WHAT IS CLAIMED IS:

1. A polypeptide consisting of human acid alpha-glucosidase or a catalytically-active fragment thereof having a modification at or near an N-terminal 70-kDa processing site.

2. A polypeptide comprising a human acid alpha-glucosidase or a catalytically-active fragment thereof having a modification at or near an N-terminal 70-kDa processing site.

3. The polypeptide of claim 1 or 2, wherein the modification is increased hydrophobicity at or near the N-terminal 70-kDa processing site.

4. The polypeptide of claim 1 or 2, wherein the modification is at one or more amino acids corresponding to positions 195-209 of SEQ ID NO: 1.

5. The polypeptide of claim 4, wherein the modification is at one or more amino acids corresponding to positions 200-204 of SEQ ID NO: 1.

6. The polypeptide of claim 5, wherein the modification is at the amino acid corresponding to position 201 of SEQ ID NO: 1.

7. The polypeptide of any one of claims 1 to 6, wherein the modification comprises

a) substitution of one or more amino acids with a more hydrophobic amino acid, or

b) insertion of one or more hydrophobic amino acids.

8. The polypeptide of claim 1 or 2, wherein the fragment is chosen from a 70-kDa, 76-kDa, 82-kDa, 95-kDa, or any other catalytically-active fragment of human acid alpha-glucosidase.

9. The polypeptide of claim 8, wherein the polypeptide further comprises a receptor targeting sequence.

10. The polypeptide of claim 9, wherein the receptor targeting sequence is IGF2.

11. The polypeptide of claim 1 or 2, wherein the polypeptide has at least 80% identity to at least 500 amino acids of SEQ ID NO: 1.

12. The polypeptide of claim 11, wherein the polypeptide has at least 90% identity to at least 500 amino acids of SEQ ID NO: 1.

13. The polypeptide of claim 12, wherein the polypeptide has at least 95% identity to at least 500 amino acids of SEQ ID NO: 1.

14. The polypeptide of claim 1 or 2, wherein the modified polypeptide exhibits more rapid lysosomal protease processing when compared to an unmodified human acid alpha-glucosidase.

15. The polypeptide of claim 14, wherein at least 50% of the polypeptide is proteolytically processed to a 70-kDa form within 20 hours of administration.

16. The polypeptide of claim 15, wherein substantially all the polypeptide is proteolytically processed to a 70-kDa form within 55 hours of administration.

17. The polypeptide of claim 1 or 2, wherein the polypeptide is conjugated to an oligosaccharide comprising at least one mannose-6-phosphate.

18. A nucleic acid encoding a polypeptide selected from any one of claims 1-17.

19. A host cell stably transfected with the nucleic acid of claim 18.

20. The host cell of claim 19, wherein the host cell is capable of secreting the polypeptide encoded by the nucleic acid of claim 18.

21. A method of reducing or preventing glycogen accumulation in a tissue, comprising administering an effective amount of a polypeptide of claim 1 or 2 to a patient in need thereof.

22. The method of claim 21, wherein the patient has a glycogen storage disease.

23. The method of claim 22, wherein the glycogen storage disease is Pompe disease.

24. A method of treating a glycogen storage disease, comprising administering a therapeutically effective amount of a polypeptide of claim 1 or 2 to a patient in need thereof.

25. The method of claim 24, wherein the glycogen storage disease is Pompe disease.

26. A pharmaceutical composition comprising a polypeptide of any one of claims 1 to 17 for use in treating a glycogen storage disease.

27. The pharmaceutical composition of claim 26, wherein the polypeptide is lyophilized.

28. A use of a polypeptide of any one of claims 1-17 in the manufacture of a medicament for reducing or preventing glycogen accumulation in a tissue.

29. The use of claim 28, wherein the glycogen accumulation is due to a glycogen storage disease.

30. The use of claim 29, wherein the glycogen storage disease is Pompe disease.

WHAT IS CLAIMED IS:

1. A polypeptide comprising a human acid alpha-glucosidase or a catalytically-active fragment thereof having a modification at or near an N-terminal 70-kDa processing site, wherein the polypeptide exhibits more rapid lysosomal protease processing when compared to an unmodified human acid alpha-glucosidase.

2. The polypeptide of claim 1, wherein the modification is increased hydrophobicity at or near the N-terminal 70-kDa processing site.

3. The polypeptide of claim 1, wherein the modification is at one or more amino acids corresponding to positions 195-209 of SEQ ID NO: 1.

4. The polypeptide of claim 3, wherein the modification is at one or more amino acids corresponding to positions 200-204 of SEQ ID NO: 1.

5. The polypeptide of claim 4, wherein the modification is at the amino acid corresponding to position 201 of SEQ ID NO: 1.

6. The polypeptide of any one of claims 1 to 5, wherein the modification comprises

a) substitution of one or more amino acids with a more hydrophobic amino acid, or

b) insertion of one or more hydrophobic amino acids.

7. The polypeptide of claim 1, wherein the fragment is chosen from a 70-kDa, 76-kDa, 82-kDa, 95-kDa, or any other catalytically-active fragment of human acid alpha-glucosidase.

8. The polypeptide of claim 1, wherein the polypeptide has at least 80% identity to at least 500 amino acids of SEQ ID NO: 1.

9. The polypeptide of claim 1, wherein at least 50% of the polypeptide is proteolytically processed to a 70-kDa form within 20 hours of administration.

10. The polypeptide of claim 9, wherein substantially all the polypeptide is proteolytically processed to a 70-kDa form within 55 hours of administration.

11. A nucleic acid encoding a polypeptide selected from any one of claims 1-10.

12. A host cell stably transfected with the nucleic acid of claim 11.

13. A pharmaceutical composition comprising a polypeptide of any one of claims 1 to 10 for use in treating a glycogen storage disease.

14. A polypeptide of any one of claims 1-10 for use in the reduction or prevention of glycogen accumulation in a tissue.