

Claims

1. A method of treating Pompe disease in a human patient in need thereof, the method comprising administering to the patient an adeno-associated viral (AAV) vector comprising a transgene encoding acid alpha-glucosidase (GAA), wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
2. A method of improving muscle function in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
3. A method of reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
4. The method of claim 3, wherein administration of the AAV vector to the patient reduces glycogen accumulation in muscle tissue and/or in neuronal tissue.
5. A method of improving pulmonary function in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
6. A method of increasing GAA expression in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
7. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of from about 2×10^{13} vg/kg to about 2×10^{14} vg/kg.
8. The method of claim 7, wherein the AAV vector is administered to the patient in an amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg.
9. The method of claim 8, wherein the AAV vector is administered to the patient in an amount of from about 4×10^{13} vg/kg to about 2×10^{14} vg/kg.
10. The method of claim 9, wherein the AAV vector is administered to the patient in an amount of from about 5×10^{13} vg/kg to about 2×10^{14} vg/kg.

11. The method of claim 10, wherein the AAV vector is administered to the patient in an amount of from about 6×10^{13} vg/kg to about 2×10^{14} vg/kg.

12. The method of claim 11, wherein the AAV vector is administered to the patient in an amount of from about 7×10^{13} vg/kg to about 2×10^{14} vg/kg.

13. The method of claim 12, wherein the AAV vector is administered to the patient in an amount of from about 8×10^{13} vg/kg to about 2×10^{14} vg/kg.

14. The method of claim 13, wherein the AAV vector is administered to the patient in an amount of from about 9×10^{13} vg/kg to about 2×10^{14} vg/kg.

15. The method of claim 14, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{14} vg/kg to about 2×10^{14} vg/kg.

16. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 3×10^{13} vg/kg.

17. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 4×10^{13} vg/kg.

18. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 5×10^{13} vg/kg.

19. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 6×10^{13} vg/kg.

20. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 7×10^{13} vg/kg.

21. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 8×10^{13} vg/kg.

22. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 9×10^{13} vg/kg.

23. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1×10^{14} vg/kg.

24. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.1×10^{14} vg/kg.

25. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.2×10^{14} vg/kg.

26. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.3×10^{14} vg/kg.

27. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.4×10^{14} vg/kg.

28. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.5×10^{14} vg/kg.

29. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.6×10^{14} vg/kg.

30. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.7×10^{14} vg/kg.

31. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.8×10^{14} vg/kg.

32. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.9×10^{14} vg/kg.

33. The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 2×10^{14} vg/kg.

34. The method of any one of claims 1-33, wherein the AAV vector is administered to the patient in a single dose comprising the amount.

35. The method of any one of claims 1-33, wherein the AAV vector is administered to the patient in two or more doses that, together, comprise the amount.

36. The method of claim 35, wherein the AAV vector is administered to the patient in from two doses to ten doses that, together, comprise the amount.

37. The method of claim 36, wherein the AAV vector is administered to the patient in two, three, or four doses that, together, comprise the amount.

38. The method of claim 37, wherein the AAV vector is administered to the patient in two doses that, together, comprise the amount.

39. The method of any one of claims 35-38, wherein the two or more doses are separated from one another by one year or more.

40. The method of any one of claims 35-38, wherein the two or more doses are administered to the patient within about 12 months of one another.

41. The method of claim 40, wherein the two or more doses are administered to the patient within from about one week to about 48 weeks of one another.

42. The method of claim 41, wherein the two or more doses are administered to the patient within from about two weeks to about 44 weeks of one another.

43. The method of claim 42, wherein the two or more doses are administered to the patient within from about three weeks to about 40 weeks of one another.

44. The method of claim 43, wherein the two or more doses are administered to the patient within from about four weeks to about 36 weeks of one another.

45. The method of claim 44, wherein the two or more doses are administered to the patient within from about five weeks to about 32 weeks of one another.

46. The method of claim 45, wherein the two or more doses are administered to the patient within from about six weeks to about 24 weeks of one another.

47. The method of claim 46, wherein the two or more doses are administered to the patient within from about 12 weeks to about 20 weeks of one another.

48. The method of claim 47, wherein the two or more doses are administered to the patient within about 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, or 19 weeks of one another.

49. The method of any one of claims 1-33, wherein the AAV vector is administered to the patient in two or more doses that each, individually, comprise the amount.

50. The method of claim 49, wherein the AAV vector is administered to the patient in from two doses to ten doses that each, individually, comprise the amount.

51. The method of claim 50, wherein the AAV vector is administered to the patient in two, three, or four doses that each, individually, comprise the amount.

52. The method of claim 51, wherein the AAV vector is administered to the patient in two doses that each, individually, comprise the amount.

53. The method of any one of claims 49-52, wherein the two or more doses are separated from one another by one year or more.

54. The method of any one of claims 49-52, wherein the two or more doses are administered to the patient within about 12 months of one another.

55. The method of claim 54, wherein the two or more doses are administered to the patient within from about one week to about 48 weeks of one another.

56. The method of claim 55, wherein the two or more doses are administered to the patient within from about two weeks to about 44 weeks of one another.

57. The method of claim 56, wherein the two or more doses are administered to the patient within from about three weeks to about 40 weeks of one another.

58. The method of claim 57, wherein the two or more doses are administered to the patient within from about four weeks to about 36 weeks of one another.

59. The method of claim 58, wherein the two or more doses are administered to the patient within from about five weeks to about 32 weeks of one another.

60. The method of claim 59, wherein the two or more doses are administered to the patient within from about six weeks to about 24 weeks of one another.

61. The method of claim 60, wherein the two or more doses are administered to the patient within from about 12 weeks to about 20 weeks of one another.

62. The method of claim 61, wherein the two or more doses are administered to the patient within about 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, or 19 weeks of one another.

63. The method of any one of claims 1-62, wherein the AAV vector is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral, intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration.

64. The method of claim 63, wherein the AAV vector is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, and/or intramuscular administration.

65. The method of claim 64, wherein the AAV vector is administered to the patient by way of intravenous and/or intrathecal administration.

66. The method of claim 65, wherein the AAV vector is administered to the patient by way of intravenous administration.

67. The method of any one of claims 1-66, wherein the AAV is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAVrh74, AAVrh.8, or AAVrh.10 serotype.

68. The method of claim 67, wherein the AAV is a pseudotyped AAV.

69. The method of claim 68, wherein the pseudotyped AAV is AAV2/8.

70. The method of claim 69, wherein the pseudotyped AAV is AAV2/9.

71. The method of any one of claims 1-66, wherein the AAV comprises a recombinant capsid protein.

72. The method of any one of claims 1-71, wherein the transgene encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell.

73. The method of claim 72, wherein the promoter is a muscle creatine kinase (MCK) promoter, desmin promoter, chicken beta actin promoter, cytomegalovirus (CMV) promoter, myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.

74. The method of claim 73, wherein the promoter is a MCK promoter.

75. The method of claim 74, wherein the MCK promoter has a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 1.

76. The method of claim 75, wherein the MCK promoter has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 1.

77. The method of claim 76, wherein the MCK promoter has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 1.

78. The method of claim 77, wherein the MCK promoter has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 1.

79. The method of claim 78, wherein the MCK promoter has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 1.

80. The method of claim 79, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.

81. The method of claim 80, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.

82. The method of claim 81, wherein the MCK promoter has a nucleic acid sequence that is 100% identical to SEQ ID NO: 1.

83. The method of any one of claims 1-82, wherein the transgene encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell.

84. The method of claim 83, wherein the enhancer is a CMV enhancer, a myocyte enhancer factor 2 (MEF2) enhancer, or a MyoD enhancer.

85. The method of any one of claims 1-84, wherein the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2.

86. The method of claim 85, wherein the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.

87. The method of claim 86, wherein the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2.

88. The method of claim 87, wherein the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2.

89. The method of claim 88, wherein the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2.

90. The method of claim 89, wherein the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2.

91. The method of claim 90, wherein the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2.

92. The method of any one of claims 1-91, wherein the patient has infantile-onset Pompe disease.

93. The method of claim 92, wherein the patient is from about one month to about one year of age.

94. The method of claim 93, wherein the patient is from about one month to about six months of age.

95. The method of any one of claims 92-94, wherein, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.

96. The method of any one of claims 1-91, wherein the patient has late-onset Pompe disease.

97. The method of claim 96, wherein the patient exhibits endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

98. The method of any one of claims 1-97, wherein the patient has not previously received GAA enzyme replacement therapy.

99. The method of any one of claims 1-98, wherein the patient has previously received GAA enzyme replacement therapy.

100. The method of any one of claims 1-99, wherein, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

101. The method of any one of claims 1-100, wherein, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.

102. A method of treating Pompe disease in a human patient in need thereof, the method comprising administering to the patient an agent that increases GAA expression, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

103. A method of improving muscle function in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an agent that increases GAA expression, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

104. A method of reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an agent that increases GAA expression, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

105. The method of claim 104, wherein administration of the agent to the patient reduces glycogen accumulation in muscle tissue and/or in neuronal tissue.

106. A method of improving pulmonary function in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an agent that increases GAA expression,

wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

107. A method of increasing GAA expression in a human patient diagnosed as having Pompe disease, the method comprising administering to the patient an agent that increases GAA expression, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

108. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 2×10^{13} vg/kg to about 2×10^{14} vg/kg.

109. The method of claim 108, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg.

110. The method of claim 109, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 4×10^{13} vg/kg to about 2×10^{14} vg/kg.

111. The method of claim 110, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 5×10^{13} vg/kg to about 2×10^{14} vg/kg.

112. The method of claim 111, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity

observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 6×10^{13} vg/kg to about 2×10^{14} vg/kg.

113. The method of claim 112, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 7×10^{13} vg/kg to about 2×10^{14} vg/kg.

114. The method of claim 113, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 8×10^{13} vg/kg to about 2×10^{14} vg/kg.

115. The method of claim 114, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 9×10^{13} vg/kg to about 2×10^{14} vg/kg.

116. The method of claim 115, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 1×10^{14} vg/kg to about 2×10^{14} vg/kg.

117. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 3×10^{13} vg/kg.

118. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 4×10^{13} vg/kg.

119. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA

activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 5×10^{13} vg/kg.

120. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 6×10^{13} vg/kg.

121. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 7×10^{13} vg/kg.

122. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 8×10^{13} vg/kg.

123. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 9×10^{13} vg/kg.

124. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1×10^{14} vg/kg.

125. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.1×10^{14} vg/kg.

126. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.2×10^{14} vg/kg.

127. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA

activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.3×10^{14} vg/kg.

128. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.4×10^{14} vg/kg.

129. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.5×10^{14} vg/kg.

130. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.6×10^{14} vg/kg.

131. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.7×10^{14} vg/kg.

132. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.8×10^{14} vg/kg.

133. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.9×10^{14} vg/kg.

134. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 2×10^{14} vg/kg.

135. The method of any one of claims 102-134, wherein the agent is administered to the patient in a single dose.

136. The method of any one of claims 102-134, wherein the agent is administered to the patient in two or more doses.

137. The method of any one of claims 102-136, wherein the agent is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral, intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration.

138. The method of any one of claims 102-137, wherein the agent comprises (i) a nucleic acid molecule encoding GAA, (ii) one or more interfering RNA molecules that collectively increase expression of endogenous GAA, (iii) one or more nucleic acid molecules encoding the one or more interfering RNA molecules, (iv) a GAA protein, and/or (v) one or more small molecules that collectively increase expression of endogenous GAA.

139. The method of claim 138, wherein the one or more interfering RNA molecules comprise short interfering RNA (siRNA), short hairpin RNA (shRNA), and/or micro RNA (miRNA).

140. The method of claim 139, wherein the agent comprises a nucleic acid molecule encoding GAA.

141. The method of claim 140, wherein the nucleic acid molecule is provided to the patient by administering to the patient a viral vector that comprises the nucleic acid molecule.

142. The method of claim 141, wherein the viral vector is an AAV, an adenovirus, a parvovirus, a coronavirus, a rhabdovirus, a paramyxovirus, a picornavirus, an alphavirus, a herpes virus, a poxvirus, or a Retroviridae family virus.

143. The method of claim 142, wherein the viral vector is an AAV.

144. The method of claim 143, wherein the AAV has a serotype selected from AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, and AAVrh74.

145. The method of claim 143, wherein the AAV is a pseudotyped AAV.

146. The method of claim 145, wherein the pseudotyped AAV is AAV2/8.

147. The method of claim 145, wherein the pseudotyped AAV is AAV2/9.

148. The method of claim 143, wherein the AAV comprises a recombinant capsid protein.

149. The method of any one of claims 138-148, wherein the nucleic acid molecule encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell.

150. The method of claim 149, wherein the promoter is a muscle MCK promoter, desmin promoter, chicken beta actin promoter, CMV promoter, myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.

151. The method of any one of claims 138-150, wherein the nucleic acid molecule encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell.

152. The method of claim 151, wherein the enhancer is a CMV enhancer, a MEF2 enhancer, or a MyoD enhancer.

153. The method of any one of claims 102-152, wherein the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2.

154. The method of claim 153, wherein the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.

155. The method of claim 154, wherein the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2.

156. The method of claim 155, wherein the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2.

157. The method of claim 156, wherein the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2.

158. The method of claim 157, wherein the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2.

159. The method of claim 158, wherein the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2.

160. The method of any one of claims 102-159, wherein the patient has infantile-onset Pompe disease.

161. The method of claim 160, wherein the patient is from about one month to about one year of age.

162. The method of claim 161, wherein the patient is from about one month to about six months of age.

163. The method of any one of claims 160-162, wherein, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.

164. The method of any one of claims 102-159, wherein the patient has late-onset Pompe disease.

165. The method of claim 164, wherein the patient exhibits endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

166. The method of any one of claims 102-165, wherein the patient has not previously received GAA enzyme replacement therapy.

167. The method of any one of claims 102-166, wherein the patient has previously received GAA enzyme replacement therapy.

168. The method of any one of claims 102-167, wherein, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

169. The method of any one of claims 102-168, wherein, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.

170. A kit comprising an AAV vector comprising a transgene encoding GAA and a package insert, wherein the package insert instructs a user of the kit to administer the AAV vector to a human patient in accordance with the method of any one of claims 1-101.

171. A kit comprising an agent that increases GAA expression and a package insert, wherein the package insert instructs a user of the kit to administer the agent to a human patient in accordance with the method of any one of claims 102-169.

172. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for treating Pompe disease in a human patient in need thereof, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

173. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for improving muscle function in a human patient diagnosed as having Pompe disease,

wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

174. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

175. The use of claim 174, wherein administration of the AAV vector to the patient reduces glycogen accumulation in muscle tissue and/or in neuronal tissue.

176. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for improving pulmonary function in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

177. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for increasing GAA expression in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

178. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of from about 2×10^{13} vg/kg to about 2×10^{14} vg/kg.

179. The use of claim 178, wherein the medicament comprises the AAV vector in an amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg.

180. The use of claim 179, wherein the medicament comprises the AAV vector in an amount of from about 4×10^{13} vg/kg to about 2×10^{14} vg/kg.

181. The use of claim 180, wherein the medicament comprises the AAV vector in an amount of from about 5×10^{13} vg/kg to about 2×10^{14} vg/kg.

182. The use of claim 181, wherein the medicament comprises the AAV vector in an amount of from about 6×10^{13} vg/kg to about 2×10^{14} vg/kg.

183. The use of claim 182, wherein the medicament comprises the AAV vector in an amount of from about 7×10^{13} vg/kg to about 2×10^{14} vg/kg.

184. The use of claim 183, wherein the medicament comprises the AAV vector in an amount of from about 8×10^{13} vg/kg to about 2×10^{14} vg/kg.

185. The use of claim 184, wherein the medicament comprises the AAV vector in an amount of from about 9×10^{13} vg/kg to about 2×10^{14} vg/kg.

186. The use of claim 185, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{14} vg/kg to about 2×10^{14} vg/kg.

187. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 3×10^{13} vg/kg.

188. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 4×10^{13} vg/kg.

189. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 5×10^{13} vg/kg.

190. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 6×10^{13} vg/kg.

191. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 7×10^{13} vg/kg.

192. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 8×10^{13} vg/kg.

193. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 9×10^{13} vg/kg.

194. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1×10^{14} vg/kg.

195. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.1×10^{14} vg/kg.

196. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.2×10^{14} vg/kg.

197. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.3×10^{14} vg/kg.

198. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.4×10^{14} vg/kg.

199. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.5×10^{14} vg/kg.

200. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.6×10^{14} vg/kg.

201. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.7×10^{14} vg/kg.

202. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.8×10^{14} vg/kg.

203. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.9×10^{14} vg/kg.

204. The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 2×10^{14} vg/kg.

205. The use of any one of claims 172-204, wherein the AAV vector is formulated for administration to the patient in a single dose comprising the amount.

206. The use of any one of claims 172-204, wherein the AAV vector is formulated for administration to the patient in two or more doses that, together, comprise the amount.

207. The use of claim 206, wherein the AAV vector is formulated for administration to the patient in from two doses to ten doses that, together, comprise the amount.

208. The use of claim 207, wherein the AAV vector is formulated for administration to the patient in two, three, or four doses that, together, comprise the amount.

209. The use of claim 208, wherein the AAV vector is formulated for administration to the patient in two doses that, together, comprise the amount.

210. The use of any one of claims 172-204, wherein the AAV vector is formulated for administration to the patient in two or more doses that each, individually, comprise the amount.

211. The use of claim 210, wherein the AAV vector is formulated for administration to the patient in from two doses to ten doses that each, individually, comprise the amount.

212. The use of claim 211, wherein the AAV vector is formulated for administration to the patient in two, three, or four doses that each, individually, comprise the amount.

213. The use of claim 212, wherein the AAV vector is formulated for administration to the patient in two doses that each, individually, comprise the amount.

214. The use of any one of claims 172-213, wherein the AAV vector is formulated for intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral,

intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration to the patient.

215. The use of claim 214, wherein the AAV vector is formulated for intravenous, intrathecal, intracisternal, intracerebroventricular, and/or intramuscular administration to the patient.

216. The use of claim 215, wherein the AAV vector is formulated for intravenous and/or intrathecal administration to the patient.

217. The use of claim 216, wherein the AAV vector is formulated for intravenous administration to the patient.

218. The use of any one of claims 172-217, wherein the AAV is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAVrh74, AAVrh.8, or AAVrh.10 serotype.

219. The use of claim 218, wherein the AAV is a pseudotyped AAV.

220. The use of claim 219, wherein the pseudotyped AAV is AAV2/8.

221. The use of claim 219, wherein the pseudotyped AAV is AAV2/9.

222. The use of any one of claims 172-217, wherein the AAV comprises a recombinant capsid protein.

223. The use of any one of claims 172-222, wherein the transgene encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell.

224. The use of claim 223, wherein the promoter is a MCK promoter, desmin promoter, chicken beta actin promoter, CMV promoter, myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.

225. The use of claim 224, wherein the promoter is a MCK promoter.

226. The use of claim 225, wherein the MCK promoter has a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 1.

227. The use of claim 226, wherein the MCK promoter has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 1.

228. The use of claim 227, wherein the MCK promoter has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 1.

229. The use of claim 228, wherein the MCK promoter has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 1.

230. The use of claim 229, wherein the MCK promoter has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 1.

231. The use of claim 230, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.

232. The use of claim 231, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.

233. The use of claim 232, wherein the MCK promoter has a nucleic acid sequence that is 100% identical to SEQ ID NO: 1.

234. The use of any one of claims 172-233, wherein the transgene encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell.

235. The use of claim 234, wherein the enhancer is a CMV enhancer, a MEF2 enhancer, or a MyoD enhancer.

236. The use of any one of claims 172-235, wherein the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2.

237. The use of claim 236, wherein the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.

238. The use of claim 237, wherein the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2.

239. The use of claim 238, wherein the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2.

240. The use of claim 239, wherein the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2.

241. The use of claim 240, wherein the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2.

242. The use of claim 241, wherein the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2.

243. The use of any one of claims 172-242, wherein the patient has infantile-onset Pompe disease.

244. The use of claim 243, wherein the patient is from about one month to about one year of age.

245. The use of claim 244, wherein the patient is from about one month to about six months of age.

246. The use of any one of claims 242-245, wherein, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.

247. The use of any one of claims 172-242, wherein the patient has late-onset Pompe disease.

248. The use of claim 247, wherein the patient exhibits endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

249. The use of any one of claims 172-248, wherein the patient has not previously received GAA enzyme replacement therapy.

250. The use of any one of claims 172-248, wherein the patient has previously received GAA enzyme replacement therapy.

251. The use of any one of claims 172-250, wherein, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

252. The use of any one of claims 172-251, wherein, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.