CLAIMS

1. A DNA polynucleotide comprising in a 5’ to 3’ direction:

(a) a 5’ inverted terminal repeat (ITR) sequence comprising the sequence of SEQ ID NO: 262;

(b) a CAG promoter;

(c) a pre-amiRNA encoding sequence comprising the sequence of SEQ ID NO: 261, wherein the CAG promoter is operably linked to the pre-amiRNA encoding sequence and a polyadenylation signal; and

(d) a 3’ inverted terminal repeat (ITR) sequence comprising the sequence of SEQ ID NO: 263.

2. The polynucleotide of claim 1, wherein the polyadenylation signal comprises the sequence of SEQ ID NOs: 264 or 252 and the CAG promoter comprises the sequence of the SEQ ID NO: 250 or 265.

3. The polynucleotide of claims 1 or 2, wherein the end of the 5’ ITR to the end 3’ ITR is up to about 2.5 kb.

4. The polynucleotide of claim 1, comprising the sequence of SEQ ID NO: 266.

5. The polynucleotide of any one of claims 1-4, wherein the polynucleotide is a plasmid further comprising an origin of replication and a selectable marker.

6. The polynucleotide of any one of claims 1-4, wherein the polynucleotide is a recombinant adeno-associated viral (rAAV) nucleic acid comprising the 5’ ITR at the 5’ terminus and 3’ ITR at the 3’ terminus.

7. A recombinant adeno-associated viral (rAAV) vector comprising:

(a) the rAAV nucleic acid of claim 6; and

(b) a rAAV capsid comprising: VP1 comprising the amino acid sequence of SEQ ID NO: 257, VP2 comprising the amino acid sequence of SEQ ID NO: 258, and VP3 comprising the amino acid sequence of SEQ ID NO: 259.

8. A recombinant adeno-associated viral (rAAV) vector comprising:

(a) an rAAV nucleic acid comprising a pre-amiRNA encoding sequence comprising the sequence of SEQ ID NO: 261 operably linked to an upstream promoter and to a downstream polyA, and

(b) a rAAV capsid comprising: VP1 comprising the amino acid sequence of SEQ ID NO: 257, VP2 comprising the amino acid sequence of SEQ ID NO: 258, and VP3 comprising the amino acid sequence of SEQ ID NO: 259.

9. A pharmaceutical composition comprising about 1.0×10^{10} vg to about 1.0×10^{13} vg of the rAAV vector of claims 7 or 8, and a pharmaceutically acceptable carrier.

10. The pharmaceutical composition of claim 9, comprising about 1.0×10^{11} vg to about 1.0×10^{12} vg.

11. The composition of claims 9 or 10, further comprising a MRI imaging agent, wherein the MRI imaging agent is gadoteridol.

12. A pharmaceutical composition comprising a sufficient amount of the rAAV vector of any one of claims 7 or 8and a pharmaceutically acceptable carrier to provide a 25% to 40% reduction in total huntingtin protein in a human subject in need thereof.

13. Use of the rAAV vector of any one of claims 7 or 8 or the pharmaceutical composition of any one of claims 9-12 for the preparation of a medicament for treating Huntington disease, wherein the medicament is to be administered intraparenchymally to a subject.

14. The use of claim 13, where said medicament is for treating Huntington disease in a human subject, wherein;

(a) the putamen and/or caudate volume in the right hemisphere and/or left hemisphere of the subject is to be determined; and

(b) the rAAV vector is to be administered intraparenchymally to the subject at a dose of about 2.0×10^{7} vg/mm^3 to about 2.0×10^{8} vg/mm^3 to the right hemisphere and/or a dose of about 2.0×10^{7} vg/mm^3 to about 2.0×10^{8} vg/mm^3 to the left hemisphere; wherein said dose is based on the volume determined in step (a).

15. The use of claim 14, wherein administration to the right hemisphere comprises direct administration to the right hemisphere putamen and caudate; and administration to the left hemisphere comprises direct administration to the left hemisphere putamen and caudate.

16. The use of claim 15, wherein the putamen and caudate volume of the right hemisphere is measured and the putamen and caudate volume of the left hemisphere is measured, and each

hemisphere independently receives a dose of 2.0 x 10^7 vg/mm^3 to 2.0 x 10^8 vg/mm^3 based on the measured volume.

17. The use of any one of claims 14-16, wherein a dose of 2.0 x 10^7 vg/mm^3 to 2.0 x 10^8 vg/mm^3 is to be administrated to the right hemisphere putamen and caudate in approximate proportion to the volume of the putamen and caudate of the right hemisphere.

18. The use of any one of claims 14-17, wherein a dose of 2.0 x 10^7 vg/mm^3 to 2.0 x 10^8 vg/mm^3 is to be administrated to the right hemisphere putamen and caudate in a ratio of about 67% putamen to about 33% caudate.

19. The use of any one of claims14-18, wherein for the left hemisphere a dose of 2.0 x 10^7 vg/mm^3 to 2.0 x 10^8 vg/mm^3 is to be administrated to the putamen and to the caudate of the left hemisphere in approximate proportion to the volume of the putamen and caudate of the left hemisphere.

20. The use of any one of claims 14-19, wherein a dose of 2.0 x 10^7 vg/mm^3 to 2.0 x 10^8 vg/mm^3 is to be administrated to the left hemisphere putamen and caudate in a ratio of about 67% putamen to about 33% caudate, wherein the same dose is to be administered to the right hemisphere and left hemisphere.

21. The use of any one of claims 14-20, wherein administration to the caudate comprises a parietal trajectory.

22. The use of any one of claims 14-21, wherein administration to the putamen comprises an occipital trajectory.

23. The use of any one of claims 14-22, wherein each hemisphere is to be administered 1.0 x 10^{10} vg to 1.0 x 10^{13} vg of the rAAV vector.

24. The use of claim 23, wherein each hemisphere is to be administered 1.0 x 10^{11} vg to 1.0 x 10^{12} vg of the rAAV vector.

25. The use of any one of claims 14-24, wherein administration comprises convection enhanced delivery.

26. The use of any one of claims 14-25, wherein expressed inhibitory RNA is measured in cerebrospinal fluid by detecting an miR155 scaffold.

27. The use of claim 26, wherein detection of expressed inhibitory nucleic acid comprises the steps of: (a) RNA purification from cerebrospinal fluid; (b) reverse transcriptase; and (c) quantitative Polymerase Chain Reaction (qPCR).