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What is claimed is:

1. A method for uncapping a mannose-6-phosphate residue on an oligosaccharide, said method comprising
 - a) providing said oligosaccharide having a mannose-1-phospho-6-mannose linkage; and
 - b) contacting said oligosaccharide with a mannosidase capable of hydrolyzing said mannose-1-phospho-6-mannose residue to phospho-6-mannose, wherein said mannosidase is a member of glycosyl hydrolase family 92.
2. The method of claim 1, wherein said mannosidase comprises an amino acid sequence having at least 90% identity to residues 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50.
3. The method of claim 1, wherein said mannosidase comprises an amino acid sequence having at least 95% identity to residues 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50.
4. The method of any one of claims 1-3, wherein said mannosidase comprises an amino acid sequence having at least 98% identity residues 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50.
5. The method of any one of claims 1-4, wherein said amino acid sequence comprises residues 1-774 of SEQ ID NO:50 or to SEQ ID NO:50.
6. The method of claim 5, wherein said amino acid sequence further comprises, N-terminal of residues 1-774 of SEQ ID NO:50 or of SEQ ID NO:50, residues 1-15 of SEQ ID NO:15.
7. The method of any one of claims 2-6, wherein for said mannosidase, the three dimensional protein coordinates of the atoms in the amino acid side chains located in the minimal catalytic center fall within 1.5 Å deviation of the coordinates of the equivalent atoms in FIG. 33.
8. The method of any one of claims 1-7, wherein said mannosidase comprises an amino acid sequence having (i) a GVGXXGXGG motif, where X is Gly, Ala, Ser, Thr, or Cys; (ii) a VRXE motif, where X is any amino acid other than Pro; (iii) an X₁YQGX₂ motif, where X₁ is Leu, Ile,

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Val, Ala, Phe, Tyr or Met, and X₂ is Thr, Ser, or Asn; or (iv) GDXGN, where X can be any amino acid other than Pro.

9. The method of any one of claims 1-8, wherein said contacting step is performed using a purified mannosidase, a recombinant mannosidase, a cell lysate containing said recombinant mannosidase, or a fungal cell containing said recombinant mannosidase.

10. The method of any one of claims 1-9, wherein said oligosaccharide is attached to a protein.

11. The method of claim 10, wherein said protein is a human protein expressed in a fungal organism.

12. The method of claim 11, wherein said fungal organism is *Yarrowia lipolytica* or *Arxula adeninivorans*.

13. The method of claim 11, wherein said fungal organism is a methylotrophic yeast.

14. The method of claim 13, wherein said methylotrophic yeast is *Pichia pastoris*, *Pichia methanolica*, *Oogataea minuta*, or *Hansenula polymorpha*.

15. The method of claim 11, wherein said fungal organism is a filamentous fungus.

16. The method of claim 15, wherein said filamentous fungus is selected from the group consisting of *Aspergillus caesiellus*, *Aspergillus candidus*, *Aspergillus carneus*, *Aspergillus clavatus*, *Aspergillus deflexus*, *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus glaucus*, *Aspergillus nidulans*, *Aspergillus niger*, *Aspergillus ochraceus*, *Aspergillus oryzae*, *Aspergillus parasiticus*, *Aspergillus penicilloides*, *Aspergillus restrictus*, *Aspergillus sojae*, *Aspergillus sydowi*, *Aspergillus tamari*, *Aspergillus terreus*, *Aspergillus ustus*, and *Aspergillus versicolor*.

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17. The method of any one of claims 10-16, wherein said protein is a pathogen protein, a lysosomal protein, a growth factor, a cytokine, a chemokine, an antibody or antigen-binding fragment thereof, or a fusion protein.
18. The method of claim 17, wherein said lysosomal protein is a lysosomal enzyme.
19. The method of claim 18, wherein said lysosomal enzyme is associated with a lysosomal storage disorder (LSD).
20. The method of claim 19, wherein said LSD is Fabry's disease, mucopolysaccharidosis I, Farber disease, Gaucher disease, GM1-gangliosidosis, Tay-Sachs disease, Sandhoff disease, GM2 activator disease, Krabbe disease, metachromatic leukodystrophy, Niemann-Pick disease, Scheie disease, Hunter disease, Sanfilippo disease, Morquio disease, Maroteaux-Lamy disease, hyaluronidase deficiency, aspartylglucosaminuria, fucosidosis, mannosidosis, Schindler disease, sialidosis type 1, Pompe disease, Pycnodysostosis, ceroid lipofuscinosis, cholesterol ester storage disease, Wolman disease, Multiple sulfatase deficiency, galactosialidosis, mucopolipidosis, cystinosis, sialic acid storage disorder, chylomicron retention disease with Marinesco-Sjögren syndrome, Hermansky-Pudlak syndrome, Chediak-Higashi syndrome, Danon disease, or Geleophysic dysplasia.
21. The method of claim 19, wherein said LSD is Pompe disease or Fabry's disease.
22. The method of any one of claims 1-20, wherein said mannosidase comprises a targeting sequence.
23. A method of producing a target protein having an uncapped phospho-6-mannose residue, said method comprising:
providing a fungal cell genetically engineered to comprise and express a nucleic acid encoding a mannosidase, said mannosidase being capable of hydrolyzing a mannose-1-phospho-6-mannose residue to phospho-6-mannose; and

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introducing into said cell a nucleic acid encoding a target protein, wherein said cell produces said target protein in which a mannose-1-phospho-6-mannose residue on the target has been converted to a phospho-6-mannose residue by said expressed mannosidase expressed in the cell.

24. The method of claim 23, wherein said mannosidase comprises a) an amino acid sequence having at least 90% sequence identity to amino acids 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50; or (b) an amino acid sequence having (i) a GVGXXGXGG motif, where X is Gly, Ala, Ser, Thr, or Cys; (ii) a VRXE motif, where X is any amino acid other than Pro; (iii) an X₁YQGX₂ motif, where X₁ is Leu, Ile, Val, Ala, Phe, Tyr or Met, and X₂ is Thr, Ser, or Asn; or (iv) GDXXGN, where X can be any amino acid other than Pro.

25. The method of claim 24, wherein for said mannosidase, the three dimensional protein coordinates of the atoms in the amino acid side chains located in the minimal catalytic center fall within 1.5 Å deviation of the coordinates of the equivalent atoms in FIG. 33.

26. The method of any one of claims 23-25, wherein said fungal cell further comprises a nucleic acid encoding a polypeptide capable of promoting mannosyl phosphorylation.

27. The method of any one of claims 23-26, wherein said fungal cell is genetically engineered to be deficient in OCH1 activity.

28. The method of any one of claims 23-27, wherein said mannosidase is a *C. cellulans*, *Streptomyces coelicolor*, or *Streptomyces lividans* mannosidase.

29. A method of producing a target protein having an uncapped phospho-6-mannose residue in a fungal organism, said method comprising

a) providing a fungal cell genetically engineered to comprise and express a nucleic acid encoding a mannosidase capable of hydrolyzing mannose-1-phospho-6-mannose to phospho-6-mannose, and said fungal cell further comprising a nucleic acid encoding a target protein in

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which a mannose-1-phospho-6-mannose residue on the target has been converted to a phospho-6-mannose residue by said expressed mannosidase expressed in the cell; and

b) isolating said target protein having said uncapped phospho-6-mannose residue.

30. The method of claim 29, wherein said mannosidase comprises (i) an amino acid sequence having at least 90% sequence identity to amino acids 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50; or (ii) an amino acid sequence having (i) a GVGXXGXGG motif, where X is Gly, Ala, Ser, Thr, or Cys; (ii) a VRXE motif, where X is any amino acid other than Pro; (iii) an X_1YQGX_2 motif, where X_1 is Leu, Ile, Val, Ala, Phe, Tyr or Met, and X_2 is Thr, Ser, or Asn; or (iv) GDXGN, where X can be any amino acid other than Pro.

31. The method of claim 30, wherein for said mannosidase, the three dimensional protein coordinates of the atoms in the amino acid side chains located in the minimal catalytic center fall within 1.5 Å deviation of the coordinates of the equivalent atoms in FIG. 33.

32. The method of any one of claims 29-31, wherein said target protein and said mannosidase are secreted by the cell.

33. An isolated fungal cell genetically engineered to produce glycoproteins comprising an uncapped phospho-6-mannose residue, said fungal cell comprising a nucleic acid encoding a mannosidase, wherein expression of said mannosidase in said fungal cell results in the production of glycoproteins comprising said terminal phospho-6-mannose residues, wherein said mannosidase is a member of glycosyl hydrolase family 92.

34. The fungal cell of claim 33, wherein said mannosidase comprises a) an amino acid sequence having at least 90% sequence identity to amino acids 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50; or b) an amino acid sequence having (i) a GVGXXGXGG motif, where X is Gly, Ala, Ser, Thr, or Cys; (ii) a VRXE motif, where X is any amino acid other than Pro; (iii) an X_1YQGX_2 motif, where X_1 is Leu, Ile, Val, Ala, Phe, Tyr or Met, and X_2 is Thr, Ser, or Asn; or (iv) GDXGN, where X can be any amino acid other than Pro.

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35. The fungal cell of claim 34, wherein for said mannosidase, the three dimensional protein coordinates of the atoms in the amino acid side chains located in the minimal catalytic center fall within 1.5 Å deviation of the coordinates of the equivalent atoms in FIG. 33.
36. The fungal cell of any one of claims 33-35, said fungal cell further comprising a nucleic acid encoding a polypeptide capable of promoting mannosyl phosphorylation.
37. The fungal cell of any one of claims 33-36, wherein said fungal cell is genetically engineered to be deficient in OCH1 (Outer CHain elongation) activity.
38. The fungal cell of any one of claims 36-37, said fungal cell further comprising a nucleic acid encoding a polypeptide capable of promoting mannosyl phosphorylation, and wherein said fungal cell is genetically engineered to be deficient in OCH1 activity.
39. The fungal cell of any one of claims 33-38, said fungal cell further comprising a nucleic acid encoding a target protein, wherein said target protein is a glycoprotein.
40. The fungal cell of claim 39, wherein said target protein is a human protein.
41. The fungal cell of claim 39 or 40, wherein said target protein is a pathogen protein, a lysosomal protein, a growth factor, a cytokine, a chemokine, an antibody or antigen-binding fragment thereof, or a fusion protein.
42. The fungal cell of claim 41, wherein said lysosomal protein is a lysosomal enzyme.
43. The fungal cell of claim 42, wherein said lysosomal enzyme is acid alpha glucosidase or alpha galactosidase.
44. The fungal cell of any one of claims 39, 40, or 41-43, wherein said target protein is a protein associated with a LSD.

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45. The fungal cell of claim 44, wherein said LSD is Fabry's disease, mucopolysaccharidosis I, Farber disease, Gaucher disease, GM1-gangliosidosis, Tay-Sachs disease, Sandhoff disease, GM2 activator disease, Krabbe disease, metachromatic leukodystrophy, Niemann-Pick disease, Scheie disease, Hunter disease, Sanfilippo disease, Morquio disease, Maroteaux-Lamy disease, hyaluronidase deficiency, aspartylglucosaminuria, fucosidosis, mannosidosis, Schindler disease, sialidosis type I, Pompe disease, Pycnodysostosis, ceroid lipofuscinosis, cholesterol ester storage disease, Wolman disease, Multiple sulfatase deficiency, galactosialidosis, mucopolipidosis, cystinosis, sialic acid storage disorder, chylomicron retention disease with Marinesco-Sjögren syndrome, Hermansky-Pudlak syndrome, Chediak-Higashi syndrome, Danon disease, or Geleophysic dysplasia.

46. The fungal cell of any one of claims 33-45, wherein said fungal cell is a *Yarrowia lipolytica* or an *Arxula adeninivorans* cell.

47. The fungal cell of claim 36, wherein said polypeptide capable of promoting mannosyl phosphorylation is a MNN4 polypeptide.

48. The fungal cell of claim 47, wherein said MNN4 polypeptide is a *Yarrowia lipolytica*, *S. cerevisiae*, *Ogataea minuta*, *Pichia pastoris*, or *C. albicans* polypeptide.

49. The fungal cell of claim 36, wherein said polypeptide capable of promoting mannosyl phosphorylation is a *P. pastoris* PNO1 polypeptide.

50. The fungal cell of any one of claims 33-49, wherein said mannosidase is a *C. cellulans*, *Streptomyces coelicolor*, or *Streptomyces lividans* mannosidase.

51. The fungal cell of any one of claims 33-50, wherein said mannosidase comprises a secretion signal.

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52. The fungal cell of any one of claims 33-51, wherein said mannosidase comprises a targeting signal to target said mannosidase to an intracellular compartment.
53. The fungal cell of any one of claims 33-52, wherein said mannosidase comprises a secretion signal and a targeting signal to target said mannosidase to an intracellular compartment.
54. A substantially pure culture of *Yarrowia lipolytica*, *Pichia pastoris*, *Hansenula polymorpha*, *Arxula adeninivorans*, *Pichia methanolica*, *Oogataea minuta*, or *Aspergillus niger* cells, a substantial number of which are genetically engineered to produce a glycoprotein comprising an uncapped phospho-6-mannose residue, said cells comprising a nucleic acid encoding a mannosidase capable of hydrolyzing mannose-1-phospho-6-mannose to phospho-6-mannose, wherein said mannosidase is a member of glycosyl hydrolase family 92.
55. The culture of claim 54, wherein said mannosidase comprises a) an amino acid sequence having at least 90% sequence identity to amino acids 1 to 774 of SEQ ID NO:50 or to the amino acid sequence of SEQ ID NO:50; or b) an amino acid sequence having (i) a GVGXXGXGG motif, where X is Gly, Ala, Ser, Thr, or Cys; (ii) a VRXE motif, where X is any amino acid other than Pro; (iii) an X₁YQGX₂ motif, where X₁ is Leu, Ile, Val, Ala, Phe, Tyr or Met, and X₂ is Thr, Ser, or Asn; or (iv) GDXGN, where X can be any amino acid other than Pro.
56. The culture of claim 55, wherein for said mannosidase, the three dimensional protein coordinates of the atoms in the amino acid side chains located in the minimal catalytic center fall within 1.5 Å deviation of the coordinates of the equivalent atoms in FIG. 33.
57. The culture of any one of claims 54-56, wherein said cells further comprise a nucleic acid encoding a polypeptide capable of promoting mannosyl phosphorylation.
58. The culture of any one of claims 54-57, wherein said cells are genetically engineered to be deficient in OCH1 activity.

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59. An isolated glycoprotein comprising an uncapped phospho-6-mannose residue, wherein the protein is produced by the method of any one of claims 1-32.

60. A composition comprising a glycoprotein, wherein at least 47% of the N-glycans on said glycoprotein comprise an uncapped phospho-6-mannose residue.

61. The composition of claim 60, wherein at least 50% of the N-glycans on said glycoprotein comprise an uncapped phospho-6-mannose residue.

62. The composition of claim 60 or 61, wherein at least 75% of the N-glycans on said glycoprotein comprise an uncapped phospho-6-mannose residues.

63. The composition of any one of claims 60-62, wherein at least 90% of the N-glycans on said glycoprotein comprise an uncapped phospho-6-mannose residue.

64. A polypeptide comprising an amino acid sequence having at least 90% identity to residues 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50, wherein the polypeptide is capable of hydrolyzing mannose-1-phospho-6-mannose to phospho-6-mannose.

65. The polypeptide of claim 64, wherein the amino acid sequence has at least 95% identity to residues 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50.

66. The polypeptide of claim 64 or 65, wherein the amino acid sequence has at least 98% identity to residues 1 to 774 of SEQ ID NO:50 or to SEQ ID NO:50.

67. The polypeptide of any of claims 64-66, wherein the amino acid sequence comprises residues 1 to 774 of SEQ ID NO:50 or SEQ ID NO:50.

68. The polypeptide of claim 67, further comprising, at the N-terminus of residues 1 to 774 of SEQ ID NO:50 or SEQ ID NO:50, residues 1-15 of SEQ ID NO:15.

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69. The polypeptide of any one of claims 64-68, wherein for said polypeptide, the three dimensional protein coordinates of atoms in the amino acid side chains located in the minimal catalytic center fall within 1.5 Å deviation of the coordinates of the equivalent atoms in FIG. 33.

70. The polypeptide of any one of claims 64-69, wherein said polypeptide comprises an amino acid sequence having (i) a GVGXXGXGG motif, where X is Gly, Ala, Ser, Thr, or Cys; (ii) a VRXE motif, where X is any amino acid other than Pro; (iii) an X_1YQGX_2 motif, where X_1 is Leu, Ile, Val, Ala, Phe, Tyr or Met, and X_2 is Thr, Ser, or Asn; or (iv) GDXGN, where X can be any amino acid other than Pro.

71. A nucleic acid comprising:

- (a) a nucleotide sequence encoding the polypeptide of any of claims 64-70; or
- (b) the complement of the nucleotide sequence.

72. The nucleic acid of claim 71, wherein the nucleotide sequence encodes residues 1 to 774 of SEQ ID NO:50 or SEQ ID NO:50.

73. The nucleic acid of claim 71 or 72, wherein the nucleotide sequence comprises nucleotides 46 to 2322 of SEQ ID NO:14 or nucleotides 46 to 4995 of SEQ ID NO:14.

74. The nucleic acid of claim 73, further comprising, 5' of nucleotides 46 to 2322 of SEQ ID NO:14 or of nucleotides 46 to 4995 SEQ ID NO:14, nucleotides 1-45 of SEQ ID NO:14.

75. An expression vector comprising the nucleic acid of any of claims 71-74, wherein the nucleic acid comprises (a).

76. A host cell comprising the expression vector of claim 75.

77. A method of making a polypeptide, the method comprising culturing the host cell of claim 76 and isolating the polypeptide from the culture.