

WHAT IS CLAIMED IS:

1. Use of i) an amount of a first composition comprising a first viral vector comprising a conditionally activatable gene or gene product, and ii) an amount of a second composition comprising a second viral vector comprising an open reading frame for expressing a gene, the product of which activates the gene in the first viral vector, in the manufacture of a medicament ~~A method~~ for targeting a specific population of mammalian neurons for activatable expression of a gene product in the central nervous system of a mammal, ~~comprising administering to the mammal~~ i) an amount of a first composition comprising a first viral vector comprising a conditionally activatable gene or gene product, and ii) an amount of a second composition comprising a second viral vector comprising an open reading frame for expressing a gene, the product of which activates the gene in the viral vector, wherein the amount of the second composition is effective to allow for expression of the gene or gene product in the first viral vector in the specific population of neurons in the mammal relative to a mammal not administered the first and second viral vector.
2. The ~~method-use~~ of claim 1 wherein the first viral vector is to be systemically administered and focused ultrasound is to be employed to target the specific population of neurons.
3. The ~~method-use~~ of claim 1 wherein the first viral vector is to be locally administered.
4. The ~~method-use~~ of any one of claims 1 to 3 wherein the second viral vector is to be systemically administered and focused ultrasound is to be employed to target the specific population of neurons.
5. The ~~method-use~~ of any one of claims 1 to 3 wherein the second viral vector is to be locally administered.
6. The ~~method-use~~ of any one of claims 1 to 5 wherein the first viral vector is a retrograde viral vector.

7. The method-use of any one of claims 1 to 5 wherein the second viral vector is a retrograde viral vector.
8. The method-use of any one of claims 1 to 7 wherein the first viral vector is to be administered before the second vector.
9. The method-use of any one of claims 1 to 7 wherein the second viral vector is to be administered before the first vector.
10. The method-use of any one of claims 1 to 9 wherein one of the viral vectors is to be targeted to a structure in the brain of the mammal to be modulated which contains axons from regulatory neurons, and the other viral vector is to be targeted to a different region of the brain containing a subset of the cell bodies that send the axons to the structure to be modulated.
11. The method-use of any one of claims 1 to 10 wherein at least one of the viral vectors comprises an adeno-associated virus, adenovirus, canine adenovirus, herpes simplex virus, or lentivirus vector.
12. The method-use of any one of claims 1 to 10 wherein one of the viral vectors comprises a retrograde form of adeno-associated virus, lentivirus or canine adenovirus.
13. The method-use of any one of claims 1 to 12, wherein the first viral vector contains recognition sites capable of recombination and activation of the gene in the first viral vector and the second viral vector encodes a recombinase that is specific for the recognition sites.
14. The method-use of claim 13 wherein the recombinase comprises Cre, PhiC31 or Flp.
15. The method-use of any one of claims 1 to 12 wherein the first viral vector comprises a transcriptional regulatory region that binds a transcriptional

activator gene product operably linked to the gene and the second viral vector encodes the transcriptional activator gene product.

5 16. The method-use of any one of claims 1 to 15 wherein the activity of the gene product encoded by the first viral vector is activatable by an exogenous agent.

10 17. The method-use of claim 16 ~~further comprising administering wherein~~ the exogenous agent is to be administered to the mammal.

18. The method-use of any one of claims 1 to 17 wherein the gene product encoded by the first viral vector prevents or inhibits one or more symptoms of a neurological disease or disorder.

15 19. The method-use of any one of claims 1 to 18 wherein the administration of the two viral vectors to the mammal is separated by at least 24 hours.

20 20. The method-use of any one of claims 1 to 19 wherein the first viral vector is to be targeted to the striatum.

21. The method-use of any one of claims 1 to 20 wherein the second viral vector is to be targeted to the substantia nigra.

25 22. The method-use of any one of claims 1 to 19 wherein the second viral vector is to be targeted to the striatum.

23. The method-use of any one of claims 1 to 19 or 22 wherein the first viral vector is to be targeted to the substantia nigra.

30 24. The method-use of any one of claims 1 to 19 wherein the first viral vector is to be targeted to the ventral tegmental area.

25. The method-use of any one of claims 1 to 19 or 24 wherein the second viral vector is to be targeted to the nucleus accumbent or the medial prefrontal cortex.
- 5 26. The method-use of any one of claims 1 to 19 wherein the second viral vector is to be targeted to the ventral tegmental area.
27. The method-use of any one of claims 1 to 19 or 26 wherein the first viral vector is to be targeted to the nucleus accumbent or the medial prefrontal cortex.
- 10 28. The method-use of any one of claims 1 to 19 wherein the first viral vector is to be targeted to the periaqueductal gray.
29. The method-use of any one of claims 1 to 19 or 28 wherein the second
- 15 viral vector is to be targeted to the nucleus ambiguus.
30. The method-use of any one of claims 1 to 19 wherein the second viral vector is to be targeted to the periaqueductal gray.
- 20 31. The method-use of any one of claims 1 to 19 or 30 wherein the first viral vector is to be targeted to the nucleus ambiguus.
32. The method-use of any one of claims 1 to 23 wherein expression of the conditionally activatable gene or gene product in the mammal prevents, inhibits
- 25 or treats one or more symptoms of Parkinson's disease.
33. The method-use of any one of claims 1 to 23 wherein the first viral vector encodes a G-protein coupled receptor.
- 30 34. The method-use of any one of claims 24 to 27 wherein expression of the conditionally activatable gene or gene product in the mammal inhibits or treats depression or drug addiction.

35. The method-use of any one of claims 28 to 31 wherein expression of the conditionally activatable gene or gene product in the mammal prevents, inhibits or treats speech or swallowing dysfunction.

5 36. The method-use of any one of claims 1 to 35 wherein the mammal is a human.

37. Use of an amount of a composition comprising a viral vector comprising a conditionally activatable gene or gene product, in the manufacture of a medicament ~~A method~~ for targeting a specific population of mammalian neurons for activatable expression of a gene product in the central nervous system of a mammal, ~~comprising administering to a mammal an amount of a composition comprising a viral vector comprising a conditionally activatable gene or gene product,~~ wherein the mammal comprises a vector comprising an open reading
10 frame for expressing a gene, the product of which activates the gene in the viral vector, wherein the amount is effective to -allow for expression of the gene or
15 gene product in the viral vector in the specific population of neurons in the mammal.

20 38. Use of an amount of a composition comprising a viral vector comprising an open reading frame for a gene, the product of which activates a conditionally activatable gene or gene product, in the manufacture of a medicament ~~A method~~ for targeting a specific population of mammalian neurons for activatable expression of a gene product in the central nervous system of a mammal,
25 ~~comprising administering to the mammal an amount of a composition comprising a viral vector comprising an open reading frame for a gene, the product of which activates a conditionally activatable gene or gene product,~~ wherein the mammal comprises a vector comprising the conditionally activatable gene or gene product, wherein the amount is effective to -allow for
30 expression of the gene or gene product in the viral vector in the specific population of neurons in the mammal.

39. Use of a first viral vector comprising a conditionally activatable gene or gene product and a second viral vector comprising an open reading frame for

expressing a gene, the product of which activates the gene in the viral vector, in the manufacture of a medicament for preventing, inhibiting or treating one or more symptoms of a neurological disease, ~~the product of which activates the gene in the viral vector, to prevent, inhibit or treat one or more symptoms of a neurological disease.~~

40. Use of a first viral vector in the manufacture of a first medicament and use of a second viral vector in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination to target a specific population of mammalian neurons for activatable expression of a gene product in the central nervous system of a mammal, wherein the first viral vector comprises a conditionally activatable gene or gene product, and wherein the second viral vector comprises an open reading frame for expressing a gene product which activates the gene in or gene product of the first viral vector, in the manufacture of a medicament for targeting a specific population of mammalian neurons for activatable expression of a gene product in the central nervous system of a mammal.