

CLAIMS:

1. An adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6, where the
5 hNeuroD1 sequence is operably linked to regulatory elements comprising:
 - (a) a glial fibrillary acidic protein (GFAP) promoter comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 12, and 15;
 - (b) an enhancer from a human elongation factor-1 alpha (EF1- α) promoter comprising the nucleic acid sequence of SEQ ID NO: 2 or a cytomegalovirus (CMV) enhancer
10 comprising the nucleic acid sequence of SEQ ID NO: 11;
 - (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or 16;
 - (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence selected from the group consisting of SEQ ID NOs: 7 and 18; and
 - 15 (e) a SV40 polyadenylation signal sequence comprising the nucleic acid sequence of SEQ ID NO: 8, a hGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 13, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 14.
2. An adeno-associated virus (AAV) vector comprising a nucleic acid coding sequence
20 encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid sequence of SEQ ID NO: 10, wherein said coding sequence is operably linked to regulatory elements comprising:
 - (a) a glial fibrillary acidic protein (GFAP) promoter comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 12, and 15;
 - 25 (b) an enhancer from a human elongation factor-1 alpha (EF1- α) promoter comprising the nucleic acid sequence of SEQ ID NO: 2 or a cytomegalovirus (CMV) enhancer comprising the nucleic acid sequence of SEQ ID NO: 11;
 - (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or 16;

- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence selected from the group consisting of SEQ ID NOs: 7 and 18; and
- (e) a SV40 polyadenylation signal sequence with a nucleic acid sequence of SEQ ID NO: 8, a hGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 13, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 14.
- 5
3. An adeno-associated virus (AAV) vector comprising a neurogenic differentiation 1 (NeuroD1) nucleic acid coding sequence encoding a NeuroD1 protein, wherein said coding sequence is operably linked to regulatory elements comprising:
- 10
- (a) a glial fibrillary acidic protein (GFAP) promoter;
- (b) an enhancer;
- (c) a chimeric intron;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE); and
- 15
- (e) a polyadenylation signal sequence.
4. A-Use of a composition comprising an adeno-associated virus (AAV) vector in the manufacture of a medicament for converting glial cells to functional neurons in a human, wherein said AAV vector comprises a human neurogenic differentiation 1 (hNeuroD1) sequence having a nucleic acid sequence of SEQ ID NO: 6, and wherein said sequence is operably linked to regulatory elements comprising:
- 20
- (a) a human glial fibrillary acidic protein (GFAP) promoter comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 12, and 15;
- (b) an enhancer from the human elongation factor-1 alpha (EF-1 alpha) promoter comprising the nucleic acid sequence of SEQ ID NO: 2 or a cytomegalovirus (CMV) enhancer comprising the nucleic acid sequence of SEQ ID NO: 11;
- 25
- (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or 16;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence selected from the group consisting of SEQ ID NOs: 7 and 18; and

(e) a SV40 polyadenylation signal sequence comprising the nucleic acid sequence of SEQ ID NO: 8, a hGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 13, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 14.

5 5. A-Use of a composition comprising an adeno-associated-virus (AAV) vector in the
manufacture of a medicament for converting glial cells to functional neurons in a human,
wherein said AAV vector comprises a nucleic acid sequence encoding a human
neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding
sequence of SEQ ID NO: 10, and wherein said coding sequence is operably linked to
10 regulatory elements comprising:

(a) a human glial fibrillary acidic protein (GFAP) promoter comprising a nucleic acid
sequence selected from the group consisting of SEQ ID NOs: 4, 12, and 15;

(b) an enhancer from the human elongation factor-1 alpha (EF-1 alpha) promoter
comprising the nucleic acid sequence of SEQ ID NO: 2 or a cytomegalovirus

15 (CMV) enhancer comprising the nucleic acid sequence of SEQ ID NO: 11;

(c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or 16;

(d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE)
comprising the nucleic acid sequence selected from the group consisting of SEQ
ID NOs: 7 and 18; and

20 (e) a SV40 polyadenylation signal sequence comprising the nucleic acid sequence of
SEQ ID NO: 8, a hGH polyadenylation sequence comprising the nucleic acid
sequence of SEQ ID NO: 13, or a bGH polyadenylation sequence comprising the
nucleic acid sequence of SEQ ID NO: 14.

25 6. A-Use of a composition comprising an adeno-associated virus (AAV) vector in the
manufacture of a medicament for the treatment of a neurological condition in a subject in
need thereof, wherein said AAV vector comprises a neurogenic differentiation 1
(NeuroD1) sequence operably linked to expression control elements comprising:

(a) a glial fibrillary acidic protein (GFAP) promoter;

(b) an enhancer;

30 (c) a chimeric intron;

- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE); and
- (e) a polyadenylation signal.

7. The AAV vector of any one of claims 1-3, or the ~~composition~~use of any one of claims 4-6, wherein said AAV vector is selected from the group consisting of AAV serotype 2, AAV serotype 5, and AAV serotype 9.

8. The AAV vector or ~~use composition~~ of claim 7, wherein said AAV vector is AAV serotype 2.

9. The AAV vector or ~~use composition~~ of claim 7, wherein said AAV vector is AAV serotype 5.

10. The AAV vector or ~~use composition~~ of claim 7, wherein said AAV vector is AAV serotype 9.

11. The ~~use composition~~ of claim 4 or 5, wherein said glial cells are reactive astrocytes.

12. The ~~use composition~~ of claim 4 or 5, wherein said functional neurons are selected from the group consisting of glutamatergic neurons, GABAergic neurons, dopaminergic neurons, cholinergic neurons, serotonergic neurons, epinephrinergic neurons, motor neurons, and peptidergic neurons.

13. The ~~use composition~~ of claim 4 or 5, wherein said human has a neurological condition.

14. The AAV vector of claim 3, or the ~~use composition~~ of claim 6, wherein said NeuroD1 is a human NeuroD1 (hNeuroD1).

15. The AAV vector of claim 3, or the ~~use composition~~ of claim 6, wherein said NeuroD1 is selected from the group consisting of a chimpanzee NeuroD1, a bonobo NeuroD1, an orangutan NeuroD1, a gorilla NeuroD1, a macaque NeuroD1, a marmoset NeuroD1, a capuchin NeuroD1, a baboon NeuroD1, a gibbon NeuroD1, and a lemur NeuroD1.

16. The AAV vector ~~or composition~~ of claim 14, wherein said hNeuroD1 comprises a nucleic acid coding sequence encoding an amino acid sequence at least 80% identical or similar to SEQ ID NO: 10.
17. The AAV vector ~~or composition~~ of claim 14, wherein said hNeuroD1 sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 6, or the complement thereof.
18. The AAV vector of claim 3, or the use composition of claim 6, wherein said GFAP promoter is a human GFAP (hGFAP) promoter.
19. The AAV vector of claim 3, or the ~~composition~~ use of claim 6, wherein said GFAP promoter is selected from the group consisting of a chimpanzee GFAP promoter, a bonobo GFAP promoter, an orangutan GFAP promoter, a gorilla GFAP promoter, a macaque GFAP promoter, a marmoset GFAP promoter, a capuchin GFAP promoter, a baboon GFAP promoter, a gibbon GFAP promoter, and a lemur GFAP promoter.
20. The AAV vector of any one of claims 1-3 or ~~composition the use~~ of any one of ~~the preceding~~ claims 4-6, wherein the AAV vector further comprises a 2A self-cleavage peptide sequence at least 80% identical to SEQ ID NO: 3 or the complement thereof.
21. The AAV vector or ~~composition~~ use of claim 18, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 4 or the complement thereof.
22. The AAV vector or use composition of claim 18, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 12 or the complement thereof.
23. The AAV vector or use composition of claim 18, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 15 or the complement thereof.

24. The AAV vector of claim 3, or the use composition of claim 6, wherein said enhancer is selected from the group consisting of an enhancer from human elongation factor-1 alpha (EF1- α) promoter and cytomegalovirus (CMV) enhancer.

25. The AAV vector or use composition of claim 24, wherein said EF1- α comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 2, or the complement thereof.

26. The AAV vector or use composition of claim 24, wherein said CMV enhancer comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 11, or the complement thereof.

27. The AAV vector of claim 3, or the use composition of claim 6, wherein said chimeric intron comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 5 or the complement thereof.

28. The AAV vector of claim 3, or the use composition of claim 6, wherein said chimeric intron comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 16 or the complement thereof.

29. The AAV vector of claim 3, or the use composition of claim 6, wherein said WPRE comprises a nucleic acid sequence at least 80% identical to a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 7 and 18, or the complement thereof.

30. The AAV vector of claim 3, or the use composition of claim 6, wherein said polyadenylation ~~polyadenylated~~ signal is selected from the group consisting of SV40 polyadenylation signal and a hGH polyadenylation signal.

31. The AAV vector or use composition of claim 30, wherein said SV40 polyadenylation ~~polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 8, or the complement thereof.

32. The AAV vector or ~~use composition~~ of claim 30, wherein said hGH polyadenylation
~~polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ
ID NO: 13, or the complement thereof.
33. The AAV vector or ~~use composition~~ of claim 30, wherein said bGH polyadenylation
~~polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ
ID NO: 14, or the complement thereof.
34. The AAV vector of claim 3, or the ~~use composition~~ of claim 6, wherein said AAV vector
further comprises a nucleic acid sequence encoding an AAV protein sequence.
35. The AAV vector of any one of claims 1-3, or the ~~use composition~~ of any one of claims 4-
6, wherein said AAV vector comprises AAV serotype 2 inverted terminal repeats (ITRs).
36. The AAV vector of any one of claims 1-3, or the ~~use composition~~ of any one of claims 4-
6, wherein said AAV vector comprises AAV serotype 5 inverted terminal repeats (ITRs).
37. The AAV vector of any one of claims 1-3, or the ~~use composition~~ of any one of claims 4-
6, wherein said AAV vector comprises AAV serotype 9 inverted terminal repeats (ITRs).
38. The AAV vector of any one of claims 1-3, or the ~~use composition~~ of any one of claims 4-
6, wherein said AAV vector comprises at least one ITR nucleic acid sequence at least
80% identical to SEQ ID NO: 1.
39. The AAV vector of any one of claims 1-3, or the ~~use composition~~ of any one of claims 4-
6, wherein said AAV vector comprises at least one ITR nucleic acid sequence at least
80% identical to SEQ ID NO: 9.
40. The ~~use composition~~ of claim 6, wherein said subject in need thereof is a mammal.
41. The ~~use composition~~ of claim 40, wherein said mammal is a human.
42. The ~~use composition~~ of claim 40, wherein said mammal is a non-human primate.
43. The ~~use composition~~ of claim 6, wherein said subject in need thereof has a neurological
condition.

44. The ~~use composition~~ of claim 13-~~or 43~~, wherein said neurological condition comprises an injury to the central nervous system (CNS) or peripheral nervous system.

45. The ~~use composition~~ of claim 13-~~or 43~~, wherein said wherein said neurological condition comprises an injury to the CNS.

5 46. The ~~use composition~~ of claim 13-~~or 43~~, wherein said neurological condition is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, amyotrophic lateral sclerosis (ALS), Huntington's Disease, epilepsy, physical injury, stroke, cerebral aneurysm, traumatic brain injury, concussion, a tumor, inflammation, infection, ataxia, brain atrophy, spinal cord atrophy, multiple sclerosis, traumatic spinal cord injury, 10 ischemic or hemorrhagic myelopathy (myelopathy), global ischemia, hypoxic ischemic encephalopathy, embolism, fibrocartilage embolism myelopathy, thrombosis, nephropathy, chronic inflammatory disease, meningitis, and cerebral venous sinus thrombosis.

15 47. The ~~use composition~~ of claim 13-~~or 43~~, wherein said neurological condition is Alzheimer's Disease.

48. The ~~use composition~~ of claim 13-~~or 43~~, wherein said neurological condition is Parkinson's Disease.

49. The ~~use composition~~ of claim 13-~~or 43~~, wherein said neurological condition is ALS.

20 50. The ~~use composition~~ of claim 13-~~or 43~~, wherein said neurological condition is Huntington's Disease.

51. The ~~use composition~~ of claim 13-~~or 43~~, wherein said neurological condition is a stroke.

52. The ~~use composition~~ of claim 51, wherein said stroke is an ischemic stroke.

53. The ~~use composition~~ of claim 51, wherein said stroke is a hemorrhagic stroke.

25 54. The ~~use composition~~ of claim 43, wherein said composition is capable of converting at least one glial cell to a neuron.

55. The ~~use composition~~ of claim 54, wherein said glial cells are selected from the group consisting of astrocytes and NG2 cells.

56. The ~~use composition~~ of claim 54, wherein said glial cells are astrocytes.

57. The ~~use composition~~ of claim 56, wherein said astrocytes are reactive astrocytes.

58. The ~~use composition~~ of claim 54, wherein said glial cells are GFAP positive.

59. The ~~use composition~~ of claim 54, wherein said neurons are functional neurons.

60. The ~~use composition~~ of claim 54, wherein said functional neurons are selected from the group consisting of glutamatergic neurons, GABAergic neurons, dopaminergic neurons, cholinergic neurons, serotonergic neurons, epinephrinergic neurons, motor neurons, and peptidergic neurons..

61. The ~~use composition~~ of claim 60, wherein said functional neurons are glutamatergic neurons.

62. The ~~use composition~~ of claim 6, wherein said composition is formulated to be delivered to a subject in need thereof.

63. The ~~use composition~~ of claim 62, wherein said composition is formulated for local delivery.

64. The ~~use composition~~ of claim 62, wherein said composition is formulated for systemic delivery.

65. The ~~use composition~~ of any one of claims 62-64, wherein said composition is formulated for delivery via intraperitoneal, intramuscular, intravenous, intrathecal, intracerebral, intracranial, intra lateral ventricle of the brain, intra cisterna magna, intra vitreous, intra-subretina, intraparenchymal, intranasal, or oral administration.

~~66. A method comprising delivering the composition of claim 6 to said subject in need thereof.~~

67. ~~The method of claim 66, wherein said composition is formulated to be delivered to a subject in need thereof.~~

68. ~~The method of claim 66, wherein said delivering comprises local administration.~~

69. ~~The method of claim 66, wherein said delivering comprises systemic administration.~~

70. ~~The method of any one of claims 66-69, wherein said delivering comprises an intraperitoneal, intramuscular, intravenous, intrathecal, intracerebral, intracranial, intra lateral ventricle of the brain, intra cisterna magna, intra vitreous, intra subretina, intraparenchymal, intranasal, or oral administration.~~

66. The use of claim 4 or 5, wherein the converting glial cells to functional neurons in a human occurs in a brain of a living human.

71. ~~A method of converting reactive astrocytes to functional neurons in a brain of a living human comprising: injecting an adeno-associated virus (AAV) into a subject in need thereof, wherein said AAV comprises a DNA vector construct comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6, wherein said sequence is operably linked to regulatory elements comprising:~~

(a) ~~a human glial fibrillary acid protein (GFAP) promoter comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 12, and 15;~~

(b) ~~an enhancer from the human elongation factor 1 alpha (EF 1 alpha) promoter comprising the nucleic acid sequence of SEQ ID NO: 2 or a cytomegalovirus (CMV) enhancer comprising the nucleic acid sequence of SEQ ID NO: 11;~~

(c) ~~a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or 16;~~

(d) ~~a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence selected from the group consisting of SEQ ID NOs: 7 and 18; and~~

~~a SV40 polyadenylation signal sequence comprising the nucleic acid sequence of SEQ ID NO: 8, a hGH polyadenylation sequence comprising the nucleic acid~~

~~sequence of SEQ ID NO: 13, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 14.~~

~~72.67. Use of a composition in the manufacture of a medicament for~~A method of

converting reactive astrocytes to functional neurons in a brain of a living human, the composition comprising: ~~injecting~~ an adeno-associated virus (AAV) ~~into a subject in need thereof, wherein said AAV comprises~~comprising a DNA vector construct comprising a nucleic acid sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding sequence of SEQ ID NO: 10, wherein said coding sequence is operably linked to expression control elements comprising:

- (a) a human glial fibrillary acid protein (GFAP) promoter comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 12, and 15;
- (b) an enhancer from the human elongation factor-1 alpha (EF-1 alpha) promoter comprising the nucleic acid sequence of SEQ ID NO: 2 or a cytomegalovirus (CMV) enhancer comprising the nucleic acid sequence of SEQ ID NO: 11;
- (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or 16;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence selected from the group consisting of SEQ ID NOs: 7 and 18; and

- (e) a SV40 polyadenylation signal sequence comprising the nucleic acid sequence of SEQ ID NO: 8, a hGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 13, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 14,

wherein the composition is to be injected into said brain of a living human.

~~73. A method of converting glial cells to neurons in a subject in need thereof comprising:~~

~~delivering an adeno-associated virus (AAV) to said subject in need thereof, wherein said AAV comprises a DNA vector construct comprising a neurogenic differentiation 1 (NeuroD1) sequence operably linked to expression control elements comprising:~~

- ~~(a) a glial fibrillary acid protein (GFAP) promoter;~~
- ~~(b) an enhancer;~~

(c) a chimeric intron;
(d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE); and
(e) and a polyadenylation signal sequence,
wherein said vector is capable of converting at least one glial cell to a neuron in said
subject in need thereof.

74.68. A ~~composition a method of treating a neurological condition in a subject in need thereof~~ comprising: ~~delivering~~ an adeno-associated virus (AAV) ~~to said subject, wherein said AAV comprises~~ comprising a DNA vector construct comprising a neurogenic differentiation 1 (NeuroD1) sequence operably linked to expression control elements comprising:

- (a) a glial fibrillary acid protein (GFAP) promoter;
- (b) an enhancer;
- (c) a chimeric intron;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE); and
- (e) a polyadenylation signal.

~~wherein said composition is to be delivered to said subject in need thereof to said subject in need thereof.~~

75.69. The ~~use of claim 67 or the composition of claim 68~~ ~~method of any one of claims 71-74~~, wherein said AAV is selected from the group consisting of AAV serotype 2, AAV serotype 5, and AAV serotype 9.

76.70. The ~~use or composition~~ ~~method~~ of claim 7569, wherein said AAV is AAV serotype 2.

77.71. The ~~use or composition~~ ~~method~~ of claim 7569, wherein said AAV is AAV serotype 5.

78.72. The ~~use or composition~~ ~~method~~ of claim 7569, wherein said AAV is AAV serotype 9.

79:73. The ~~use method~~ of claims ~~67 71 or 72~~, wherein said functional neurons are glutamatergic neurons, GABAergic neurons, dopaminergic neurons, cholinergic neurons, serotonergic neurons, epinephrinergic neurons, motor neurons, and peptidergic neurons.

80:74. The ~~method composition~~ of claims ~~6873 or 74~~, wherein said NeuroD1 is human NeuroD1 (hNeuroD1).

81:75. The ~~composition method~~ of claims ~~6873 or 74~~, wherein said NeuroD1 is selected from the group consisting of a chimpanzee NeuroD1, a bonobo NeuroD1, an orangutan NeuroD1, a gorilla NeuroD1, a macaque NeuroD1, a marmoset NeuroD1, a capuchin NeuroD1, a baboon NeuroD1, a gibbon NeuroD1, and a lemur NeuroD1.

82:76. The ~~composition method~~ of claim ~~7480~~, wherein said hNeuroD1 comprises a amino acid sequence encoding an amino acid coding sequence at least 80% identical or similar to SEQ ID NO: 10.

83:77. The ~~composition method~~ of claim ~~7480~~, wherein said hNeuroD1 sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 6, or the complement thereof.

84:78. The ~~composition method~~ of claims ~~6873 or 74~~, wherein said GFAP promoter is a human GFAP (hGFAP) promoter.

85:79. The ~~composition method~~ of claims ~~6873 or 74~~, wherein said GFAP promoter is selected from the group consisting of a chimpanzee GFAP promoter, a bonobo GFAP promoter, an orangutan GFAP promoter, a gorilla GFAP promoter, a macaque GFAP promoter, a marmoset GFAP promoter, a capuchin GFAP promoter, a baboon GFAP promoter, a gibbon GFAP promoter, and a lemur GFAP promoter.

86:80. The ~~use of any one of claims 67 or 69 to 73, or the composition method~~ of any one of claims ~~68 to 72 or 75 to 7971-85~~, wherein the DNA vector construct further comprises a 2A self-cleavage peptide sequence at least 80% identical to SEQ ID NO: 3 or the complement thereof.

87.81. The composition method of claim 7884, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 4, or the complement thereof.

88.82. The composition method of claim 7884, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 12, or the complement thereof.

89.83. The composition method of claim 7884, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 15, or the complement thereof.

90.84. The composition method of claims 6873 or 74, wherein said enhancer is selected from the group consisting of an enhancer from human elongation factor-1 alpha (EF1- α) promoter and cytomegalovirus (CMV) enhancer.

91.85. The composition method of claim 8490, wherein said EF1- α comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 2, or the complement thereof.

92.86. The composition method of claim 8490 wherein said CMV enhancer comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 11, or the complement thereof.

93.87. The composition method of claims 6873 or 74, wherein said chimeric intron comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 5, or the complement thereof.

94.88. The composition method of claims 73 or 7468, wherein said chimeric intron comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 16, or the complement thereof.

95.89. The composition method of claims 73 or 7468, wherein said WPRE comprises a nucleic acid sequence at least 80% identical to a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 7 and 18, or the complement thereof.

96:90. The ~~composition method~~ of claims ~~73 or 7468~~, wherein said polyadenylation
~~polyadenylated~~ signal is selected from the group consisting of SV40 polyadenylation
signal, a hGH polyadenylation signal, and a bGH polyadenylation signal.

5 97:91. The ~~composition method~~ of claims ~~73 or 7468~~, wherein said SV40
polyadenylation ~~polyadenylated~~ signal comprises a nucleic acid sequence at least 80%
identical to SEQ ID NO: 8, or the complement thereof.

98:92. The ~~composition method~~ of claims ~~73 or 7468~~, wherein said hGH polyadenylation
~~polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ
ID NO: 13, or the complement thereof.

10 99:93. The ~~composition method~~ of claims ~~73 or 7468~~, wherein said bGH polyadenylation
~~polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ
ID NO: 14, or the complement thereof.

100:94. The ~~composition method~~ of claims ~~73 or 7468~~, wherein said vector further
comprises a nucleic acid sequence encoding an AAV protein sequence.

15 101:95. The ~~use of claim 67 or the composition method of any one~~ of claims ~~71-7468~~,
wherein said vector comprises AAV serotype 2 inverted terminal repeats (ITRs).

102:96. The ~~use of claim 67 or the composition method of any one~~ of claims ~~6871-74~~,
wherein said vector comprises AAV serotype 5 inverted terminal repeats (ITRs).

20 103:97. The ~~use of claim 67 or the composition method of any one~~ of claims ~~6871-74~~,
wherein said vector comprises AAV serotype 9 inverted terminal repeats (ITRs).

104:98. The ~~use of claim 67 or the composition method of any one of~~ claims ~~6871-74~~,
wherein said vector comprises at least one ITR nucleic acid sequence at least 80%
identical to SEQ ID NO: 1.

25 105:99. The ~~use of claim 67 or the composition method of any one of~~ claims ~~6871-74~~,
wherein said vector comprises at least one ITR nucleic acid sequence at least 80%
identical to SEQ ID NO: 9.

~~106. The method of claim 71, wherein said converting occurs in the central nervous system (CNS) or peripheral nervous system.~~

~~107. The method of claim 73, wherein said converting occurs in the CNS.~~

100108. The ~~method~~composition of claim ~~73 or 7468~~, wherein said subject in need thereof is a mammal.

101109. The ~~composition~~method of claim 100108, wherein said mammal is a human.

102110. The ~~composition~~method of claim 100108, wherein said mammal is a non-human primate.

103111. The ~~composition~~method of claim ~~73 or 7468~~, wherein said delivering comprises a local administration.

104112. The ~~composition~~method of claim ~~73 or 7468~~, wherein said delivering comprises systemic administration.

105113. The ~~composition~~method of claim ~~73 or 7468~~, wherein said delivering comprises an administration selected from the group consisting of an intraperitoneal administration, intramuscular administration, intravenous administration, intrathecal administration, intracerebral administration, intracranial, intra lateral ventricle of the brain, intra cisterna magna, intra vitreous, intra-subretina, intraparenchymal administration, intranasal administration, and oral administration.

106114. The ~~method~~use of claim ~~71 or 7267~~, wherein said injecting comprises an injection selected from the group consisting of an intraperitoneal injection, intramuscular injection, intravenous injection, intrathecal injection, intracerebral injection, intracranial, intra lateral ventricle of the brain, intra cisterna magna, intra vitreous, intra-subretina, intraparenchymal injection, intranasal injection, and oral injection.

107115. The ~~composition~~method of claims ~~73 or 7468~~, wherein said delivering comprises injecting.

108116. The ~~method-use~~ of ~~any one of~~ claims ~~6771, 72, or 115~~, wherein said injecting is performed at a concentration of between 10^{10} particles/mL and 10^{14} particles/mL.

109117. The ~~composition method~~ of claim ~~116108~~, wherein said injecting further comprises a flow rate of between 0.1 $\mu\text{L}/\text{min}$ and 5.0 $\mu\text{L}/\text{min}$.

~~118. The method of claim 73, wherein said at least one glial cell is selected from the group consisting of at least one astrocyte and at least one NG2 cell.~~

~~119. The method of claim 71, wherein said at least one glial cell is at least one astrocyte.~~

~~120. The method of claim 118 or 119, wherein said at least one astrocyte is a reactive astrocyte.~~

~~121. The method of claim 73, wherein said neuron is a functional neuron.~~

~~122. The method of any one of claims 71, 72, and 121, wherein said functional neurons are selected from the group consisting of glutamatergic neurons, GABAergic neurons, dopaminergic neurons, cholinergic neurons, serotonergic neurons, epinephrinergic neurons, motor neurons, and peptidergic neurons.~~

~~123. The method of claim 73, wherein said subject exhibits an improvement of at least one neurological condition symptom as compared to said subject prior to said delivering.~~

~~124. The method of claim 123, wherein said improvement is measured within 1 year of said delivering.~~

110125. The ~~method of any one use~~ of claims ~~71, 72, or 115~~ 67, or the ~~composition of claim 107~~, wherein said ~~method comprises directly injecting said AAV~~ is to be directly injected into the brain of said subject.

111126. The ~~method of any one use~~ of claims ~~71 or 72~~ 67, wherein said converting is in the cerebral cortex of said brain.

112127. The ~~method of any one use~~ of claims ~~71, 72, or 115~~ 67, or the composition of claim 107, wherein said ~~method comprises directly injecting said~~ AAV is to be directly injected into the spinal cord of said subject.

113128. The ~~composition method~~ of claim 6874, wherein said neurological condition comprises an injury to the central nervous system (CNS) or peripheral nervous system.

114129. The ~~composition method~~ of claim 6874, wherein said neurological condition is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, amyotrophic lateral sclerosis (ALS), Huntington's Disease, epilepsy, physical injury, stroke, cerebral aneurysm, traumatic brain injury, concussion, a tumor, inflammation, infection, ataxia, brain atrophy, spinal cord atrophy, multiple sclerosis, traumatic spinal cord injury, ischemic or hemorrhagic myelopathy (myelopathy), global ischemia, hypoxic ischemic encephalopathy, embolism, fibrocartilage embolism myelopathy, thrombosis, nephropathy, chronic inflammatory disease, meningitis, and cerebral venous sinus thrombosis.

115130. The ~~composition method~~ of claim 6874, wherein said neurological condition is Alzheimer's Disease.

116131. The ~~composition method~~ of claim 6874, wherein said neurological condition is Parkinson's Disease.

117132. The ~~composition method~~ of claim 6874, wherein said neurological condition is ALS.

118133. The ~~composition method~~ of claim 6874, wherein said neurological condition is Huntington's Disease.

119134. The ~~composition method~~ of claim 6874, wherein said neurological condition is a stroke.

120135. The ~~composition method~~ of claim 119134, wherein said stroke is an ischemic stroke.

121136. The ~~composition method~~ of claim 119134, wherein said stroke is a hemorrhagic stroke.

122137. The ~~composition method~~ of claim 6874, wherein said ~~composition method~~ is capable of converting at least one glial cell into a neuron.

5 123138. The ~~composition method~~ of claim 122137, wherein said glial cells are selected from the group consisting of astrocytes and NG2 cells.

124139. The ~~composition method~~ of claim 122137, wherein said glial cells are astrocytes.

125140. The ~~composition method~~ of claim 124139, wherein said astrocytes are reactive astrocytes.

10 126141. The ~~composition method~~ of claim 122137, wherein said glial cells are GFAP positive.

127142. The ~~composition method~~ of claim 122137, wherein said neurons are functional neurons.

15 128143. The ~~composition method~~ of claim 127142, wherein said functional neurons are selected from the group consisting of glutamatergic neurons, GABAergic neurons, dopaminergic neurons, cholinergic neurons, serotonergic neurons, epinephrinergic neurons, motor neurons, and peptidergic neurons.-

129144. The ~~method use~~ of claims ~~71 or 72~~ 67, wherein a therapeutically effective dose of said AAV vector is to be injected into said subject.

20 130145. The ~~composition method~~ of claims ~~73 or 74~~ 68, wherein a therapeutically effective dose of said AAV vector is to be delivered to said subject.

131146. The ~~use method~~ of claim ~~144 or 145~~ 129, wherein said therapeutically effective dose is to be administered with a pharmaceutically acceptable carrier.

25 132. The composition of claim 130, wherein said therapeutically effective dose is to be administered with a pharmaceutically acceptable carrier.

133147. An adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6, where the hNeuroD1 sequence is operably linked to regulatory elements comprising:

a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 15;

an enhancer from a human elongation factor-1 alpha (EF1- α) promoter comprising the nucleic acid sequence of SEQ ID NO: 2;

a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 16;

a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 18; and

a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 14.

134148. An adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6, where the hNeuroD1 sequence is operably linked to regulatory elements comprising:

a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 15;

a cytomegalovirus (CMV) enhancer comprising the nucleic acid sequence of SEQ ID NO: 11;

a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 16;

a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 18; and

a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 14.