Claims

1. A recombinant adeno-associated virus (rAAV) comprising: (a) a variant AAV capsid protein comprising a heterologous peptide insertion with a length of 7 to 20 amino acids covalently inserted in the GH-loop of the capsid protein relative to a corresponding parental AAV capsid protein, wherein the peptide insertion comprises the amino acid sequence NKTTNKD and (ii) a heterologous nucleic acid comprising a nucleotide sequence encoding human α-galactosidase A (AGA) protein, wherein said nucleic acid is codon optimized for expression in human cells, wherein said nucleic acid comprises a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 1.

2. The rAAV according to claim 1, wherein the insertion peptide has from 1 to 3 spacer amino acids (Y_1-Y_3) at the amino and/or carboxyl terminus of amino acid sequence NKTTNKD.

3. The rAAV according to claim 1 or 2, wherein the insertion peptide is LANKTTNKDA.

4. The rAAV according to any one of claims 1 to 3, wherein the variant capsid protein comprises a V708I amino acid substitution relative to VP1 of AAV2 (SEQ ID NO:2) or the corresponding position in the capsid protein of another AAV serotype and wherein the variant capsid protein comprises an amino acid sequence at least 90% identical to the entire length of the amino acid sequence set forth as SEQ ID NO:4.

5. The rAAV according to claim 4, wherein the variant capsid protein comprises an amino acid sequence at least 95% identical to the entire length of the amino acid sequence set forth as SEQ ID NO:4.

6. The rAAV according to any one of claims 1 to 5, wherein the insertion site is located between two adjacent amino acids at a position between amino acids 570 and 611 of VP1 of AAV2, or the corresponding position in the capsid protein of another AAV serotype.

7. The rAAV according to any one of claims 1 to 6, wherein the insertion site is located between amino acids corresponding to amino acids 587 and 588 of VP1 of AAV2 or

between amino acids corresponding to amino acids 588 and 589 of VP1 of AAV2 or the corresponding position in the capsid protein of another AAV serotype.

8. The rAAV according to any one of claims 1 to 7, wherein said rAAV vector comprises a heterologous nucleic acid comprising a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 1.

9. The rAAV according to any one of claims 1 to 8, wherein said rAAV vector comprises a heterologous nucleic acid comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 1.

10. The rAAV according to any one of claims 1 to 9, wherein the rAAV vector comprises a nucleic acid comprising from 5' to 3': (a) an AAV2 terminal repeat (b) a CAG promoter (c) the nucleic acid set forth in SEQ ID NO: 1, (d) a polyadenylation sequence and (e) an AAV2 terminal repeat.

11. A host cell comprising the rAAV according to any one of claims 1 to 10.

12. The host cell of claim 11, wherein the host cell is a CHO cell, an HEK293T cell, an HEK293 cell, a HeLa cell, a BHK21 cell or a Vero cell and/or wherein the host cell is grown in a suspension or adherent culture and/or wherein the host cell is a cardiac or skeletal muscle cell.

13. A pharmaceutical composition comprising the rAAV according to any one of claims 1 to 10, and at least one pharmaceutically acceptable excipient.

14. The pharmaceutical composition of claim 13 for use in therapy.

15. Use of the pharmaceutical composition of claim 13 in the manufacture of a medicament for the treatment of Fabry disease.

16. The use of claim 15, wherein said pharmaceutical composition is to be administered by intravenous and/or intramuscular injection.

17. The use of claim 16, wherein the use comprises a single intravenous administration of at least 1×10^{8} vg/kg of the rAAV vector.

18. The use of claim 16 or 17, wherein the use comprises a single intravenous administration of 1×10^{12} vg/kg to 1×10^{14} vg/kg of the rAAV vector.

19. The use of the rAAV according to any one of claims 1 to 10 in the manufacture of a medicament for the treatment of Fabry disease.

20. The use according to claim 19, wherein the medicament is to be administered by intravenous and/or intramuscular injection.