CLAIMS

[Claim 1]

Use of a pharmaceutical composition in the manufacture of a medicament for the treatment of Duchenne muscular dystrophy in a human patient, wherein the pharmaceutical composition comprises an antisense oligomer consisting of a base sequence complementary to a sequence consisting of nucleotides at positions 36 to 56 from the 5'-terminus of exon 53 of a human dystrophin gene or a pharmaceutically acceptable salt thereof, or a hydrate thereof,

wherein the antisense oligomer is Viltolarsen,

wherein the Viltolarsen is to be intravenously administered to the human patient at a dose of between 40 mg/kg inclusive and 80 mg/kg inclusive once a week.

[Claim 2]

The use according to claim 1, wherein the Viltolarsen is to be intravenously administered to the human patient at a dose of 40 mg/kg once a week.

[Claim 3]

The use according to claim 1, wherein the Viltolarsen is to be intravenously administered to the human patient at a dose of 80 mg/kg once a week.

[Claim 4]

The use according to claim 1, wherein the human patient has a mutation that results in a deficiency of any exon selected from the group consisting of exons 43-52, 45-52, 47-52, 48-52, 49-52, 50-52, or 52, in a dystrophin gene.

[Claim 5]

The use according to claim 1, wherein the expression of a dystrophin protein in the human patient before the treatment is 1% or less compared with that of a healthy subject, as measured by Western blotting or mass spectrometry.

[Claim 6]

The use according to claim 5, wherein the expression of a dystrophin protein is not found in the human patient before the treatment.

[Claim 7]

The use according to claim 1, wherein the pharmaceutical composition comprises the Viltolarsen in a concentration of between 2.5 mg/ml inclusive and 500 mg/ml inclusive, or between 10 mg/ml inclusive and 100 mg/ml inclusive.

[Claim 8]

The use according to claim 1, wherein the pharmaceutical composition comprises the Viltolarsen in a concentration of 25 mg/ml.

[Claim 9]

The use according to claim 1, wherein the pharmaceutical composition comprises the Viltolarsen in a concentration of 50 mg/ml.

[Claim 10]

The use according to claim 1, wherein the pharmaceutical composition further comprises at least one component selected from the group consisting of a tonicity agent, a pH adjuster, and a solvent.

[Claim 11]

The use according to claim 10, wherein the tonicity agent is at least one selected from the group consisting of sodium chloride, potassium chloride, glucose, fructose, maltose, sucrose, lactose, mannitol, sorbitol, xylitol, trehalose, and glycerin.

[Claim 12]

The use according to claim 10 or 11, wherein the pH adjuster is at least one selected from the group consisting of hydrochloric acid, sodium hydroxide, citric acid, lactic acid, phosphate (sodium hydrogen phosphate, sodium dihydrogen phosphate, and potassium dihydrogen phosphate), and monoethanolamine.

[Claim 13]

The use according to claim 10 or 11, wherein the solvent is water.

[Claim 14]

The use according to claim 12, wherein the solvent is water.

[Claim 15]

The use according to claim 1, wherein the pharmaceutical composition comprises the Viltolarsen in a concentration of between 2.5 mg/ml inclusive and 500 mg/ml inclusive, or between 10 mg/ml inclusive and 100 mg/ml inclusive, and sodium chloride in a concentration of between 8 mg/ml inclusive and 10 mg/ml inclusive, and which is an aqueous solution with pH 7.2 to 7.4.

[Claim 16]

The use according to claim 1, wherein the treatment provides at least one effect selected from the group consisting of the following effects (1) to (6):

(1) the average value of the expression level of a dystrophin protein in the skeletal muscle of the patient is 9-fold or more increased in comparison to baseline, after administration of the pharmaceutical composition for 24 weeks;

(2) a change in the velocity obtained from time to stand (TTSTAND) is -0.055 times/sec or more in comparison to baseline, at the time of the 25th week after administration of the pharmaceutical composition for 24 weeks;

(3) a change in the velocity obtained from time to run/walk 10 meters (TTRW) is -0.025 meters/sec or more in comparison to baseline, at the time of the 25th week after administration of the pharmaceutical composition for 24 weeks;

(4) a change in the velocity obtained from time to climb 4 stairs (TTCLIMB) is -0.060 times/sec or more in comparison to baseline, at the time of the 25th week after administration of the pharmaceutical composition for 24 weeks;

(5) a change in the score of North Star Ambulatory Assessment (NSAA) is -2.2 scores or more in comparison to baseline, at the time of the 25th week after administration of the pharmaceutical composition for 24 weeks; and

(6) a change in 6-minute walk test (6MWT) is -7.5 meters or more in comparison to baseline, at the time of the 25th week after administration of the pharmaceutical composition for 24 weeks.

[Claim 17]

The use according to claim 1, wherein when the treatment is performed on 7- to 9-year-old human patients with Duchenne muscular dystrophy for 84 weeks, at least one effect selected from the group consisting of the following effects (1) to (6) is provided:
(1) the percentage of patients who lose rise ability is less than 20% by the time of the 85th week after initiation of the treatment;
(2) the percentage of patients who lose ability to climb 4 stairs is less than 10% by the time of the 85th week after initiation of the treatment;
(3) the percentage of patients who lose independent walking ability is less than 10% by the time of the 85th week after initiation of the treatment;
(4) a reduction in the velocity of running/walking 10 meters due to aging is not observed by the time of the 85th week after initiation of the treatment;
(5) a reduction in the velocity of climbing 4 stairs due to aging is not observed by the time of the 85th week after initiation of the treatment; and
(6) a reduction in rise velocity due to aging is not observed by the time of the 85th week after initiation of the treatment.

[Claim 18]

The use according to claim 1, wherein when the treatment is performed on 10- to 12-year-old human patients with Duchenne muscular dystrophy for 84 weeks, at least one effect selected from the group consisting of the following effects (1) to (6) is provided:
(1) the percentage of patients who lose rise ability is less than 60% by the time of the 85th week after initiation of the treatment;
(2) the percentage of patients who lose ability to climb 4 stairs is less than 50% by the time of the 85th week after initiation of the treatment;
(3) the percentage of patients who lose independent walking ability is less than 50% by the time of the 85th week after initiation of the treatment;
(4) a reduction in the velocity of running/walking 10 meters due to aging is not observed by the time of the 85th week after initiation of the treatment;
(5) a period in which the velocity of climbing 4 stairs increases is observed by the time of the 85th week after initiation of the treatment; and
(6) a period in which rise velocity increases is observed by the time of the 85th week after initiation of the treatment.

[Claim 19]

The use according to any one of claims 1-11, 13, and 15-18, wherein the pharmaceutical composition does not comprise a phosphate buffer.

[Claim 20]

The use according to claim 19, wherein the pharmaceutical composition does not comprise a buffer.

[Claim 21]

The use according to claim 19 or 20, wherein the pharmaceutical composition comprises the Viltolarsen in a concentration of 50mg /ml, and sodium chrolide in a concentration 8.55 mg/mL to 9.45 mg/mL, and wherein the pharmaceutical composition is an aqueous solution with pH 7.0-7.5.

[Claim 22]

The use according to claim 21, wherein the pH is 7.2-7.4.

[Claim 23]

The use according to claim 21, wherein the pH is 7.3.