

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
5 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 for targeting a specific population of mammalian neurons for activatable expression of a gene product in the central nervous system of a mammal, wherein the amount of the second
10 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 use of claim 1 wherein the first viral vector is to be systemically
15 administered and focused ultrasound is to be employed to target the specific population of neurons.
3. The use of claim 1 wherein the first viral vector is to be locally
20 administered.
4. The 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.
- 25 5. The use of any one of claims 1 to 3 wherein the second viral vector is to be locally administered.
6. The use of any one of claims 1 to 5 wherein the first viral vector is a retrograde viral vector.
30
7. The use of any one of claims 1 to 5 wherein the second viral vector is a retrograde viral vector.

8. The use of any one of claims 1 to 7 wherein the first viral vector is to be administered before the second vector.
9. The use of any one of claims 1 to 7 wherein the second viral vector is to be administered before the first vector.
10. The 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 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 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 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 use of claim 13 wherein the recombinase comprises Cre, PhiC31 or Flp.
15. The 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.

16. The 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.
17. The use of claim 16 wherein the exogenous agent is to be administered to the mammal.
18. The 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.
19. The 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. The use of any one of claims 1 to 19 wherein the first viral vector is to be targeted to the striatum.
21. The use of any one of claims 1 to 20 wherein the second viral vector is to be targeted to the substantia nigra.
22. The use of any one of claims 1 to 19 wherein the second viral vector is to be targeted to the striatum.
23. The use of any one of claims 1 to 19 or 22 wherein the first viral vector is to be targeted to the substantia nigra.
24. The 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 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.
26. The 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 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.
28. The use of any one of claims 1 to 19 wherein the first viral vector is to be
5 targeted to the periaqueductal gray.
29. The use of any one of claims 1 to 19 or 28 wherein the second viral vector is to be targeted to the nucleus ambiguus.
- 10 30. The use of any one of claims 1 to 19 wherein the second viral vector is to be targeted to the periaqueductal gray.
31. The use of any one of claims 1 to 19 or 30 wherein the first viral vector is to be targeted to the nucleus ambiguus.
- 15 32. The use of any one of claims 1 to 23 wherein expression of the conditionally activatable gene or gene product in the mammal prevents, inhibits or treats one or more symptoms of Parkinson's disease.
- 20 33. The use of any one of claims 1 to 23 wherein the first viral vector encodes a G-protein coupled receptor.
34. The 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
25 depression or drug addiction.
35. The 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.
- 30 36. The 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 for targeting a specific population of mammalian neurons for
activatable expression of a gene product in the central nervous system of a
mammal, wherein the mammal comprises a vector comprising an open reading
frame for expressing a gene, the product of which activates the gene in the viral
5 vector, wherein the amount is effective to allow for expression of the gene or
gene product in the viral vector in the specific population of neurons in the
mammal.

38. Use of an amount of a composition comprising a viral vector comprising
10 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 for
targeting a specific population of mammalian neurons for activatable expression
of a gene product in the central nervous system of a mammal, wherein the
mammal comprises a vector comprising the conditionally activatable gene or
15 gene product, wherein the amount is effective to allow for 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
20 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.

25 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
30 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.