

CLAIMS

1. Use of one or more compositions comprising a nucleic acid encoding retromer core protein VPS35 and at least one nucleic acid encoding a retromer core protein chosen from the group consisting of VPS26a, VPS26b, and combinations thereof, in the manufacture of a medicament for the treating, preventing and/or curing a neurodegenerative disease of a neurogenerative disease or disorder in a subject.
2. The use of claim 1, wherein the nucleic acid encoding retromer core protein VPS35 and the at least one nucleic acid encoding a retromer core protein chosen from the group consisting of VPS26a, VPS26b, and combinations thereof, are provided in one or more viral vectors.
3. The use of claim 2, wherein the one or more compositions comprise a first composition comprising at least one viral vector comprising a transgene encoding retromer core protein VPS35 and a second composition comprising at least one viral vector comprising a transgene encoding a retromer core protein chosen from the group consisting of VPS26a, VPS26b, and combinations thereof.
4. The use of claim 3, wherein a therapeutically effective amount of a third composition comprising at least one viral vector comprising a transgene encoding a retromer core protein chosen from the group consisting of VPS26a, VPS26b, and combinations thereof is administered to the subject.
5. The use of claim 3, wherein the first and second composition are administered sequentially.
6. The use of claim 3, wherein the first and second composition are administered simultaneously.
7. The use of claim 4, wherein the first, second and third composition are administered sequentially.

8. The use of claim 4, wherein the first, second and third composition are administered simultaneously.
9. The use of any one of claims 1-8, wherein the one or more compositions further comprise a pharmaceutical carrier.
10. The use of any one of claims 1-9, wherein the neurodegenerative disease or disorder is chosen from the group consisting of Alzheimer's disease (AD), Parkinson's disease, neuronal ceroid lipofuscinosis (NCL), transmissible spongiform encephalopathies (TSEs or prion disease), multiple system atrophy (MSA), progressive supranuclear palsy (PSP), frontotemporal lobar dementia linked to chromosome 17q21-22 and its subtypes (FTLD-17/FTLD-Tau), Lewy Body Disease (LBD), amyotrophic lateral sclerosis (ALS), frontal-temporal degeneration (FTD), ALS-FTD, and chronic traumatic encephalopathy (CTE).
11. A viral vector comprising at least one transgene encoding retromer core protein VPS35 and encoding a retromer core protein chosen from the group consisting of VPS26a, VPS26b, and combinations thereof.
12. The vector of claim 11, wherein the retromer core protein VPS35 encoded by the transgene has the amino acid sequence of VPS35 (SEQ ID NO: 1).
13. The vector of claim 11, wherein the transgene has the nucleic acid sequence of SEQ ID NO: 10.
14. The vector of claim 11, wherein the retromer core protein VPS26a encoded by the transgene has the amino acid sequence of VPS26a (SEQ ID NO: 2).
15. The vector of claim 11, wherein the retromer core protein VPS26b encoded by the transgene has the amino acid sequence of VPS26b (SEQ ID NO: 3).
16. The vector of any one of claims 2-15, wherein the vector is selected from the group consisting of adeno-associated virus (AAV), adenovirus, lentivirus, retrovirus, poxvirus,

baculovirus, herpes simplex virus, vaccinia virus, and a synthetic virus.

17. A composition comprising at least one viral vector comprising a transgene encoding retromer core protein VPS35 and a transgene encoding a retromer core protein chosen from the group consisting of VPS26a, VPS26b, and combinations thereof.

18. The composition of claim 17, wherein the retromer core protein VPS35 encoded by the transgene has the amino acid sequence of VPS35 (SEQ ID NO: 1).

19. The composition of claim 17, wherein the transgene has the nucleic acid sequence of SEQ ID NO: 10.

20. The composition of claim 17, wherein the retromer core protein Vps26a encoded by the transgene has the amino acid sequence of VPS26a (SEQ ID NO: 2).

21. The composition of claim 17, wherein the retromer core protein VPS26b encoded by the transgene has the amino acid sequence of VPS26b (SEQ ID NO: 3).

22. The composition of claim 17, wherein the vector is selected from the group consisting of adeno-associated virus (AAV), adenovirus, lentivirus, retrovirus, poxvirus, baculovirus, herpes simplex virus, vaccinia virus, and a synthetic virus.