

CLAIMS:

1. A method for reducing the progression of abnormal muscle pathology and/or reversing abnormal muscle pathology in a patient, wherein the patient has been diagnosed with Pompe disease or is suspected of having Pompe disease, the method comprising administering to the patient a recombinant AAV (rAAV) having an AAV capsid and a vector genome packaged therein, wherein the vector genome comprises:
 - (a) a 5' inverted terminal repeat (ITR);
 - (b) a promoter;
 - (c) a nucleotide sequence encoding a chimeric fusion protein comprising a signal peptide and a vIGF2 peptide fused to a human acid- α -glucosidase (hGAA), wherein the sequence encoding the chimeric fusion protein is operable linked to regulatory sequences that direct its expression, and comprises SEQ ID NO: 7 or a sequence at least 95% identical thereto that encodes amino acids 1 to 982 of SEQ ID NO: 6;
 - (d) a polyA; and
 - (e) a 3' ITR.
2. The method according to claim 1, wherein the promoter is a constitutive promoter, optionally a CAG promoter or a CB7 promoter.
3. The method according to claim 1, wherein the abnormal muscle pathology is characterized by one or more of i) an elevated percentage of muscle cells with central nuclei; ii) muscle fiber atrophy, iii) anisocytosis in muscle cell fibers, iv) autophagic buildup, v) vacuolation, and vi) weakness.
4. The method according to claim 1, wherein the patient has late-onset Pompe disease.
5. The method according to claim 1, wherein the patient has infantile-onset Pompe disease.
6. The method according to claim 1, wherein the vector genome further comprises at least four, at least five, at least six, at least seven, or at least eight miR target sequences, optionally wherein each of the miR target sequences is specific for miR-183.

7. The method according to claim 1, wherein the AAV capsid is an AAVhu68 capsid.
8. The method according to claim 1, wherein the rAAV is administered intravenously and/or intrathecally.
9. The method according to claim 1, wherein the rAAV is administered to the patient via dual routes of administration, optionally wherein the dual routes are intravenous administration and intra-cisterna magna (ICM) administration.
10. The method according to claim 1, wherein the rAAV is administered intravenously at a dosage of about 1×10^{11} genome copies(GC)/kg to about 5×10^{13} GC/kg.
11. The method according to claim 1, wherein the rAAV is administered via the ICM at a dosage of about 1×10^{12} GC to about 5×10^{13} GC.
12. The method according to claim 1, wherein the rAAV is administered IV at a dosage of about 1×10^{11} GC/kg to about 5×10^{13} GC/kg and via the ICM at a dosage of about 1×10^{12} GC to about 5×10^{13} GC.
13. The method according to claim 1, further comprising administering a co-therapy to the patient receives, optionally wherein the co-therapy is a bronchodilator, an acetylcholinesterase inhibitor, respiratory muscle strength training (RMST), enzyme replacement therapy, and/or diaphragmatic pacing therapy.
14. A pharmaceutical composition comprising a recombinant AAV (rAAV) having an AAV capsid and a vector genome packaged therein, wherein the vector genome comprises:
 - (a) a 5' inverted terminal repeat (ITR);
 - (b) a promoter;
 - (c) a nucleotide sequence encoding a chimeric fusion protein comprising a signal peptide and a vIGF2 peptide fused to a human acid- α -glucosidase (hGAA), wherein the sequence encoding the chimeric fusion protein is operable linked to regulatory sequences

that direct its expression, and comprises SEQ ID NO: 7, or a sequence at least 95% identical thereto that encodes amino acids 1 to 982 of SEQ ID NO: 6;

(d) a poly A; and

(e) a 3' ITR.

15. The pharmaceutical composition according to claim 14, wherein the promoter is a constitutive promoter, optionally a CAG promoter or a CB7 promoter.

16. The pharmaceutical composition according to claim 14 or 15, wherein the vector genome further comprises at least four, at least five, at least six, at least seven, or at least eight miR target sequences, optionally wherein each of the miR target sequences is specific for miR-183.

17. The pharmaceutical composition according to any one of claims 14 to 16, wherein the AAV capsid is an AAVhu68 capsid.

18. The pharmaceutical composition according to any one of claims 14 to 17, wherein the composition is formulated for intravenous and/or intrathecal delivery.

19. The pharmaceutical composition according to any one of claims 14 to 18 for use in the treatment of a patient with Pompe disease, wherein the treatment reduces the progression of abnormal muscle pathology and/or reverses abnormal muscle pathology in the patient.

20. The pharmaceutical composition for use according to claim 19, wherein the abnormal muscle pathology is characterized by one or more of i) an elevated percentage of muscle cells with central nuclei; ii) muscle fiber atrophy, iii) anisocytosis in muscle cell fibers, iv) autophagic buildup, v) vacuolation, and vi) weakness.

21. The pharmaceutical composition for use according to claim 19 or 20, wherein the patient has late-onset Pompe disease.

22. The pharmaceutical composition for use according to claim 19 or 20, wherein the patient has infantile-onset Pompe disease.

23. The pharmaceutical composition for use according to any one of claims 19 to 22 wherein the rAAV is administered to the patient via dual routes of administration, optionally wherein the dual routes are intravenous administration and intra-cisterna magna (ICM) administration.

24. A pharmaceutical composition according to any one of claims 14 to 18, suitable for administration to a post-symptomatic patient has been diagnosed with Pompe disease.

25. A pharmaceutical composition according to any one of claims 14 to 18, which is suitable for reversing abnormal muscle pathology in a post-symptomatic patient with Pompe disease.

26. A pharmaceutical composition according to claim 25, wherein the abnormal muscle pathology is characterized by one or more of i) an elevated percentage of muscle cells with central nuclei; ii) muscle fiber atrophy, iii) anisocytosis in muscle cell fibers, iv) autophagic buildup, v) vacuolation, and vi) weakness.

27. A pharmaceutical composition according to any one of claims 14 to 18 or 24 to 26, which is suitable for use in a co-therapy, optionally characterized in that the patient further receives treatment with a bronchodilator, an acetylcholinesterase inhibitor, respiratory muscle strength training (RMST), enzyme replacement therapy, and/or diaphragmatic pacing therapy.

28. Use of the pharmaceutical composition according to any one of claims 14 to 18 for treating Pompe disease in a patient in need thereof, wherein the treatment reduces the progression of abnormal muscle pathology and/or reverses abnormal muscle pathology in the patient.