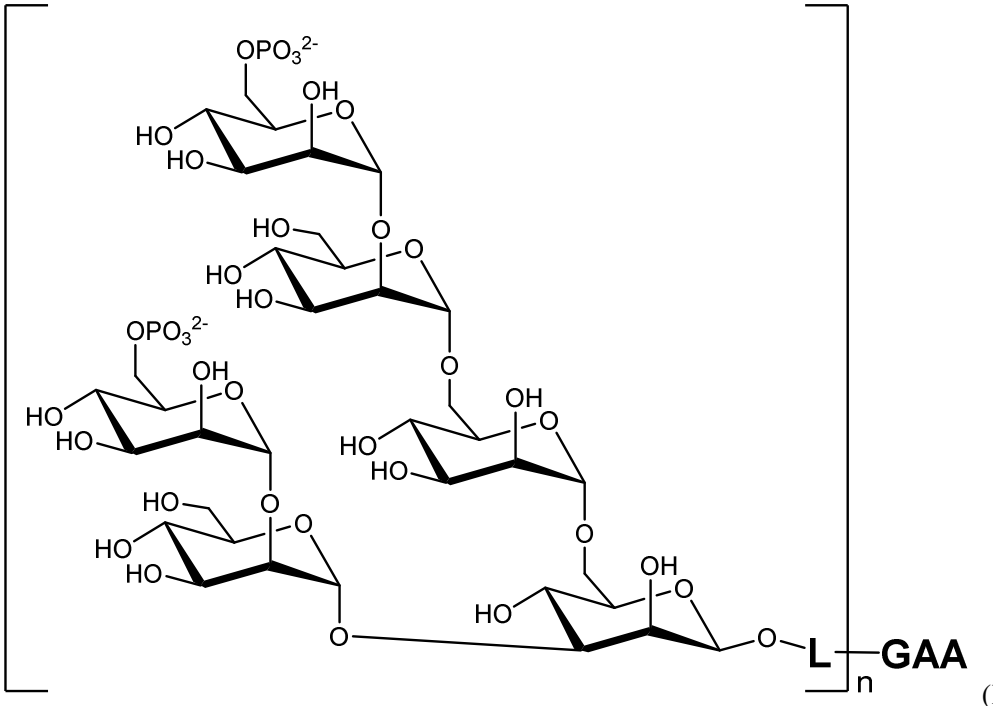
CLAIMS

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 infantile-onset Pompe disease (IOPD) in a human individual, wherein the oligosaccharide-protein conjugate has a structure of Formula I:



(I),

wherein GAA is acid α-glucosidase, L is a chemical linker connecting the oligosaccharide and the GAA, and n is 1 to 10, and

wherein the pharmaceutical composition is to be administered at a dose of about 20 mg/kg to about 40 mg/kg.

2. The use of claim 1, wherein the pharmaceutical composition is to be administered at a dose of about 20 mg/kg or about 40 mg/kg.

3. The use of claim 1 or 2, wherein the pharmaceutical composition is to be administered:

a. to the individual once every two weeks;

b. intravenously; and/or

c. administered to the individual for at least about 25 weeks.

4. The use of any one of claims 1-3, wherein the pharmaceutical composition is reconstituted from a lyophilized formulation comprising the oligosaccharide-protein conjugate.

5. The use of claim 4, wherein the pharmaceutically acceptable carrier comprises a sugar that is not degraded by GAA, optionally wherein the sugar that is not degraded by GAA is mannitol.

6. The use of claim 4 or 5, wherein the pharmaceutically acceptable carrier further comprises glycine and/or histidine.

7. The use of any one of claims 4-6, wherein the pharmaceutical composition has a pH of about 6.2.

8. The use of any one of claims 4-7, wherein the pharmaceutically acceptable carrier comprises about 10-50 mM histidine, about 0.25-2% glycine, about 1-4% mannitol, and about 0.005-0.05% polysorbate 80.

9. The use of claim 8, wherein the pharmaceutically acceptable carrier comprises about 10 mM histidine, about 2% glycine, about 2% mannitol, and about 0.01% polysorbate 80.

10. The use of any one of claims 1-9, wherein the individual:

a. has cardiomyopathy at the time of diagnosis in the first year of life;

b. has arrhythmia;

c. has cardiomegaly;

d. is 18 years old or younger;

e. is 6 months old or younger; and/or

f. has not received treatment with a recombinant GAA.

11. The use of any one of claims 1-10, wherein the individual has received at least 6 months of treatment with a recombinant GAA, optionally, wherein the individual shows clinical decline after treatment with the recombinant GAA, wherein the clinical decline is determined by assessing one or more parameters selected from the group consisting of respiratory functions, motor skills and cardiac parameters.

12. The use of claim 11, wherein the individual has suboptimal clinical response to treatment with the recombinant GAA, wherein the clinical response is determined by assessing one or more parameters selected from the group consisting of respiratory functions, motor skills and cardiac parameters.

13. The use of claim 11 or 12, wherein the recombinant GAA is alglucosidase alfa.

14. The use of any one of claims 1-13, wherein the individual is cross-reactive immunologic material (CRIM)-negative or the individual is CRIM-positive.

15. The use of any one of claims 1-14, further comprising administering to the individual an effective amount of methotrexate, optionally, wherein the effective amount of methotrexate is administered in a single cycle or in three cycles.

16. The use of claim 15, further comprising administering to the individual an effective amount of an additional immune tolerance induction therapy, optionally, wherein the additional immune tolerance induction therapy comprises rituximab and intravenous immunoglobulin (IVIG).

17. The use of any one of claims 1-16, wherein:

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

b. creatine kinase (CK) level of the individual decreases by at least about 100 IU/L when measured after at least about 25 weeks of treatment;

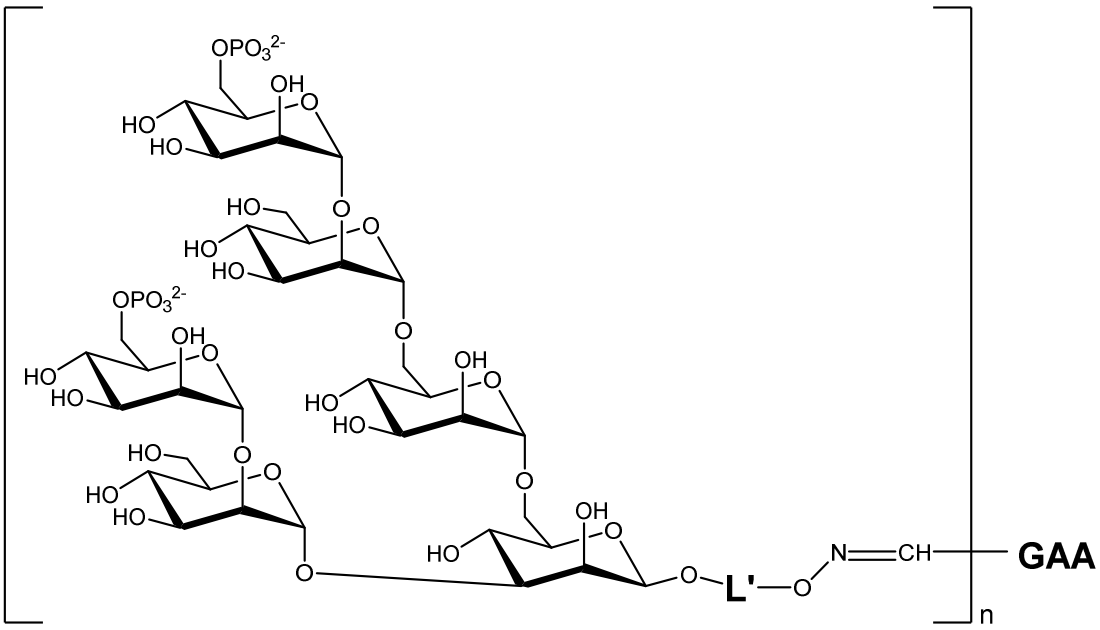
c. urinary hexose tetrasaccharide (Hex4) level of the individual decreases by at least about 10 mmol/mol when measured after at least about 25 weeks of treatment;

d. Gross Motor Function Measure (GMFM-88) score of the individual increases by at least 5% when measured after at least about 25 weeks of treatment; and/or

e. the individual shows improvement or stabilization of one or more parameters selected from the group consisting of respiratory functions, motor skills, cardiac parameters and eyelid positions.

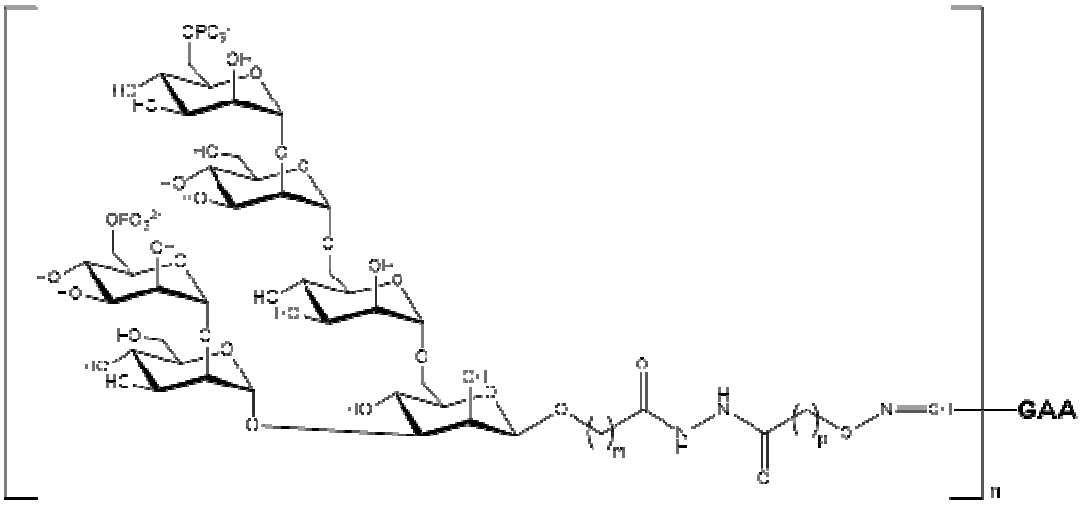
18. The use of claim 17, wherein the improvement or stabilization is assessed based on one or more parameters selected from the group consisting of Alberta Infant Motor Scale (AIMS) score, Pompe-Pediatric Evaluation of Disability Inventory (PEDI) functional skills scale, Echocardiographic (ECHO)-left ventricular mass (LVM) Z-score, ECHO LVMI score, Gross Motor Function Classification System-Expanded and Revised (GMFCS-E&R) score, Quick Motor Function Test, 6 Minute Walk test (6MWT), interpalpebral fissure distance (IPFD), margin reflex distance-1 (MRD-1), margin pupil distance (MPD), onset of ptosis, and use of respiratory support.

19. The use of any one of claims 1-18, wherein the oligosaccharide-protein conjugate has a structure of Formula II:



(II),

wherein GAA is acid a-glucosidase, L' is a chemical linker, and n is 1 to 10, or wherein the oligosaccharide-protein conjugate has a structure of Formula (III):

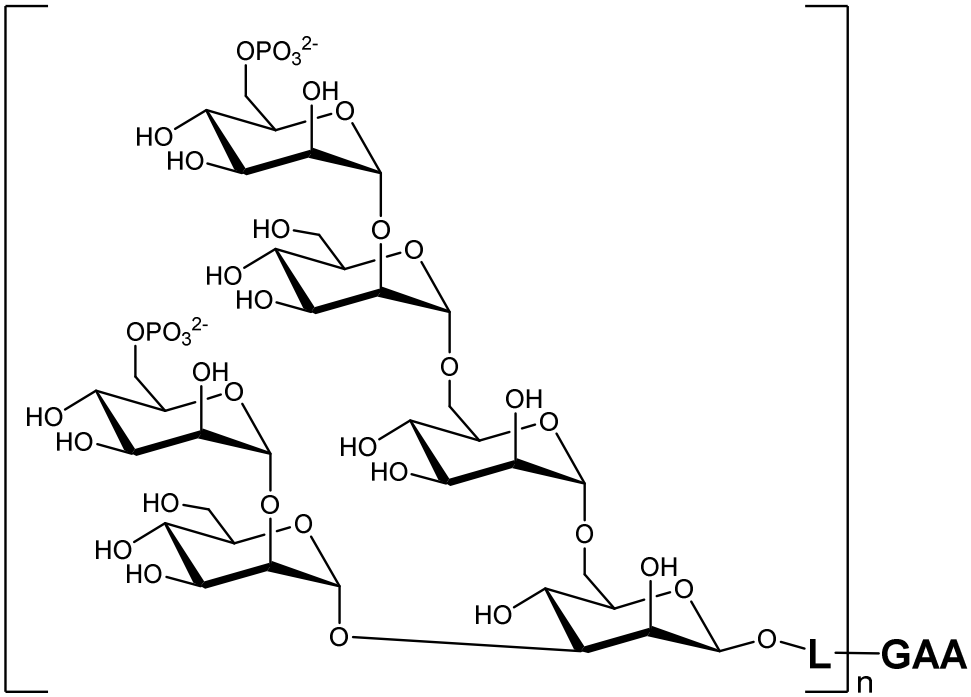


wherein GAA is acid a-glucosidase, n is 1 to 10, and wherein m and p are independently chosen from integers ranging from 1 to 10, optionally, wherein m is 3, p is 1, and/or n is 5-7.

20. The use of any one of claims 1-19, wherein the GAA is a human GAA produced in Chinese hamster ovary (CHO) cells.

21. The use of claim 20, wherein the human GAA has glycoform alfa and/or the oligosaccharide-protein conjugate is avalglucosidase alfa.

22. A formulation comprising: (a) an oligosaccharide-protein conjugate; and (b) one or more cryoprotectants comprising a sugar that is not degraded by acid α-glucosidase; wherein the oligosaccharide-protein conjugate has a structure of Formula I:



(I),

wherein GAA is acid a-glucosidase, L' is a chemical linker, and n is 1 to 10.

23. An article of manufacture comprising a container comprising the formulation of claim 22.

24. The article of manufacture of claim 23, wherein the container is a vial, optionally, wherein the formulation is a lyophilized formulation.

25. Use of an effective amount of a pharmaceutical composition comprising the formulation of claim 22, in the manufacture of a medicament for treating Pompe disease in a human individual, optionally, wherein the Pompe disease is IOPD.

26. A kit comprising the formulation of claim 22, optionally, further comprising instructions for use in treating Pompe disease.