CLAIMS

What is claimed is:

1. Use of a recombinant adeno-associated virus (rAAV) particle in the manufacture of a medicament for the treatment of a disorder of the central nervous system (CNS), wherein the rAAV particle is to be administered to the CNS of the individual, wherein the rAAV particle comprises

a) a rAAV capsid comprising AAV2 capsid proteins comprising one or more amino acid substitutions at one or more of positions R484, R487, K527, K532, R585 and/or R588, numbering based on VP1 numbering of AAV2,

wherein the one of more amino acid substitutions is with a hydrophobic amino acid residue,

and

wherein the one or more amino acid substitutions reduces binding of the rAAV particle to a heparan sulfate proteoglycan, and

b) a rAAV vector comprising a heterologous nucleic acid and at least one AAV inverted terminal repeat.

2. Use of a recombinant adeno-associated virus (rAAV) particle in the manufacture of a medicament for:

(a) the treatment of a disorder of the central nervous system (CNS), wherein the capsid of said rAAV particle is modified to improve rAAV transduction of cells in the CNS of an individual compared to transduction of cells with a rAAV comprising a wild-type capsid, or

(b) the treatment of a disorder of the CNS, wherein the capsid of said rAAV particle is modified to improve expression of a heterologous nucleic acid in the CNS of an individual compared to the level of expression of a heterologous nucleic acid of a rAAV particle comprising a wild-type rAAV capsid protein, wherein the rAAV particle comprises

a) a rAAV capsid comprising AAV2 capsid proteins comprising one or more amino acid substitutions at one or more of positions R484, R487, K527, K532, R585 and/or R588, numbering based on VP1 numbering of AAV2, wherein

the one of more amino acid substitutions is with a hydrophobic amino acid residue, andwherein the one or more amino acid substitutions reduces binding of the rAAV particle to a heparan sulfate proteoglycan, and

b) a rAAV vector comprising a heterologous nucleic acid and at least one AAV inverted terminal repeat.

3. Use of a recombinant adeno-associated virus (rAAV) particle in the manufacture of a composition for the treatment of a disorder of the central nervous system (CNS) of an individual, wherein the composition is to be administered to the striatum of the individual, wherein the rAAV particle comprises

a) a rAAV capsid comprising AAV2 capsid proteins comprising one or more amino acid substitutions at one or more of positions R484, R487, K527, K532, R585 and/or R588, numbering based on VP1 numbering of AAV2, wherein the one of more amino acid substitutions is with a hydrophobic amino acid residue, and wherein the one or more amino acid substitutions reduces binding of the rAAV particle to a heparan sulfate proteoglycan, and

b) a rAAV vector comprising a heterologous nucleic acid and at least one AAV inverted terminal repeat.

4. The use according to claim 3, wherein the disorder of the CNS is Huntington's Disease or Parkinson's Disease.

5. The use according to any one of claims 1- 4, wherein the rAAV particle is to be administered at a single site.

6. The use according to any one of claims 1-5, wherein the one or more amino acid substitutions reduces binding of the rAAV particle to the heparan sulfate proteoglycan by at least 10%, at least 25%, at least 50%, at least 75%, or 100%.

7. The use according to any one of claims 1-6, wherein the one or more amino acid substitutions comprises substitution of an arginine or lysine residue with an alanine residue.

8. The use according to any one of claims 1-7, wherein the one or more amino acid substitutions comprises substitutions at positions R484 and R487 or at positions R585

and R588, numbering based on VP1 of AAV2.

9. The use according to any one of claims 1-8, wherein the AAV2 capsid proteins comprise amino acid substitutions R585A and R588A, numbering based on VP1 of AAV2.

10. The use according to any one of claims 1-9, wherein the AAV2 capsid proteins comprise amino acid substitution K532A, numbering based on VP1 of AAV2.

11. The use according to any one of claims 1-10, wherein the rAAV particle comprises one or more AAV2 capsid proteins having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 2, 4, or 6.

12. The use according to any one of claims 1-11, wherein the heterologous nucleic acid encodes a polypeptide selected from the group consisting of an antioxidant, a neurotrophic factor, an anti-apoptotic factor, an anti- angiogenic factor, and an anti-inflammatory factor.

13. The use according to any one of claims 1-11, wherein the heterologous nucleic acid encodes a therapeutic nucleic acid.

14. The use according to any one of claims 1-13, wherein the rAAV vector is a self-complementary rAAV vector.