Claims

We claim:

1. A nucleic acid comprising, in order from 5' to 3':

(i) a first AAV2 inverted terminal repeat sequence (ITR);

(ii) an MCK enhancer comprising nucleotides 236-442 of SEQ ID NO: 2;

(iii) a muscle creatine kinase core promoter sequence set out in nucleotides 443-793 of SEQ ID NO: 2;

(iv) a nucleotide sequence encoding a human GALGT2 polypeptide comprising nucleotides 1002-2522 of SEQ ID NO: 2; and

(v) a second AAV2 ITR sequence.

2. The nucleic acid of claim 1 further comprising 3' to said core promoter, a mouse MCK exon 1 sequence set out in nucleotides 794-846 of SEQ ID NO: 2.

3. The nucleic acid of any one of claims 1-2 further comprising 3' to said core promoter, an SV40 intron sequence set out in nucleotides 847-943 of SEQ ID NO: 2.

4. The nucleic acid of any one of claims 1-3 further comprising 3' to said core promoter, a 5' untranslated region set out in nucleotides 944-1000 of SEQ ID NO: 2.

5. The nucleic acid of any one of claims 1-4 further comprising 3' to said nucleotide sequence encoding a human GALGT2 polypeptide, a Syn pA sequence set out in nucleotides 2531-2579 of SEQ ID NO: 2.

6. The nucleic acid of any one of claims 1-5,

wherein said first ITR is set out in nucleotides 53-230 of SEQ ID NO: 2, and/or

wherein said second ITR is set out in nucleotides 2581-2762 of SEQ ID NO: 2.

7. The nucleic acid of claim 6,

wherein said first ITR is set out in nucleotides 53-230 of SEQ ID NO: 2; and

wherein said second ITR is set out in nucleotides 2581-2762 of SEQ ID NO: 2.

8. A nucleic acid comprising an rAAV.rh74.MCK.GALGT2 genome that is at least 90% identical to the nucleotide sequence set out in SEQ ID NO: 2.

9. A nucleic acid comprising the rAAV.rh74.MCK.GALGT2 genome set out in SEQ ID NO: 2.

10. A recombinant adeno-associated virus particle (rAAV) comprising the nucleic acid of any one of claims 1-9, wherein the rAAV is infectious.

11. The rAAV of claim 10, wherein the rAAV is serotype AAV-1, AAV-2, AAV-3, AAV-4, AAV-5, AAV-6, AAV-7, AAV-8, AAV-9, AAV-10, AAV-11, or AAVrh.74.

12. The rAAV of claim 10 or 11, wherein the AAV DNA in the rAAV genome is from AAV rh.74.

13. The rAAV of any one of claims 10-12, wherein the polynucleotide sequence of the AAV rh.74 genome is set out in SEQ ID NO: 1.

14. A composition comprising the rAAV of any one of claims 10-13 and a pharmaceutically acceptable carrier.

15. Use of the composition of claim 14 in the manufacture of a medicament for the treatment of a neuromuscular disorder, wherein the neuromuscular disorder is Duchenne Muscular Dystrophy (DMD); Becker Muscular Dystrophy; Congenital Muscular Dystrophy (MDC) 1A, 1B, 1C and 1D; Limb Girdle Muscular Dystrophy (LGMD) 1A, 1B, 1C, 1D, 1E, 1F, 1G, 1H, 2A, 2B, 2C, 2D, 2E, 2F, 2G 2H, 2I, 2J, 2K, 2L, 2M, 2N, 2O and 2Q; Bethlem Myopathy; Ullrich Congenital Muscular Dystrophy; Muscle Eye Brain Disease; Fukuyama Congenital Muscular Dystrophy; Walker Warburg Syndrome; Myotonic Dystrophy; Myasthenic syndromes; Congenital Myasthenias; Inclusion Body Myopathy; Inclusion Body Myositis; Emery Dreifuss Muscular Dystrophy; Distal Muscular Dystrophy; Dermatomyositis; Centronuclear Myopathy; Faciosacpulohumeral Muscular Dystrophy; Myoshi Myopathy;

Mitochondrial Myopathy; Nemaline Myopathy; Nonaka Myopathy; Myasthenia Gravis; or Polymyositis.

16. Use of the composition of claim 14 in the manufacture of a medicament for the treatment of a neuromuscular disorder, wherein the neuromuscular disorder is a muscular dystrophy.

17. The use of claim 16, wherein the muscular dystrophy is Duchenne Muscular Dystrophy.

18. The use of claim 16, wherein the muscular dystrophy is Congenital Muscular Dystrophy 1A.

19. The use of claim 16, wherein the muscular dystrophy is Limb Girdle Muscular Dystrophy 2D.

20. The use of any one of claims 15-19, wherein the composition is formulated for intramuscular (IM), isolated limb infusion or perfusion (ILP), or intravenous (IV) administration.

21. The use of claim 20 which is formulated for IM administration.

22. The use of claim 20 or 21 comprising a dose of the rAAV from ~~about~~ $3x10^{11}$ to at least ~~about~~ $5x10^{12}$ vg/injection.

23. The use of claim 20 which is formulated for infusion or ILP administration.

24. The use of claim 20 or 23 comprising a dose of the rAAV from ~~about~~ $2x10^{12}$ to at least ~~about~~ $4.8x10^{13}$ vg/kg/limb, or a total dose of from ~~about~~ $4x10^{12}$ to at least ~~about~~ $9.6x10^{13}$.

25. The use of claim 20 which is formulated for IV administration.

26. The use of claim 20 comprising a dose of the rAAV from ~~about~~ $2x10^{14}$ to at least ~~about~~ $6x10^{15}$ vg/kg.

27. The use of claim 20 comprising a dose of the rAAV from ~~about~~ $5x10^{13}$ vg/kg to ~~about~~ $5x10^{15}$ vg/kg.