

CLAIMS:

1. An adeno-associated virus (AAV) comprising an AAVhu68 capsid having packaged therein a vector genome, the vector genome comprising an expression cassette comprising a nucleic acid sequence encoding at least one hairpin forming miRNA that comprises a targeting sequence that binds a miRNA target site on the mRNA of human androgen receptor, operably linked to regulatory sequences which direct expression of the nucleic acid sequence in the subject, wherein the miRNA inhibits expression of human androgen receptor, and wherein the expression cassette is flanked by a 5' AAV ITR and 3' AAV ITR.
2. The AAV of claim 1, wherein the miRNA target site comprises:
GAA CTA CAT CAA GGA ACT CGA (SEQ ID NO: 1); or
CTA CAT CAA GGA ACT CGA TCG (SEQ ID NO: 27).
3. The AAV of claim 1 or claim 2, wherein the miRNA coding sequence comprises the sequence of TCG AGT TCC TTG ATG TAG TTC (SEQ ID NO: 2) or a sequence having up to 10 substitutions.
4. The AAV of claim 1 or claim 2, wherein the miRNA coding sequence comprises the sequence of CGA TCG AGT TCC TTG ATG TAG (SEQ ID NO: 3) or a sequence having up to 10 substitutions.
5. The AAV of any one of claims 1 to 4, wherein the miRNA coding sequence comprises SEQ ID NO: 4 or SEQ ID NO: 5, or a sequence having up to 30 substitutions.
6. The AAV of any one of claims 1 to 5, wherein the miRNA coding sequence comprises SEQ ID NO: 11 or SEQ ID NO: 12, or a sequence having up to 60 substitutions.
7. The AAV according to any one of claims 1 to 6, wherein the regulatory sequences comprise one or more of a promoter, intron, WPRE, and poly A.

8. The AAV according to claim 7, wherein the promoter is a CB7 promoter.
9. The AAV according to any one of claims 7 or 8, wherein the regulatory sequences comprise a WPRE.
10. The AAV according to any one of claims 7 to 9, wherein the regulatory sequences comprise an intron.
11. The AAV according to any one of claims 7 to 10, wherein the regulatory sequences comprise a rabbit beta globin poly A.
12. A pharmaceutical composition comprising the AAV according to any one of claims 1 to 11, and a pharmaceutically acceptable aqueous suspending liquid, excipient, and/or diluent.
13. An expression cassette comprising a nucleic acid sequence encoding at least one hairpin forming miRNA that comprises a targeting sequence that binds a miRNA target site on the mRNA of human androgen receptor, operably linked to regulatory sequences which direct expression of the nucleic acid sequence in the subject, wherein the miRNA inhibits expression of human androgen receptor, and wherein the expression cassette is flanked by a 5' AAV ITR and 3' AAV ITR.
14. The expression cassette of claim 13, wherein the miRNA target site comprises:
GAA CTA CAT CAA GGA ACT CGA (SEQ ID NO: 1); or
CTA CAT CAA GGA ACT CGA TCG (SEQ ID NO: 27).
15. The expression cassette of claim 13 or claim 14, wherein the miRNA coding sequence comprises the sequence of TCG AGT TCC TTG ATG TAG TTC (SEQ ID NO: 2) or a sequence having up to 10 substitutions.
16. The expression cassette of claim 13 or claim 14, wherein the miRNA coding sequence comprises the sequence of CGA TCG AGT TCC TTG ATG TAG (SEQ ID NO: 3) or a sequence having up to 10 substitutions.

17. The expression cassette according to any one of claims 13 to 16, wherein the regulatory sequences comprise one or more of a promoter, intron, WPRE, and poly A.
18. The expression cassette according to claim 17, wherein the promoter is a CB7 promoter.
19. The expression cassette according to any one of claims 17 or 18, wherein the regulatory sequences comprise a WPRE.
20. The expression cassette according to any one of claims 17 to 19, wherein the regulatory sequences comprise an intron.
21. The expression cassette according to any one of claims 17 to 20, wherein the regulatory sequences comprise a rabbit beta globin poly A.
22. Use of the AAV according to any one of claims 1 to 11, or a composition according to claim 12, or the expression cassette according to any one of claims 13 to 21, in the preparation of a medicament for the treatment of a subject having Spinal and Bulbar Muscular Atrophy (SBMA) .
23. The use according to claim 22, wherein the AAV, composition or cassette is formulated to be administered intrathecally at a dose of 1×10^{10} GC/g brain mass to 3.33×10^{11} GC/g brain mass of the rAAV.
24. The use according to any one of claims 22 or 23, wherein the subject is a human adult and is to be administered a dose of 1.44×10^{13} to 4.33×10^{14} GC of the rAAV.
25. The use according to any one of claims 22 to 24, wherein the rAAV is to be delivered intrathecally, via intracerebroventricular delivery, or via intraparenchymal delivery.
26. The use according to any one of claims 22 to 25, wherein the composition is to be administered as a single dose via a computed tomography- (CT-) guided sub-occipital injection into the cisterna magna (intra-cisterna magna).

27. The use according to any one of claims 22 to 26, wherein the subject has SBMA.
28. The use according to any one of claims claim 22 to 27, wherein the patient is to be administered an AAV according to any one of claims 1 to 11, a composition according to claim 12 or a cassette according to any one of claims 13 to 21.
29. The use according to any one of claims 13 to 28, wherein the subject is to be administered a dose of 1×10^{10} GC/g brain mass to 3.33×10^{11} GC/g brain mass of the rAAV intrathecally.
30. The use according to any one of claims 13 to 29, wherein the subject is a human adult and is to be administered a dose of 1.44×10^{13} to 4.33×10^{14} GC of the rAAV.
31. The use according to any one of claim 13 to 30, wherein the rAAV comprising the miR coding sequence is to be delivered intrathecally, via intracerebroventricular delivery, or via intraparenchymal delivery.
32. The use according to any one of claims 13 to 31, wherein the rAAV is to be administered as a single dose via a computed tomography- (CT-) guided sub-occipital injection into the cisterna magna (intra-cisterna magna).