CLAIMS:

1. A recombinant adeno-associated virus (rAAV) comprising an adeno-associated virus (AAV) capsid and a vector genome, wherein the vector genome comprises an AAV 5' inverted terminal repeat (ITR), an expression cassette, and an AAV 3'ITR, wherein the expression cassette comprises an engineered nucleic acid sequence encoding for a functional human N-sulfoglycosamine sulfohydrolase (hSGSH), wherein the hSGSH coding sequence comprises a signal peptide sequence and a mature hSGSH coding sequence, wherein the mature hSGSH coding has the nucleic acid sequence of SEQ ID NO: 16 or a nucleic acid sequence which is (a) at least 85% or (b) at least 99% identical thereto and encodes SEQ ID NO: 23; and wherein the hSGSH coding sequence is operably linked to regulatory control sequences which direct expression of the hSGSH in a cell.

2. The rAAV according to claim 1, wherein:

(i) the mature hSGSH coding sequence 99% identical to SEQ ID NO: 16 is SEQ ID NO: 22 which encodes SEQ ID NO: 23 (hSGSH.A482Y-E488V);

(ii) the mature hSGSH coding sequence is SEQ ID NO: 16;

(iii) the mature hSGSH coding sequence has the nucleic acid sequence of SEQ ID NO: 16, or a nucleic acid sequence which is 85% identical thereto and encodes SEQ ID NO: 23; or

(iv) the signal peptide sequence is a native signal sequence having nucleic acid sequence of SEQ ID NO: 31, or a sequence at least about 95% identical thereto which encodes SEQ ID NO: 32.

3. The rAAV according to claim 1 or 2, wherein the regulatory control sequences comprise:

(i) a CMV IE enhancer, a chicken-beta actin (CB) promoter, and a chicken beta actin intron; or

(ii) one or more of a Kozak sequence, an intron, an enhancer, a TATA signal and a polyA sequence, optionally

wherein the regulatory control sequences comprise a rabbit globin polyadenylation sequence.

4. The rAAV according to any one of claims 1 to 3, wherein the regulatory control sequences further comprise a mutant WPRE element.

5. The rAAV according to any one of claims 1 to 4, wherein the vector genome further comprises at least one, two, three, four or more tandem repeats of dorsal root ganglion (drg)-specific miRNA target sequences, wherein the at least one, two, three, four or more tandem repeats comprise at least a first miRNA target sequence, at least a second, at least third, and/or at least fourth miRNA target sequence, optionally wherein the miRNA target sequence comprises at least a first miRNA target sequence, at least a second, at least third, and/or at least fourth miRNA target sequence which target is miR182 or miR183.

6. The rAAV according to claim 5, wherein the miRNA target sequence for the at least first, at least second, at least third, and/or at least fourth miRNA target sequence for the expression cassette mRNA or DNA positive strand is AGTGTGAGTTCTACCATTGCCAAA (miR182, SEQ ID NO: 47); and/or AGTGAATTCTACCAGTGCCATA (miR183, SEQ ID NO: 28).

7. The rAAV according to any one of claims 1 to 6, wherein the vector genome further comprises at least eight tandem repeats comprising at least a first, at least second, at least third, at least fourth, at least fifth, at least sixth, at least seventh and at least eighth miRNA target sequence, which may be the same or different, and target miR183 or miR182, optionally wherein the at least eight tandem repeats comprise at least four tandem repeats of dorsal root ganglion (drg)-specific miRNA182 target sequences and at least four tandem repeats of drg-specific miRNA183 target sequences.

8. The rAAV according to claim 7, wherein the drg-specific miRNA target sequence for the

(a) at least a first, at least second, at least third, at least fourth, at least fifth, at least sixth, at least seventh and/or at least eighth miRNA target sequence for the expression cassette mRNA or DNA positive strand is (i) AGTGAATTCTACCAGTGCCATA (miR183, SEQ ID NO: 28); and (ii) AGTGTGAGTTCTACCATTGCCAAA (miR182, SEQ ID NO: 47); and/or

(b) at least first, at least second, at least third and/or at least fourth miRNA target sequence for a the expression cassette mRNA or DNA positive strand is AGTGTGAGTTCTACCATTGCCAAA (miR182, SEQ ID NO: 47) and at least fifth, at least sixth, at least seventh and/or at least eighth miRNA target sequence for the expression cassette mRNA or DNA positive strand is AGTGAATTCTACCAGTGCCATA (miR183, SEQ ID NO: 28).

9. The rAAV according to any one of claims 5 to 7, wherein two, three, four or more or the at least eight of the miRNA target sequences are separated by a spacer, optionally wherein the spacer is independently selected from one or more of (A) GGAT; (B) CACGTG; (C) GCATGC; (D) gcggccgc; (E) cgat; (F) atcggt; and/or (G) tcac, further optionally wherein the spacer located between the miRNA target sequences may be located 3' to the first miRNA target sequence and/or 5' to the last miRNA target sequence.

10. The rAAV according to any one of claims 5 to 9, wherein the least one, two, three, four or more or the at least eight tandem repeats of dorsal root ganglion (drg)-specific miRNA target sequences are operably linked to:
(i) a 3' untranslated region (UTR) of the hSGSH; or (ii) a 5' untranslated region (UTR) of the hSGSH.

11. The rAAV according to any one of claims 1 to 3, wherein the rAAV vector genome comprises the nucleic acid sequence of SEQ ID NO: 10 (AAV.CB7.CI.hSGSHcoV1.rBG).

12. The rAAV according to any one of claims 1 to 6, wherein the rAAV vector genome comprises the nucleic acid sequence of SEQ ID NO: 13 (CB7.CI.hSGSHcoV1-4xmiR183.rBG).

13. The rAAV according to any one of claims 1 to 12, wherein the AAV capsid is a Clade F AAV, AAVhu68 or
AAVrh91.

14. The rAAV according to any of claims 1 to 13, for use in the treatment of Mucopolysaccharidosis III A (MPS IIIA or Sanfilippo syndrome type A) and/or improving gait or mobility, reducing tremors, reducing spasms, improving posture, or reducing the progression of vision loss in a subject in need thereof.

15. A composition comprising a stock of rAAV according to any of claims 1 to 14 and an aqueous suspension media.

16. A pharmaceutical composition comprising a rAAV according to any of claims 1 to 14 in a formulation buffer.

17. Use of the rAAV according to any of claims 1 to 13 in the preparation of a pharmaceutical composition for treating Mucopolysaccharidosis III A (MPS IIIA or Sanfilippo syndrome type A) and/or improving gait or mobility, reducing tremors, reducing spasms, improving posture, or reducing the progression of vision loss in a subject in need thereof.

18. The use according to claim 45, wherein the pharmaceutical composition is to be delivered via intracerebroventricular (ICV), intrathecal (IT), intracistemal or intravenous (IV) injection.

19. The use according to claim 17 or 18, wherein the pharmaceutical composition is to be administered at a dose 1 x 10^9 GC of rAAV per gram of brain mass to about 1 x 10^{13} GC of rAAV per gram of brain mass.

20. The pharmaceutical composition according to claim 16, which is formulated to have a pH of about 7.28 to about 7.32.

20. A vector comprising an expression cassette, wherein the expression cassette comprises a hSGSH-coding sequence, which is a nucleic acid sequence encoding a functional human N-sulfoglycosamine sulfohydrolase (hSGSH), under control of regulatory control sequences which direct the hSGSH expression, wherein the hSGSH coding sequence comprises a signal peptide sequence and a mature hSGSH, and wherein the mature hSGSH-

coding sequence is selected from SEQ ID NO: 16 or a sequence at least about 95% identical to SEQ ID NO: 16, or SEQ ID NO: 22, or a sequence at least about 95% identical thereto.

21. The vector according to claim 20, wherein the vector is a viral vector selected from a recombinant parvovirus, a recombinant lentivirus, a recombinant retrovirus, or a recombinant adenovirus; or a non-viral vector selected from naked DNA, naked RNA.

22. A nucleic acid molecule comprising an expression cassette comprising an engineered functional human N-sulfoglycosamine sulfohydrolase (hSGSH) gene and regulatory control sequences, said expression cassette being flanked by a 5' inverted terminal repeat (ITR) and a 3' ITR, wherein the engineered hSGSG gene encodes a functional hSGSH, wherein the hSGSH coding sequence comprises a signal peptide sequence and a mature hSGSH, and wherein the mature hSGSH-coding sequence is selected from SEQ ID NO: 16 and 22.

23. The nucleic acid sequence according to claim 21, wherein the expression cassette is selected from SEQ ID NO: 11 and SEQ ID NO: 14.

24. A packaging host cell comprising a nucleic acid molecule according to claim 22 or 23.

25. The packaging host cell according to claim 24, wherein

(i) the host cell further comprises AAV rep coding sequences operably linked to sequences which express rep protein in the packaging host cell, AAV capsid coding sequences operably linked to sequences which express AAV capsid proteins in the packaging host cell, and helper virus functions necessary to permit packaging of the expression cassette and ITRs into the AAV capsid; and/or

(ii) the AAV capsid is selected from a AAVhu68 and AAVrh91.

26. An rAAV production system useful for producing the rAAV according to any of claims 1 to 12, wherein the production system comprises a cell culture comprising:

(a) a nucleic acid sequence encoding a AAV capsid protein;

(b) a vector genome; and

(c) sufficient AAV rep functions and helper functions to permit packaging of the vector genome into the AAV capsid.

27. The rAAV production system according to claim 26, wherein
(i) the AAV capsid is selected from a AAVhu68 and AAVrh91 or(ii) the vector genome is selected from SEQ ID NO: 10 and SEQ ID NO: 13.