

What is claimed is:

1. A method for producing recombinant human lysosomal proteins, the method comprising:
culturing host cells in a bioreactor that secrete a recombinant human lysosomal protein;
5 removing media from the bioreactor;
filtering the media to provide a filtrate;
loading the filtrate onto an anion exchange chromatography (AEX) column to capture
the lysosomal protein; and
eluting a first protein product from the AEX column.
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2. The method of claim 1, wherein the recombinant human lysosomal protein is recombinant
human α -glucosidase (rhGAA).
3. The method of claim 2, wherein the rhGAA comprises an amino acid sequence that is at
15 least 95% identical to SEQ ID NO: 2.
4. The method of any of claims 1-3, further comprising:
loading the first protein product onto an immobilized metal affinity chromatography
(IMAC) column; and
20 eluting a second protein product from the IMAC column.
5. The method of claim 4, further comprising:
loading the second protein product onto a third chromatography column; and
eluting a third protein product from the third chromatography column.
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6. The method of claim 5, wherein the third chromatography column is selected from a cation
exchange chromatography (CEX) column and a size exclusion chromatography (SEC) column.
7. The method of any of claims 1-6, wherein filtering the media is selected from alternating
30 tangential flow filtration (ATF) and tangential flow filtration (TFF).

8. The method of any of claims 1-7, further comprising inactivating viruses in one or more of the first protein product, the second protein product and the third protein product.
9. The method of any of claims 1-8, further comprising filtering the second protein product or the third protein product to provide a filtered product and filling a vial with the filtered product.
10. The method of any of claims 1-9, further comprising lyophilizing the filtered product.
11. The method of any of claims 1-10, wherein the host cells comprise Chinese hamster ovary (CHO) cells.
12. The method of any of claims 1-11, wherein the host cells comprise CHO cell line GA-ATB-200 or ATB-200-001-X5-14 or a subculture thereof.
13. The method of any of claims 1-12, wherein:
- (i) at least 90% of the first protein product or the second protein product or the third protein product binds to cation-independent manose-6-phosphate receptor (CIMPR) or
 - (ii) at least 90% of the first protein product or the second protein product or the third protein product contains an N-glycan carrying mono-mannose-6-phosphate (mono-M6P) or bis-mannose-6-phosphate (bis-M6P).
14. The method of any of claims 1-13, wherein the rhGAA comprises seven potential N-glycosylation sites, at least 50% of molecules of the rhGAA comprise an N-glycan unit bearing two mannose-6-phosphate residues at the first site, at least 30% of molecules of the rhGAA comprise an N-glycan unit bearing one mannose-6-phosphate residue at the second site, at least 30% of molecules of the rhGAA comprise an N-glycan unit bearing two mannose-6-phosphate residue at the fourth site, and at least 20% of molecules of the rhGAA comprise an N-glycan unit bearing one mannose-6-phosphate residue at the fourth site.
15. A recombinant protein product made by the method of any of claims 1-14.

16. A pharmaceutical composition comprising the recombinant protein product of claim 15 and a pharmaceutically acceptable carrier.

5 17. Use of the pharmaceutical composition of claim 16 for treating a lysosomal storage disorder.

18. The use of claim 17, wherein the lysosomal storage disorder is Pompe disease and the recombinant protein is rhGAA.

10 19. The use of claim 18, wherein the patient is co-administered a pharmacological chaperone for α -glucosidase within 4 hours of the administration of the pharmaceutical composition comprising the rhGAA product.

15 20. The use of claim 19, wherein the pharmacological chaperone is selected from 1-deoxynojirimycin and N-butyl-deoxynojirimycin.

21. The use of claim 19 or 20, wherein the pharmacological chaperone is co-formulated with the rhGAA product.