What is claimed is:

1. A method of producing an altered N-glycosylation form of a target protein or polypeptide, the method comprising:

providing a ~~*Yarrowia lipolytica* or an *Arxula adeninivorans* cell~~ cell genetically engineered to comprise at least one modified N-glycosylation activity relative to a non-genetically engineered cell of the same species, the cell being a *Yarrowia lipolytica* or an *Arxula adeninivorans* cell or a cell from a related species of dimorphic yeast, the at least one modified N-glycosylation activity comprising; ~~and~~

~~introducing into the cell a nucleic acid encoding a target protein, wherein the cell produces the target protein in an altered N-glycosylation form~~

expression of a phosphorylation-promoting protein or biologically active variant thereof that promotes mannosyl phosphorylation of the target protein or polypeptide, wherein the phosphorylation-promoting protein or biologically active variant thereof is MNN4 or PNO1; and

introducing into the cell a nucleic acid encoding a target protein or polypeptide, wherein the cell produces the target protein or polypeptide in an altered N-glycosylation form relative to a non-genetically engineered cell of the same species.

2. The method of claim 1, further comprising isolating the altered N-glycosylation form of the target protein.

3. The method of claim 1 or 2, wherein the target protein is an exogenous protein.

4. The method of any of claims 1-3, wherein the target protein is an endogenous protein.

5. The method of any of claims 1-4, wherein the target protein is a mammalian protein.

6. The method of claim 5, wherein the target protein is a human protein.

7. The method of any of claims 1-6, wherein the 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.

8. The method of claim 7, wherein the fusion protein is a fusion of a pathogen protein, a lysosomal protein, a growth factor, a cytokine, or a chemokine with an antibody or an antigen-binding fragment thereof.

9. The method of any of claims 1-8, wherein the target protein is a protein associated with a lysosomal storage disorder (LSD).

10. The method of any of claims 1-9, wherein the target protein is glucocerebrosidase or galactocerebrosidase.

11. The method of any of claims 1-9, wherein the target protein is selected from the group consisting of alpha-L-iduronidase, beta-D-galactosidase, beta-glucosidase, beta-hexosaminidase, beta-D-mannosidase, alpha-L-fucosidase, arylsulfatase B, arylsulfatase A, alpha-N-acteylgalactosaminidase, aspartylglucosaminidase, iduronate-2-sulfatase, alpha-glucosaminide-N-acetyltransferase, beta-D-glucoronidase, hyaluronidase, alpha-L-mannosidase, alpha- neuraminidase, phosphotransferase, acid lipase, acid ceramidase, sphinogmyelinase, thioesterase, cathepsin K, and lipoprotein lipase.

12. The method of any of claims 1-11, wherein the altered N-glycosylation form of the target protein or polypeptide protein comprises one or more N-glycan structures.

~~13. The method of claim 12, wherein the one or more N-glycans are $Man_5GlcNAc_2$.~~

~~14. The method of claim 12, wherein the one or more N-glycans are $Man_8GlcNAc_2$.~~

~~15. The method of claim 12, wherein the one or more N-glycans are $Man_9GlcNAc_2$.~~

~~16. The method of claim 12, wherein the one or more N-glycans are $Man_3GlcNAc_2$.~~

~~17. The method of claim 12, wherein the one or more N-glycans are $Glc_1Man_5GlcNAc_2$.~~

~~18. The method of claim 12, wherein the one or more N-glycans are $Glc_2Man_5GlcNAc_2$.~~

13~~9~~. The method of ~~any of~~ claims 12~~-18~~, wherein the altered N-glycosylation form of the target protein is homogenous.

~~20~~14. The method of ~~any~~ either of claims 12~~-18~~ or 13, wherein the altered N-glycosylation form of the target protein is substantially homogenous.

1521. The method of claim ~~20~~14, wherein the fraction of altered target molecules that contain the altered glycosylation is at least about 20%.

~~22~~16. The method of claim ~~20~~14, wherein the fraction of altered target molecules that contain the altered glycosylation is at least about 30%.

~~23~~17. The method of claim ~~20~~14, wherein the fraction of altered target molecules that contain the altered glycosylation is at least about 40%.

~~24. The method of any of claims 19-23, wherein the altered glycosylation is $Man_5GlcNAc_2$.~~

~~25. The method of any of claims 19-23, wherein the altered glycosylation is $Man_8GlcNAc_2$.~~

~~26. The method of any of claims 19-23, wherein the altered glycosylation is $Man_9GlcNAc_2$.~~

~~27. The method of any of claims 19-23, wherein the altered glycosylation is $Man_3GlcNAc_2$.~~

~~28. The method of any of claims 19-23, wherein the altered glycosylation is $Glc_1Man_5GlcNAc_2$.~~

~~29. The method of any of claims 19-23, wherein the altered glycosylation is $Glc_2Man_5GlcNAc_2$.~~

~~30~~18. The method of any of claims 1-~~29~~17, wherein the cell is genetically engineered to ~~be deficient in~~comprise at least one further N-glycosylation activity.

~~31. The method of claim 30, wherein N-glycosylation activity is ALG3 activity.~~

~~32~~19. The method of claim ~~30~~18, wherein N-glycosylation activity is OCH1 activity.

~~33. The method of claim 30, wherein N-glycosylation activity is MNS1 activity.~~

~~34. The method of claim 30, wherein N-glycosylation activity is MNN9 activity.~~

~~32~~05. The method of ~~any~~ either of claims 181~~-3~~ or 194, wherein the at least one further modification comprises deletion of a gene encoding a protein having the N-glycosylation activity.

~~32~~16. The method of any of claims 181~~-35~~20, wherein the at least one further modification comprises expression of a mutant form of a protein having the N-glycosylation activity.

~~37~~22. The method of any of claims ~~1~~18~~-32~~16, wherein the at least one further modification comprises introduction or expression of an RNA molecule that interferes with the functional expression of a protein having the N-glycosylation activity.

~~38~~23. The method of ~~any of~~ claim 181~~-37~~, wherein the at least one further modification comprises expression of a protein having N-glycosylation activity.

~~39~~24. The method of claim ~~38~~23, wherein the expressed protein is a protein encoded by an exogenous nucleic acid in the cell.

~~40. The method of claim 38, wherein the N-glycosylation activity is a glucosyltransferase activity.~~

~~41. The method of any of claims 38-40, wherein the protein having N-glycosylation activity is ALG6.~~

~~42. The method of claim 38, wherein the protein having N-glycosylation activity is an alpha-mannosidase.~~

~~43. The method of claim 38, wherein the alpha-mannosidase is targeted to the endoplasmic reticulum.~~

~~44. The method of claim 42 or 43, wherein the protein having N-glycosylation activity is a fusion protein comprising an alpha-mannosidase polypeptide and an HDEL endoplasmic reticulum retention peptide.~~

~~45. The method of claim 42, wherein the alpha-mannosidase has a pH optimum below 5.1.~~

~~46. The method of claim 38, wherein the protein having N-glycosylation activity is a protein is capable of removing glucose residues from $Man_5GlcNAc_2$.~~

~~47. The method of claim 38 or 46, wherein the protein having N-glycosylation activity is a protein having α-1,3-glucosidase activity.~~

~~48. The method of claim 46 or 47, wherein the protein is a glucosidase II.~~

~~49. The method of any one of claims 46-48, wherein the protein comprises one or both of the alpha and beta subunit of a glucosidase II.~~

~~50. The method of claim 46, wherein the protein is a mutanase.~~

~~51. The method of claim 1, wherein the cell is genetically engineered to comprise at least two modified N-glycosylation activities.~~

~~52. The method of claim 51, wherein the at least two modified N-glycosylation activities comprise a deficiency in an ALG3 activity and an elevated level of an ALG6 activity.~~

~~53. The method of claim 1, wherein the cell is genetically engineered to comprise at least three modified N-glycosylation activities.~~

~~54. The method of claim 51, wherein the at least three modified N-glycosylation activities comprise a deficiency in an ALG3 activity; an elevated level of an ALG6 activity; and an elevated level of a a-glucosidase II activity.~~

~~52~~55. The method of ~~any~~ either of claims ~~32~~38-~~5~~ or 244, wherein the protein having N-glycosylation activity is an exogenous protein.

~~52~~66. The method of any of claims ~~32~~38-~~52~~54, wherein the protein having N-glycosylation activity is a mammalian protein.

~~52~~77. The method of claim ~~52~~66, wherein the protein having N-glycosylation activity is a human protein.

~~58~~28. The method of ~~any one of~~either claims ~~38~~23- or ~~54~~24, wherein the protein having N-glycosylation activity is a lower eukaryotic protein.

~~59~~29. The method of claim ~~45~~28, wherein the lower eukaryote is a fungus, a trypanosome, or a protozoan.

~~60~~30. The method of claim ~~58~~28, wherein the lower eukaryote is selected from the group consisting of *Typanosoma brucei*, *Trichoderma harzianum*, and an *Aspergillus*.

~~61. The method of any of claims 1-60, wherein modification comprises expression of a protein or biologically active variant thereof capable of effecting mannosyl phosphorylation of the target protein.~~

~~62. The method of claim 61, wherein the protein or biologically active variant thereof capable of effecting mannosyl phosphorylation is MNN4.~~

~~63. The method of claim 61, wherein the protein or biologically active variant thereof is capable of effecting mannosyl phosphorylation is PNO1.~~

~~64. The method of claim 61, wherein the protein or biologically active variant thereof is capable of effecting mannosyl phosphorylation is MNN6.~~

~~65~~31. The method of ~~any one of~~ claims ~~61-64~~, wherein at least about 30% of the mannosyl residues of a glycoprotein are phosphorylated.

~~66. The method of any one of claims 1-65, wherein the cell is not genetically engineered to be deficient in an OCH1 activity.~~

~~63~~27. The method of any of claims 1-~~66~~31, further comprising additional processing of the glycoprotein.

~~68~~33. The method of claim ~~67~~47, wherein the additional processing occurs *in vitro*.

~~69~~34. The method of claim ~~64~~77, wherein the additional processing occurs *in vivo*.

~~70~~35. The method of any of claims ~~67~~32-~~69~~34, wherein the additional processing comprises addition of a heterologous moiety to the modified glycoprotein.

~~71~~36. The method of claim ~~55~~35, wherein the heterologous moiety is a polymer or a carrier.

~~72~~37. The method of any of claims ~~67~~32-~~71~~36, wherein the additional processing comprises enzymatic or chemical treatment of the altered N-glycosylation form of the target protein.

~~73~~38. The method of claim ~~67~~32, wherein the additional processing comprises treatment of the altered N-glycosylation form of the- target protein with a mannosidase, a mannanase, a phosphodiesterase, a glucosidase, or a glycosyltransferase.

~~74~~39. The method of claim ~~72~~37, wherein the additional processing comprises treatment of the altered N-glycosylation form of the target protein with hydrofluoric acid.

~~75~~40. The method of any of claims ~~67~~32-~~74~~39, wherein the additional processing comprises phosphorylation of the altered N-glycosylation form of the -target protein.

~~76~~41. An isolated protein having altered N-glycosylation, wherein the protein is produced by the method of any of claims 1-~~40~~75.

~~77~~42. An isolated ~~*Yarrowia lipolytica* or *Arxula adeninivorans* cell~~ cell genetically engineered to comprise at least one modified N-glycosylation activity relative to a non-genetically engineered cell, the cell being a *Yarrowia lipolytica, or Arxula adeninivorans* cell or a cell from a related species of dimorphic yeast of the same species~~.~~
, the at least one modified N-glycosylation activity comprising expression of a phosphorylation-promoting protein or biologically active variant thereof that promotes mannosyl phosphorylation of the target protein or polypeptide, wherein the phosphorylation-promoting protein or biologically active variant thereof is MNN4 or PNO1.

~~78~~43. The isolated cell of claim ~~77~~42, wherein the cell comprises at least one further modification of N-glycosylation activity.
~~N-glycosylation activity is ALG3 activity.~~

~~44~~79. The isolated cell of claim ~~77 or 74~~38, wherein N-glycosylation activity is OCH1 activity.

~~80. The isolated cell of any of claims 77-79, wherein N-glycosylation activity is MNS1 activity.~~

~~81. The isolated cell of any of claims 77-79, wherein N-glycosylation activity is MNN9 activity.~~

~~82~~45. The isolated cell of ~~any~~ either of claims ~~74~~37~~-~~ or ~~44~~79, wherein the further modification comprises deletion of a gene encoding a protein having the N-glycosylation activity.

~~83~~46. The isolated cell of either of claims 43 or 44~~any of claims 77-79~~, wherein the modification comprises expression of a mutant form of a protein having the N-glycosylation activity.

~~84~~47. The isolated cell of either of claims 43 or 44~~any of claims 77-83~~, wherein the modification comprises introduction or expression of an RNA molecule that interferes with the functional expression of a protein having the N-glycosylation activity.

~~85~~48. The isolated cell of claim 43~~any of claims 77-83~~, wherein the modification comprises expression of a protein having N-glycosylation activity.

~~86. The isolated cell of claim 85, wherein the N-glycosylation activity is a glucosyltransferase activity.~~

~~87. The isolated cell of claim 85 or 86, wherein the protein having N-glycosylation activity is ALG6.~~

~~88. The isolated cell of claim 85, wherein the protein having N-glycosylation activity is an alpha-mannosidase.~~

~~89. The isolated cell of claim 88, wherein the alpha-mannosidase is targeted to the endoplasmic reticulum.~~

~~90. The isolated cell of claim 88 or 89, wherein the protein having N-glycosylation activity is a fusion protein comprising an alpha-mannosidase polypeptide and an HDEL endoplasmic reticulum retention peptide.~~

~~91. The isolated cell of claim 85, wherein the protein having N-glycosylation activity is a protein is capable of removing glucose residues from $Man_5GlcNAc_2$.~~

~~92. The isolated cell of claim 85 or 91, wherein the protein having N-glycosylation activity is a protein having α-1,3-glucosidase activity.~~

~~93. The isolated cell of claim 91 or 92, wherein the protein is a glucosidase II.~~

~~94. The isolated cell of any one of claims 91-93, wherein the protein comprises one or both of the alpha and beta subunit of a glucosidase II.~~

~~95. The isolated cell of claim 91, wherein the protein is a mutanase.~~

~~96. The isolated cell of any one of claims 77-95, wherein the cell is genetically engineered to comprise at least two modified N-glycosylation activities.~~

~~97. The isolated cell of claim 96, wherein the at least two modified N-glycosylation activities comprise a deficiency in an ALG3 activity and an elevated level of an ALG6 activity.~~

~~98. The isolated cell of any one of claims 77-97, wherein the cell is genetically engineered to comprise at least three modified N-glycosylation activities.~~

~~99. The isolated cell of claim 98, wherein the at least three modified N-glycosylation activities comprise a deficiency in an ALG3 activity; an elevated level of an ALG6 activity; and an elevated level of a a glucosidase II activity.~~

~~100. The isolated cell of any one of claims 77-99, wherein the cell is not genetically engineered to be deficient in an OCH1 activity.~~

~~101~~49. The isolated cell of ~~any one of~~ claims ~~85~~48-~~100~~, wherein the protein having N-glycosylation activity is a human protein.

~~102. The isolated cell of any of claims 77-101, wherein the modification comprises expression of a protein or biologically active variant thereof capable of promoting mannosyl phosphorylation of the modified glycoprotein.~~

~~103. The isolated cell of claim 102, wherein the protein or biologically active variant thereof that effects mannosyl phosphorylation is MNN4.~~

~~104. The isolated cell of claim 103, wherein the protein or biologically active variant thereof that effects mannosyl phosphorylation is PNO1.~~

~~105~~50. ~~A method of treating a disorder treatable by administration of a protein having altered N-glycosylation, the method comprising:~~

~~administering to a subject~~ Use of a protein of claim ~~74~~16 in the manufacture of a medicament for treating a disorder in a subject, the disorder is treatable by administration of a protein having altered N-glycosylation, and wherein the subject is one having, or suspected of having, a disease treatable by administration of a protein having altered N-glycosylation.

~~106~~51. The ~~method~~ use of claim ~~105~~50, wherein the disorder is a metabolic disorder.

~~107~~52. The ~~method~~ use of claim ~~106~~51, wherein the metabolic disorder is a lysosomal storage disorder (LSD).

~~108~~53. The ~~method~~ use of claim ~~107~~52, wherein the lysosomal storage disorder is Gaucher disease, Tay-Sachs disease, Pompe disease, Niemann-Pick disease, or Fabry disease.

~~109~~54. The ~~method~~ use of any of claims ~~105~~50-~~108~~53, wherein the protein is one associated with a LSD.

~~110~~55. The ~~method~~ use of claim ~~109~~54, wherein the protein is glucocerebrosidase or alpha-galactosidase.

~~111~~56. The ~~method~~ use of claim ~~109~~54, wherein the protein is selected from the group consisting of alpha-L-iduronidase, beta-D-galactosidase, beta-glucosidase, beta-hexosaminidase, beta-D-mannosidase, alpha-L-fucosidase, arylsulfatase B, arylsulfatase A, alpha-N-acteylgalactosaminidase, aspartylglucosaminidase, iduronate-2-sulfatase, alpha-glucosaminide-N-acetyltransferase, beta-D-glucoronidase, hyaluronidase, alpha-L-mannosidase, alpha-

neurominidase, phosphotransferase, acid lipase, acid ceramidase, sphinogmyelinase, thioesterase, cathepsin K, and lipoprotein lipase.

~~112~~57. The ~~method~~ use of any of claims ~~105~~50-~~111~~56, further comprising determining whether the subject has a disease treatable by administration of a protein having altered N-glycosylation.

~~113~~58. The ~~method~~ use of any of claims ~~105~~50-~~112~~57, wherein the subject is a human.

~~114~~59. A method of producing an altered N-glycosylation form of a target protein, the method comprising:

contacting a target protein with a cell lysate prepared from a cell genetically engineered to comprise at least two modifications of N-glycosylation activity relative to a non-genetically engineered cell of the same species, the cell being a *Yarrowia lipolytica* or an *Arxula adeninivorans* cell or a cell from a related species of dimorphic yeast, the at least two modifications of N-glycosylation activity comprising~~Yarrowia lipolytica or an Arxula adeninivorans cell genetically engineered to comprise at least one modified N-glycosylation activity,~~: a deficiency in OCH1 activity; and

expression of a phosphorylation-promoting protein or biologically active variant thereof that promotes mannosyl phosphorylation of the target protein or polypeptide, wherein the phosphorylation-promoting protein or biologically active variant thereof is MNN4 or PNO1, and

wherein the contacting of the target protein with the cell lysate results in an altered N-glycosylation form of the target protein.

~~115~~60. A method of producing an altered N-glycosylation form of a target protein, the method comprising contacting a target protein with one or more proteins having N-glycosylation activity, wherein the one or more proteins having N-glycosylation activity are obtained from a cell genetically engineered to comprise at least two modifications of N-glycosylation activity relative to a non-genetically engineered cell of the same species, the cell being a *Yarrowia lipolytica* or an *Arxula adeninivorans* cell or a cell from a related species of dimorphic yeast, the at least two modifications of N-glycosylation activity comprising:

a deficiency in OCH1 activity; and

expression of a phosphorylation-promoting protein or biologically active variant thereof that promotes mannosyl phosphorylation of the target protein or polypeptide, wherein the phosphorylation-promoting protein or biologically active variant thereof is MNN4 or PNO1, and

~~*Yarrowia lipolytica* or an *Arxula adeninivorans* cell genetically engineered to comprise at least one modified N-glycosylation activity and~~ wherein contacting the target molecule with the one or more proteins having N-glycosylation activity results in an altered N-glycosylation form of the target protein.

~~116~~61. A substantially pure culture of *Yarrowia lipolytica* or *Arxula adeninivorans* cells, a substantial number of which are genetically engineered to comprise at least two modifications of N-glycosylation activity comprising:

a deficiency in OCH1 activity; and expression of a phosphorylation-promoting protein or biologically active variant thereof that promotes mannosyl phosphorylation of the target protein or polypeptide, wherein the phosphorylation-promoting protein or biologically active variant thereof is MNN4 or PNO1~~one modified N-glycosylation activity~~.

~~117~~62. The substantially pure culture of cells of claim ~~87~~61, wherein the culture of cells contains one or more subpopulations of cells, each subpopulation comprising a different modified glycosylation activity.

~~118. An isolated nucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:2.~~

~~119. An isolated nucleotide sequence comprising a sequence that is at least 80% identical to SEQ ID NO:1 or SEQ ID NO:2.~~

~~120. A polypeptide encoded by the isolated nucleotide sequence of claims 118 or 119.~~

~~121. An isolated nucleic acid comprising:~~

~~(a) a nucleotide sequence that hybridizes under highly stringent conditions to the complement of SEQ ID NO:1 or SEQ ID NO:2; or~~

~~(b) the complement of the nucleotide sequence.~~

~~122. A vector comprising the nucleic acid sequence of any of claims 118-121.~~

~~123. An expression vector comprising the nucleic acid sequence of any of claims 118-121.~~

~~124. A cultured cell comprising the expression vector of claim 123, or a progeny of the cell, wherein the cell expresses the polypeptide.~~

~~125. A method of producing a protein, the method comprising culturing a cell of claim 124 under conditions permitting the expression of the polypeptide.~~

~~126. The method of claim 125, further comprising after culturing the cell, isolating the polypeptide from the cell or the medium in which the cell was cultured.~~