12 to 28, or a pharmaceutically acceptable salt thereof, or a hydrate thereof, and (iii) a pharmaceutical composition comprising the third antisense oligomer according to any one of claims 12 to 28, or a pharmaceutically acceptable salt thereof, or a hydrate thereof.

[Claim 31]

The pharmaceutical composition or the pharmaceutical combination according to claim 29 or 30, wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

[Claim 32]

The pharmaceutical composition or the pharmaceutical combination according to any one of claims 29 to 31 for use in the treatment of muscular dystrophy.

[Claim 33]

The pharmaceutical composition or the pharmaceutical combination for use according to any one of claims 29 to 32, wherein the composition or combination is to be administered to a human patient.

[Claim 34]

Use of (i) the first and second antisense oligomers according to any one of claims 1 to 28, or pharmaceutically acceptable salts thereof, or hydrates thereof, (ii) the first to third antisense oligomers according to any one of claims 12 to 28, or pharmaceutically acceptable salts thereof, or hydrates thereof, or (iii) the pharmaceutical composition or the pharmaceutical combination according to any one of claims 29 to 33 in the manufacture of a medicament for the treatment of muscular dystrophy in a patient.

[Claim 35]

The use according to claim 34, wherein the muscular dystrophy patient is a patient with a mutation that is a target of exon 45 to 55 skipping in dystrophin gene.

[Claim 36]

The use according to claim 34 or 35, wherein the patient is a human.