CLAIMS

What is claimed is:

1. Use of a composition in the manufacture of a medicament for~~A method of~~ treating a disease or disorder in a subject in need thereof, wherein the composition comprises ~~comprising administering~~ a dose comprising ~~an~~ a therapeutically effective amount of ribitol for administration to the subject, wherein the dose is ~~optionally~~ an immediate-release dose and/or not a~~n~~ controlled-release dose, and wherein the disease or disorder is associated with a defect in fukutin (FKNT) or Fukutin-related protein (FKRP).

2. Use of a composition in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof, wherein the composition comprises a dose comprising an amount of ribitol effective to achieve an area under the concentration-time curve (AUC_{0-24}) steady-state level of between 100 (µg·h)/mL and 2500 (µg·h)/mL upon administration to the subject, and wherein the disease or disorder is associated with a defect in fukutin (FKTN) or Fukutin-related protein (FKRP).

3. The use of claim 1 or 2, wherein the defect causes a partial or complete loss of function in FKRP or FKTN.

~~2.~~ 4. The ~~method~~use of claim 1 to 3, wherein the dose is to be administered at most four times daily, at most three times daily, or at most twice daily.

~~3. The method of claim 2, wherein the dose is administered at most twice daily.~~

~~4. The method of claim 1, wherein the dose is administered three times daily.~~

~~5. The method of claim 3, wherein the dose is administered twice daily.~~

~~6. The method of claim 3, wherein the dose is administered once daily.~~

~~7~~5. The ~~method~~use of any of claims ~~1~~ 1 to ~~5~~4, wherein the ~~method comprises administering~~ dose is to be administered between ~~at least~~ 0.5 grams per day (g/day), ~~at least 1 g/day, at least 2 g/day, at least 3 g/day, at least 4 g/day, at least 5 g/day, at least 7.5 g/day, at least 10 g/day, at least~~

~~12.5 g/day, at least 15 g/day, at least 20 g/day, at least 25 g/day, at least 30 g/day, at least 35 g/day, at least 40 g/day, at least 45 g/day, at least 50 g/day, at least 55 g/day, or at least~~ and ~~60~~ 40 g/day of ribitol.

~~8. The method of any of claims 1 to 6, wherein the method comprises administering at most 0.5 g/day, at most 1 g/day, at most 2 g/day, at most 3 g/day, at most 4 g/day, at most 5 g/day, at most 7.5 g/day, at most 10 g/day, at most 12.5 g/day, or at most 15 g/day, at most 20 g/day, at most 25 g/day, at most 30 g/day, at most 35 g/day, at most 40 g/day, at most 45 g/day, at most 50 g/day, at most 55 g/day, or at most 60 g/day.~~

~~9. The method of any of claims 1 to 5, wherein the method comprises administering 0.5 g/day, 1 g/day, 1.5 g/day, 2 g/day, 3 g/day, 4 g/day, 5 g/day, 6 g/day, 7.5 g/day, 10 g/day, 12 g/day, 12.5 g/day, 15 g/day, 20 g/day, 25 g/day, 30 g/day, 35 g/day, 40 g/day, 45 g/day, 50 g/day, 55 g/day, or 60 g/day.~~

~~10. The method of claim 8, wherein the method comprises administering 0.5 g/day.~~

~~11. The method of claim 8, wherein the method comprises administering 1.5 g/day.~~

~~12. The method of claim 8, wherein the method comprises administering 3 g/day.~~

~~13. The method of claim 8, wherein the method comprises administering 6 g/day.~~

~~14. The method of claim 8, wherein the method comprises administering 10 g/day.~~

~~15. The method of claim 8, wherein the method comprises administering 12 g/day.~~

~~16. The method of claim 8, wherein the method comprises administering 15 g/day.~~

~~17. The method of claim 8, wherein the method comprises administering 20 g/day.~~

~~18. The method of claim 8, wherein the method comprises administering 25 g/day.~~

~~19. The method of claim 8, wherein the method comprises administering 30 g/day.~~

~~20. The method of claim 8, wherein the method comprises administering 35 g/day.~~

~~21. The method of claim 8, wherein the method comprises administering 40 g/day.~~

~~22. The method of claim 8, wherein the method comprises administering 45 g/day.~~

~~23. The method of claim 8, wherein the method comprises administering 50 g/day.~~

~~24. The method of claim 8, wherein the method comprises administering 55 g/day.~~

~~25. The method of claim 8, wherein the method comprises administering 60 g/day.~~

~~26. The method of any one of claims 1 to 25, comprising administering the dose of ribitol for at least one week, two weeks, or four weeks.~~

~~27~~6. The ~~method~~use of any one of claims ~~1~~ 1 to ~~25~~5, ~~comprising administering~~ wherein the dose of ribitol is to be administered for between one week and ~~at least one month, two months, or~~ four months.

~~28~~7. The ~~method~~use of any one of claims ~~1~~ 1 to ~~25~~6, ~~comprising administering~~ wherein the dose of ribitol is to be chronically.

~~29. The method of any one of claims 1 to 28, wherein the disease or disorder is associated with a defect in Fukutin-related protein (FKRP).~~

~~30. The method of any one of claims 1 to 29, wherein a mammal has a mutation in the gene encoding Fukutin-related protein (FKRP) that causes a partial or complete loss-of-function in FKRP.~~

~~31~~8. The ~~method~~use of any one of claims ~~1~~ 1 to ~~30~~7, wherein the disease or disorder is a muscular dystrophy.

~~32~~9. The ~~method~~use of claim ~~31~~8, wherein the muscular dystrophy is an FKRP-related alpha-dystroglycanopathy, an FKTN-related alpha-dystroglycanopathy, Isoprenoid Synthase Domain-Containing Protein (ISPD)-related alpha-dystroglycanopathy, Muscle Eye Brain Disease (MEB), or Congenital Muscular Dystrophy (CMD).

~~33~~10. The ~~method~~use of claim ~~32~~9, wherein the disease or disorder is Limb-Girdle Muscular Dystrophy type 2i (LGMD2i/R9), Limb-Girdle Muscular Dystrophy Type 2M (LGMD2M), Limb-Girdle Muscular Dystrophy Type 2U (LGMD2U), or Fukuyama congenital muscular dystrophy (FCMD).

~~34. The method of claim 31, wherein the muscular dystrophy is a fukutin (FKTN)-related alpha-dystroglycanopathy.~~

~~35. The method of claim 34, wherein the FKTN-related alpha-dystroglycanopathy is Fukuyama Syndrome.~~

~~36~~11. The ~~method~~use of any one of claims ~~1~~ 1 to ~~35~~10, wherein the maximum observed concentration (C_{max}) of ribitol is between 50 and ~~2500~~ 400 µg/mL.

~~37. The method of any one of claims 1 to 36, wherein the area under the concentration-time curve (AUC_{0-24}) for ribitol is between 100 (µg·h)/mL and 8000 (µg·h)/mL or between 350 (µg·h)/mL and 8000 (µg·h)/mL.~~

~~38. The method of any one of claims 1 to 36, wherein the AUC_{0-24} for ribitol is at least about 100 (µg·h)/mL or about 100 (µg·h)/mL to about 700 (µg·h)/mL.~~

~~39. The method of any one of claims 1 to 36, wherein the AUC_{0-24} for ribitol is at least about 182 (µg·h)/mL or about 182 (µg·h)/mL to about 700 (µg·h)/mL.~~

~~40. The method of any one of claims 1 to 36, wherein the AUC_{0-24} for ribitol is at least about 200 (µg·h)/mL or about 200 (µg·h)/mL to about 700 (µg·h)/mL.~~

~~41. The method of any one of claims 1 to 36, wherein the AUC_{0-24} for ribitol is at least about 700 (µg·h)/mL or about 500 (µg·h)/mL to about 700 (µg·h)/mL.~~

~~42. The method of any one of claims 1 to 41, wherein the subject is a mammal.~~

~~43~~12. The ~~method~~use of any one of claims ~~1~~ 1 to ~~41~~11, wherein the subject is a human.

13. The use of claim 12, wherein the human is a child.~~.~~

~~44. The method of any one of claims 1 to 43, wherein the subject is a human child.~~

~~45~~14. The ~~method~~use of any one of claims ~~1~~ 1 to ~~44~~13, wherein the ~~method~~medicament restores and/or enhances functional glycosylation of α-DG.

~~46. The method of any one of claims 1 to 44, wherein the method treats the disease or disorder.~~

~~47. A method of treating a disease or disorder in a subject in need thereof, comprising administering ribitol at dose effective to achieve steady-state AUC(0-24) level.~~

~~48. The method of claim 47, wherein the dose is administered at most four times daily.~~

~~49. The method of claim 48, wherein the dose is administered at most twice daily.~~

~~50. The method of claim 47, wherein the dose is administered three times daily.~~

~~51. The method of claim 49, wherein the dose is administered twice daily.~~

~~52. The method of claim 49, wherein the dose is administered once daily.~~

~~53. The method of any of claims 47 to 52, wherein the method comprises administering at least 0.5 grams per day (g/day), at least 1 g/day, at least 2 g/day, at least 3 g/day, at least 4 g/day, at least 5 g/day, at least 7.5 g/day, at least 10 g/day, at least 12.5 g/day, at least 15 g/day, at least 20 g/day, at least 25 g/day, at least 30 g/day, at least 35 g/day, at least 40 g/day, at least 45 g/day, at least 50 g/day, at least 55 g/day, or at least 60 g/day.~~

~~54. The method of any of claims 47 to 52, wherein the method comprises administering at most 0.5 g/day, at most 1 g/day, at most 2 g/day, at most 3 g/day, at most 4 g/day, at most 5 g/day, at most 7.5 g/day, at most 10 g/day, at most 12.5 g/day, or at most 15 g/day, at most 20 g/day, at most 25 g/day, at most 30 g/day, at most 35 g/day, at most 40 g/day, at most 45 g/day, at most 50 g/day, at most 55 g/day, or at most 60 g/day.~~

~~55. The method of any of claims 47 to 52, wherein the method comprises administering 0.5 g/day, 1 g/day, 1.5 g/day, 2 g/day, 3 g/day, 4 g/day, 5 g/day, 6 g/day, 7.5 g/day, 10 g/day, 12 g/day,~~

~~12.5 g/day, 15 g/day, 20 g/day, 25 g/day, 30 g/day, 35 g/day, 40 g/day, 45 g/day, 50 g/day, 55 g/day, or 60 g/day.~~

~~56. The method of claim 54, wherein the method comprises administering 0.5 g/day.~~

~~57. The method of claim 54, wherein the method comprises administering 1.5 g/day.~~

~~58. The method of claim 54, wherein the method comprises administering 3 g/day.~~

~~59. The method of claim 54, wherein the method comprises administering 6 g/day.~~

~~60. The method of claim 54, wherein the method comprises administering 10 g/day.~~

~~61. The method of claim 54, wherein the method comprises administering 12 g/day.~~

~~62. The method of claim 54, wherein the method comprises administering 15 g/day.~~

~~63. The method of claim 54, wherein the method comprises administering 20 g/day.~~

~~64. The method of claim 54, wherein the method comprises administering 25 g/day.~~

~~65. The method of claim 54, wherein the method comprises administering 30 g/day.~~

~~66. The method of claim 54, wherein the method comprises administering 35 g/day.~~

~~67. The method of claim 54, wherein the method comprises administering 40 g/day.~~

~~68. The method of claim 54, wherein the method comprises administering 45 g/day.~~

~~69. The method of claim 54, wherein the method comprises administering 50 g/day.~~

~~70. The method of claim 54, wherein the method comprises administering 55 g/day.~~

~~71. The method of claim 54, wherein the method comprises administering 60 g/day.~~

~~72. The method of any one of claims 1 to 71, comprising administering the dose of ribitol for at least one week, two weeks, or four weeks.~~

~~73. The method of any one of claims 1 to 71, comprising administering the dose of ribitol for at least one month, two months, or four months.~~

~~74. The method of any one of claims 1 to 71, comprising administering the dose of ribitol chronically.~~

~~75. The method of any one of claims 1 to 71, wherein the disease or disorder is associated with a defect in Fukutin-related protein (FKRP).~~

~~76. The method of any one of claims 47 to 75, wherein a mammal has a mutation in the gene encoding Fukutin-related protein (FKRP) that causes a partial or complete loss-of-function in FKRP.~~

~~77. The method of any one of claims 47 to 76, wherein the disease or disorder is a muscular dystrophy.~~

~~78. The method of claim 77, wherein the muscular dystrophy is FKRP-related alpha-dystroglycanopathy.~~

~~79. The method of claim 78, wherein the disease or disorder is Limb-Girdle Muscular Dystrophy type 2i (LGMD2i).~~

~~80. The method of claim 77, wherein the muscular dystrophy is a fukutin (FKTN)-related alpha-dystroglycanopathy.~~

~~81. The method of claim 80, wherein the FKTN-related alpha-dystroglycanopathy is Fukuyama Syndrome.~~

~~82. The method of any one of claims 47 to 81, wherein the maximum observed concentration (C_{max}) of ribitol is between 50 and 2500 µg/mL.~~

~~83. The method of any one of claims 47 to 82, wherein the area under the serum concentration-time curve (AUC_{0-24}) for ribitol is between 350 (µg·h)/mL and 8000 (µg·h)/mL.~~

~~84. The method of any one of claims 47 to 82, wherein the AUC_{0-24} for ribitol is at least about 100 (µg·h)/mL.~~

~~85. The method of any one of claims 47 to 82, wherein the AUC_{0-24} for ribitol is at least about 182 (μg·h)/mL.~~

~~86. The method of any one of claims 47 to 82, wherein the AUC_{0-24} for ribitol is at least about 200 (μg·h)/mL.~~

~~87. The method of any one of claims 47 to 82, wherein the AUC_{0-24} for ribitol is at least about 700 (μg·h)/mL.~~

~~88. The method of any one of claims 47 to 87, wherein the subject is a mammal.~~

~~89. The method of any one of claims 47 to 87, wherein the subject is a human.~~

~~90. The method of any one of claims 1 to 89, wherein the subject is a human child.~~

~~91. The method of any one of claims 1 to 90, wherein the method restores and/or enhances functional glycosylation of α-DG.~~

~~92. The method of any one of claims 1 to 89, wherein the method treats the disease or disorder.~~

~~93~~15. A pharmaceutical composition~~,~~ comprising ribitol and a pharmaceutically acceptable carrier or excipient.

~~94~~16. The pharmaceutical compositions of claim ~~93~~15, wherein the pharmaceutical composition is a solid~~, optionally a tablet or capsule~~.

17~~95~~. The pharmaceutical compositions of claim ~~93~~15, wherein the pharmaceutical composition is a solution.

~~96~~18. The pharmaceutical composition of claim ~~95~~17, wherein the solution comprises a carrier, and wherein the carrier is water or saline.

~~97~~19. The pharmaceutical composition of claim ~~96~~18, wherein the carrier is substantially pure water.

~~98. The pharmaceutical composition of claim 97, wherein the carrier is saline.~~

20~~99~~. The pharmaceutical composition of any one of claims ~~93~~ 15 to ~~98~~19, wherein the pharmaceutical composition comprises ribitol at between 0.2 g/mL and 10 g/mL.

~~100~~21. A kit comprising the pharmaceutical composition of any one of claims ~~93~~ 15 to ~~99~~ 20 and instructions for use in treating a disease or disorder.

~~101~~22. A unit dose, comprising between 0.5 g and ~~60~~ 40 g of ribitol.

~~102. The unit dose of claim 101, wherein the unit dose comprising 0.5 g of ribitol.~~

~~103. The unit dose of claim 101, wherein the unit dose comprising 1.5 g of ribitol.~~

~~104. The unit dose of claim 101, wherein the unit dose comprising 3 g of ribitol.~~

~~105. The unit dose of claim 101, wherein the unit dose comprising 6 g of ribitol.~~

~~106. The unit dose of claim 101, wherein the unit dose comprising 9 g of ribitol.~~

~~107. The unit dose of claim 101, wherein the unit dose comprising 12 g of ribitol.~~

~~108. The unit dose of claim 101, wherein the unit dose comprising 15 g of ribitol.~~

~~109~~23. The unit dose of ~~any one of~~ claim ~~s 101-108~~22, wherein the ribitol is dissolved in water.

~~110~~24. A unit dose, comprising an amount of ribitol that is effective to achieve a steady-state $AUC_{(0-24)}$ level for ribitol of between 100 (µg·h)/mL and ~~8000~~ 2500 (µg·h)/mL.

~~111. The unit dose of claim 110, wherein the AUC_{0-24} for ribitol is at least about 100 (µg·h)/mL or about 100 (µg·h)/mL to about 700 (µg·h)/mL.~~

~~112. The unit dose of claim 110, wherein the AUC_{0-24} for ribitol is at least about 182 (µg·h)/mL or about 182 (µg·h)/mL to about 700 (µg·h)/mL.~~

~~113. The unit dose of claim 110, wherein the AUC_{0-24} for ribitol is at least about 200 (µg·h)/mL or about 200 (µg·h)/mL to about 700 (µg·h)/mL.~~

~~114. The unit dose of claim 110, wherein the AUC_{0-24} for ribitol is at least about 700 (µg·h)/mL or about 500 (µg·h)/mL to about 700 (µg·h)/mL.~~

25~~115~~. The unit dose of ~~any one of claims 101-114~~claim 24, wherein the unit dose is formulated as a solid~~, optionally a tablet or capsule~~.

~~116~~26. The unit dose of claim 24~~dose of any one of claims 101-114~~, wherein the unit dose is formulated as a liquid~~, optionally wherein the ribitol is dissolved in water~~.

27. The unit dose of claim 24, wherein the ribitol is dissolved in water.

~~117~~28. The unit dose of any one of claims ~~101~~22-~~116~~27, wherein the unit dose is formulated for oral administration.

~~118~~29. Use of ~~The~~ the pharmaceutical composition of any one of claims ~~93-99~~15-20 or unit dose of any one of claims ~~101-106~~22-28 in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof, wherein the disease or disorder is associated with a defect in fukutin (FKTN) or Fukutin-related protein (FKRP)~~ for use in a method of treatment according to any one of claims 1-92~~.

30. The use of claim 29, wherein the defect causes a partial or complete loss-of-function in FKRP or FKTN.