~~We claim:~~

CLAIMS

1. A ~~rhGAA~~ composition ~~derived from CHO cells that contains a higher amount of rhGAA containing N-glycans carrying mono-~~comprising recombinant human alpha glucosidase (rhGAA), wherein 40%-60% of the N-glycans on the rhGAA are complex type N-glycans, and wherein each rhGAA molecule on average comprises at least one bis-phosphorylated mannose-6-phosphate (bis-M6P~~) or~~ glycan).

2. The composition of claim 1, wherein at least 17% of the total glycans on the rhGAA are bis-M6P ~~than conventional rhGAA as exemplified by Lumizyme® (Alglucosidase Alfa; CAS 420794-05-0).~~ glycans.

3. The ~~rhGAA~~ composition of claim 1, wherein the rhGAA comprises ~~an~~the amino acid sequence that is at least ~~95~~90% identical to ~~that described by~~ SEQ ID NO: ~~1~~4.

4. The ~~rhGAA~~ composition of claim 1, wherein ~~30% or more of~~ the rhGAA ~~binds to cation-independent manose~~comprises at least 3.0 mol mannose-6-phosphate ~~receptor (CIMPR) or 30% or more of the rhGAA contains an N-glycan carrying mono-~~(M6P~~-or bis-M6P~~) residues per mol rhGAA.

5. The ~~rhGAA~~ composition of claim ~~1~~4, wherein ~~50% or more of~~ the rhGAA ~~binds to cation-independent manose-6-phosphate receptor (CIMPR) or 50% or more of the rhGAA contains an N-glycan carrying mono-~~comprises at least 4.0 mol M6P ~~or bis-M6P~~residues per mol rhGAA.

~~1. The rhGAA composition of claim 1, wherein 90% to 100% of the rhGAA binds to cation- independent manose-6-phosphate receptor (CIMPR) or 90% to 100% or more of the rhGAA contains an N-glycan carrying mono-M6P or bis-M6P.~~

6. The ~~rhGAA~~ composition of claim ~~1~~4, wherein the ~~average content of N-glycans carrying~~rhGAA comprises at least 5.0 mol M6P ~~ranges from 0.5 to~~ residues per mol rhGAA.

~~2. 7.0 mol/mol rhGAA.~~

The ~~rhGAA~~ composition of claim ~~1~~4, wherein the ~~average content of N-glycans carrying M6P ranges from 1.0 to 4~~rhGAA comprises at least 6.0 mol~~/~~ M6P residues per mol rhGAA.

8. The ~~rhGAA~~ composition of claim ~~1~~4, wherein the ~~average content of N-glycans carrying M6P ranges from 5.0 to 6~~rhGAA comprises at least 7.0 mol~~/~~ M6P residues per mol rhGAA.

9. The ~~rhGAA~~ composition of claim ~~1~~4, wherein ~~on average~~ the ~~N-glycans contain greater than~~rhGAA comprises from 3.0 mol~~/~~ to 6.0 mol ~~of~~ M6P ~~and greater than 4~~residues per mol~~/mol sialic acid~~ rhGAA.

10. The ~~rhGAA~~ composition of claim ~~1~~4, wherein ~~on average 40~~the rhGAA comprises from 3.0 mol to ~~60% of the N-glycans on the~~7.0 mol M6P residues per mol rhGAA ~~are complex type N-glycans; wherein no more than 6.5% of N-glycans on~~.

11. A pharmaceutical composition comprising the rhGAA ~~are hybrid-type N-glycans,~~of claim 1 and ~~wherein no more than 15% of the high mannose-type N-glycans on the rhGAA are non-phosphorylated,~~ at least ~~10% of the high mannose-type N-glycans on the rhGAA are mono-M6P phosphorylated, and/~~one pharmaceutically acceptable carrier or ~~at least 2% of the high mannose-type N-glycans on the rhGAA are bis-M6P phosphorylated~~excipient.

12. The pharmaceutical composition of claim ~~1~~11, wherein the ~~rhGAA on average carries 2.0 to 8.0 sialic acid residues per mol of rhGAA.~~ pharmaceutically acceptable carrier is water.

13. The pharmaceutical composition of claim ~~1~~11, wherein the ~~rhGAA is produced by CHO cell line ATB200-001-X5~~ composition is in the form of a lyophilized powder.

~~3. 14 or by a subculture thereof.~~

. The pharmaceutical composition of claim ~~1, further comprising a chaperone~~11, wherein the composition comprises mannitol.

~~A method for making the~~15. The pharmaceutical composition of claim ~~1 comprising culturing a CHO cell line and recovering said composition from the culture of CHO cells.~~ 11, wherein the composition comprises polysorbate 80.

~~4. A CHO cell line that produces the~~16. The pharmaceutical composition of claim ~~1.~~

~~5. CHO cell line GA-ATB-200 or a subculture thereof that produces the composition of claim 1.~~

~~6. A method for making the CHO cell line of claim 15, comprising transforming a CHO cell with DNA encoding rhGAA, selecting a CHO cell that stably integrates the DNA encoding rhGAA into its chromosome(s) and that stably expresses rhGAA, and selecting a CHO cell that expresses rhGAA having a high content of glycans bearing M6P or bis-M6P, and, optionally, selecting a CHO cell having N-glycans with high sialic acid content and and/or having N-glycans with a low non-phosphorylated high-mannose content.~~

~~7. A method for treating a condition, disorder or disease associated with insufficient lysosomal rhGAA comprising administering the composition of claim 1 to a subject in need thereof.~~

~~8. The method of claim 18, wherein the subject has Glycogen Storage Disease Type II (Pompe Disease).~~

~~9. The method of claim 18, comprising administering said composition to cardiac muscle of the subject.~~

~~10. The method of claim 18, comprising administering~~ 11, wherein the composition ~~to quadriceps, triceps or other skeletal muscle of the subject.~~

~~11. The method of claim 18, comprising administering said composition to the diaphragm of the subject.~~

~~12. The method of claim 18, wherein said composition is combined with, coadministered with, or separately administered along with, a pharmacological chaperone.~~

~~13. The method of claim 18, wherein said composition is combined with, coadministered with, or separately administered along with, AT2220 or a salt thereof.~~

~~14. The method of claim 18, wherein said composition is combined with, coadministered with, or separately administered along with, AT2221or a salt thereof.~~

~~26. A method for metabolizing, degrading, removing or otherwise decreasing glycogen in tissue, muscle, muscle fiber, muscle cells, lysosomes, organelles, cellular compartments, or cytoplasm, comprising administering the composition of claim 1 to a subject, optionally along with a chaperone or a drug that reduces immunological responses to rhGAA.~~

~~27. A method for modulating lysosomal proliferation, autophagy, or exocytosis in a cell comprising administering the composition of claim 1, optionally in combination with a chaperone, to a subject in need thereof.~~

comprises a pH buffer.