CLAIMS

What is claimed is:

1. Use of a pharmaceutical composition comprising an oligosaccharide-protein conjugate and a pharmaceutically acceptable carrier, in the manufacture of a medicament for treating late-onset Pompe disease (LOPD) in a human individual, wherein the oligosaccharide-protein conjugate is avalglucosidase alfa,

wherein the human individual shows the first symptom of Pompe Disease at an age of at least 18 years old,

wherein the pharmaceutical composition is to be administered at a dose of 20 mg/kg, and

wherein administration of the pharmaceutical composition to a plurality of human individuals for 49 weeks results in one or more of the following:

(a) an average increase of FVC% in an upright position of at least 1.1%, at least 2.3%, or at least 4.6%;

(b) an average increase of 6-minute walk test (6MWT) distance of at least 12.5 m, at least 23 m, or at least 50 m;

(c) an average increase in 6MWT percentage of predicted value (6MWT%) of at least 2%, at least 3.5%, or at least 8%;

(d) an average increase in maximum inspiratory pressure percentage of predicted value (MIP%) in an upright position of at least 4.5%, at least 8.7%, or at least 12.5%;

(e) an average increase in maximum expiratory pressure percentage (MEP%) in an upright position of at least 5.2%, at least 10.9%, at least 14.3%, or at least 16.5%;

(f) an average increase in hand-held dynamometry (HHD) score for lower extremities of at least 170 Newtons (N), at least 250 N, or at least 350 N;

(g) an average increase in HHD score for upper extremities of at least 95 N, at least 190 N, or at least 245N;

(h) an average increase in quick motor function test (QMFT) total score of at least 2.7, at least 3.3, or at least 5.2;

(i) an average change of Gait, Stair, Gower's Maneuver, and Chair (GSGC) score of at least -0.9, at least -0.35, or at least 0.40;

(j) an average increase of GMFM-88 Dimension D score of at least 2.2, at least 3.3, or at least 5.8;

(k) an average increase of GMFM-88 Dimension E score of at least 0.7, at least 4.5, or at least 5.2;

(l) an average increase in health-related quality of life Short Form 12 Health Survey (SF-12) physical component score (PCS) of at least 0.4, at least 3.7, or at least 4.3%;

(m) an average increase in SF-12 mental component score (MCS) of at least 0.45, at least 3.4, or at least 5.3;

(n) an average decrease in urinary HEX4 level of at least 30%, at least 43%, or at least 78%;

(o) an average decrease in creatine kinase level of at least 13%, at least 39%, or at least 63%;

(p) an average decrease in alanine aminotransferase (ALT) level of at least 19%, at least 38%, or at least 68%; and

(q) an average decrease in aspartate aminotransferase (AST) level of at least 26%, at least 33%, or at least 66%.

2. The use of claim 1, wherein the individual is at least 45 years old or between 18 years old and 45 years old.

3. The use of claim 1 or 2, wherein the individual is diagnosed with Pompe disease at an age of at least 18 years old.

4. The use of any one of the preceding claims, wherein administration of the pharmaceutical composition to a plurality of human individuals for 49 weeks results in one or more of the following:

(a) an average increase of FVC% in an upright position of 2.89% within a 95% confidence interval of 1.1% to 4.7%;

(b) an average increase of 6-minute walk test (6MWT) distance of 32.2 meters within a 95% confidence interval of 12.4 meters to 52 meters;

(c) an average increase in 6MWT percentage of predicted value (6MWT%) of 5.0% within a 95% confidence interval of 1.9% to 8.1%;

(d) an average increase in maximum inspiratory pressure percentage of predicted value (MIP%) in an upright position of 8.7% within a 95% confidence interval of 4.5% to 12.9%;

(e) an average increase in maximum expiratory pressure percentage (MEP%) in an upright position of at least 10.9% within a 95% confidence interval of 5.2% to 16.5%;

(f) an average increase in hand-held dynamometry (HHD) score for lower extremities of 260 Newtons (N) within a 95% confidence interval of 169 N to 352 N;

(g) an average increase in HHD score for upper extremities of 174 N within a 95% confidence interval of 97.8 N to 249N;

(h) an average increase in quick motor function test (QMFT) total score of 4.0 within a 95% confidence interval of 2.7 to 5.2;

(i) an average change of Gait, Stair, Gower's Maneuver, and Chair (GSGC) score of -0.25 within a 95% confidence interval of -0.94 to 0.43;

(j) an average increase of GMFM-88 Dimension D score of 4.0 within a 95% confidence interval of 2.2 to 5.8;

(k) an average increase of GMFM-88 Dimension E score of 2.6 within a 95% confidence interval of 0.72 to 4.5;

(l) an average increase in health-related quality of life Short Form 12 Health Survey (SF-12) physical component score (PCS) of 2.4 within a 95% confidence interval of 0.40 to 4.4;

(m) an average increase in SF-12 mental component score (MCS) of 2.9 within a 95% confidence interval of 0.45 to 5.3;

(n) an average decrease in urinary HEX4 level of 10.8% with a standard deviation of 24.0%;

(o) an average decrease in creatine kinase level of 38.0% with a standard deviation of 24.9%;

(p) an average decrease in alanine aminotransferase (ALT) level of 43.3% with a standard deviation of 24.7%; and

(q) an average decrease in aspartate aminotransferase (AST) level of 46.1% with a standard deviation of 20.2%.

5. The use of any one of the preceding claims, wherein the individual

a. has not previously received treatment with a recombinant GAA; or

b. has previously received treatment with a recombinant GAA .

6. The use of claim 5, wherein the recombinant GAA is alglucosidase alfa.

7. The use of any one of the preceding claims, wherein prior to the treatment, the individual has a forced vital capacity percentage of predicted value (FVC%) in an upright position between 30% and 85%, optionally, wherein prior to the treatment, the individual is able to ambulate for at least 40 meters without stopping and without an ambulation assistance device.

8. The use of any one of the preceding claims, wherein the individual:

a. does not have Pompe-specific cardiac hypertrophy;

b. has confirmed GAA enzyme deficiency from any tissue source and/or at least 2 confirmed GAA gene variants;

c. is to be administered with the pharmaceutical composition for at least 49 weeks;

d. has stable Mercuri scores, 3-point Dixon fat fraction, and/or T2 water with or without B1 correction according to skeletal muscle magnetic resonance imaging (MRI) over the course of the treatment;

e. has lower risk of infusion-associated reaction (IARs) after receiving the treatment compared to that after treatment with alglucosidase alfa; and/or

f. has decreasing level of antidrug antibody (ADA) against the oligosaccharide-protein conjugate over time.

9. The use of any one of the preceding claims, wherein the pharmaceutical composition is to be administered:

a. to the individual once every two weeks; and/or

b. intravenously.

10. The use of any one of the preceding claims, wherein the pharmaceutical composition is reconstituted from a lyophilized formulation comprising the oligosaccharide-protein conjugate.

11. The use of claim 10, wherein the pharmaceutically acceptable carrier comprises 10-50 mM histidine, 0.25-2% glycine, 1-4% mannitol, and 0.005-0.05% polysorbate 80, optionally, wherein the pharmaceutically acceptable carrier comprises 10 mM histidine, 2% glycine, 2% mannitol, and 0.01% polysorbate 80.

12. The use of any one of the preceding claims, wherein the GAA is a human GAA produced in Chinese hamster ovary (CHO) cells, optionally, wherein the human GAA has glycoform alfa.

13. The use of any one of the preceding claims, wherein administration of the pharmaceutical composition to the plurality of human individuals for 49 weeks results in one or more of the following:

(a) an increase of FVC% in an upright position that is at least 2.43% higher compared to the increase of FVC% in an upright position in a plurality of human individuals treated with alglucosidase alfa;

(b) an increase in 6MWT distance that is at least 30.01 meters longer compared to the increase in 6MWT distance in a plurality of human individuals treated with alglucosidase alfa;

(c) an increase in 6MWT percentage of predicted value (6MWT%) that is at least 4.71% longer compared to the percent increase of 6MWT% in a plurality of human individuals treated with alglucosidase alfa;

(d) an increase in maximum inspiratory pressure percentage of predicted value (MIP%) in an upright position that is at least 4.40% higher compared to the increase in MIP% in a plurality of human individuals treated with alglucosidase alfa;

(e) an increase in maximum expiratory pressure percentage of predicted value (MEP%) in an upright position that is at least 2.51% higher compared to the increase in MEP% in a plurality of human individuals treated with alglucosidase alfa;

(f) an increase in hand-held dynamometry (HHD) score for lower extremities that is at least 106.97 N higher compared to the increase in HHD score for lower extremities in a plurality of human individuals treated with alglucosidase alfa;

(g) an increase in HHD score for upper extremities that is at least 63.87 N higher compared to the increase in HHD score for upper extremities in a plurality of human individuals treated with alglucosidase alfa;

(h) an increase in quick motor function test (QMFT) total score that is at least 2.08 higher compared to the increase in QMFT total score in a plurality of human individuals treated with alglucosidase alfa;

(i) an increase in health-related quality of life Short Form 12 Health Survey (SF-12®) physical component score (PCS) that is at least 0.77 higher compared to the increase in SF-12® PCS in a plurality of human individuals treated with alglucosidase alfa;

(j) an increase in SF-12® mental component score (MCS) that is at least 2.12 higher compared to the increase in SF-12® MCS in a plurality of human individuals treated with alglucosidase alfa;

(k) a decrease in urinary hexose tetrasaccharide (HEX4) level that is at least 43.41% lower compared to the decrease in HEX4 level in a plurality of human individuals treated with alglucosidase alfa;

(l) a decrease in creatine kinase level that is at least 23.89% lower compared to the decrease in creatine kinase level in a plurality of human individuals treated with alglucosidase alfa;

(m) a decrease in alanine aminotransferase (ALT) level that is at least 33.9% lower compared to the decrease in ALT level in a plurality of human individuals treated with alglucosidase alfa; and

(n) a decrease in aspartate aminotransferase (AST) level that is at least 32.28% lower compared to the decrease in AST level in a plurality of human individuals treated with alglucosidase alfa,

wherein the plurality of human individuals treated with alglucosidase alfa is to be administered alglucosidase alfa at a dose of 20 mg/kg for 49 weeks.