

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 and a human distal-less homeobox 2 (hDlx2) sequence comprising the nucleic acid sequence of SEQ ID NO: 13, wherein said hNeuroD1 sequence and said hDlx2 sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 sequence and said hDlx2 sequence are 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 26;
 - (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 selected from the group consisting of SEQ ID NOs: 5 and 27;
 - (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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

2. An adeno-associated virus (AAV) vector comprising a nucleic acid sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding sequence of SEQ ID NO: 10 and a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, (iii) or an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 coding sequence and said hDlx2 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 26;
 - (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 selected from the group consisting of SEQ ID NOs: 5 and 27;
 - (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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

3. An adeno-associated virus (AAV) vector comprising a neurogenic differentiation 1 (NeuroD1) nucleic acid coding sequence encoding a NeuroD1 protein and a distal-less homeobox 2 (Dlx2) nucleic acid coding sequence encoding a Dlx2 protein, wherein said NeuroD1 coding sequence and said Dlx2 coding sequence are separated by a linker sequence, wherein said NeuroD1 coding sequence and said Dlx2 coding sequence are operably linked to regulatory elements comprising:
- (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
 - (e) a polyadenylation signal sequence.
4. Use of a A composition comprising an adeno-associated virus (AAV) vector in the preparation of medicine 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 a human distal-less homeobox 2 (hDlx2) sequence having a nucleic acid sequence of SEQ ID NO: 13, wherein said hNeuroD1 sequence and said hDlx2 sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 sequence and hDlx2 sequence are operably linked to 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 26;

- (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 selected from the group consisting of SEQ ID NOs: 5 and 27;
- (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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

5. Use of a A composition comprising an adeno-associated-virus (AAV) vector in the preparation of medicine for converting glial cells to functional neurons in a human, wherein said AAV vector comprises a nucleic acid coding sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid sequence of SEQ ID NO: 10 and a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence are separated by
 - (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence are operably linked to 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 26;
- (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 selected from the group consisting of SEQ ID NOs: 5 and 27;
- (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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

6. Use of aA composition comprising an adeno-associated virus (AAV) vector in the preparation of medicine for the treatment of a subject in need thereof, wherein said AAV vector comprises a neurogenic differentiation 1 (NeuroD1) sequence and a distal-less homeobox 2 (Dlx2) sequence, wherein said NeuroD1 sequence and said Dlx2 sequence are separated by a linker sequence, wherein said NeuroD1 sequence and Dlx2 sequence are operably linked to expression control elements comprising:

- (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

(e) a polyadenylation signal.

7. The AAV vector of any one of claims 0-3, 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 ~~composition~~use of claim 7, wherein said AAV vector is AAV serotype 2.
9. The AAV vector or ~~composition~~use of claim 7, wherein said AAV vector is AAV serotype 5.
10. The AAV vector or ~~composition~~use of claim 7, wherein said AAV vector is AAV serotype 9.
11. The ~~composition~~use of claim 4 or 5, wherein said glial cells are reactive astrocytes.
12. The ~~composition~~use 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 ~~composition~~use of claim 4 or 5, wherein said human has a neurological condition.
14. The AAV vector of claim 3, or the ~~composition~~use of claim 6, wherein said NeuroD1 is a human NeuroD1 (hNeuroD1).
15. The AAV vector of claim 3, or the ~~composition~~use of claim 6, wherein said Dlx2 is a human Dlx2 (hDlx2).
16. The AAV vector of claim 3, or the ~~composition~~use 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.

17. The AAV vector of claim 3, or the ~~composition~~use of claim 6, wherein said Dlx2 is selected from the group consisting of a chimpanzee Dlx2, a bonobo Dlx2, an orangutan Dlx2, a gorilla Dlx2, a macaque Dlx2, a marmoset Dlx2, a capuchin Dlx2, a baboon Dlx2, a gibbon Dlx2, and a lemur Dlx2.
18. The AAV vector or ~~composition~~use of claim 14, wherein said hNeuroD1 comprises a nucleic acid sequence encoding an amino acid sequence at least 80% identical or similar to SEQ ID NO: 10.
19. The AAV vector or composition of claim 15, wherein said hDlx2 comprises a nucleic acid sequence encoding an amino acid sequence at least 80% identical or similar to SEQ ID NO: 14.
20. The AAV vector or composition of claim 14, wherein said hNeuroD1 coding sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 6, or the complement thereof.
21. The AAV vector or composition of claim ~~14~~15, wherein said hDlx2 coding sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 13, or the complement thereof.
22. The AAV vector of claim 3, or the composition of claim 6, wherein said linker is selected from the group consisting of P2A and T2A.
23. The AAV vector or composition of claim 22, wherein said linker is said P2A.
24. The AAV vector or composition of claim 22, wherein said linker is said T2A.
25. The AAV vector or composition of claim 22, wherein said P2A linker comprises a nucleic acid sequence at least 80% identical to the sequence

selected from the group consisting of SEQ ID NO: 15 and 18, or the complement thereof.

26. The AAV vector or composition of claim 22, wherein said T2A linker comprises a nucleic acid sequence at least 80% identical to the sequence selected from the group consisting of SEQ ID NO: 16 and 19, or the complement thereof.
27. The AAV vector of claim 3, or the ~~composition~~use of claim 6, wherein said GFAP promoter is a human GFAP (hGFAP) promoter.
28. 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.
29. The AAV vector of any one of claims 1–3 or ~~composition~~the use of any one of ~~the preceding~~ claims 4–6, wherein said IRES sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 3, or the complement thereof.
30. The AAV vector or composition of claim 27, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 4 or the complement thereof.
31. The AAV vector or composition of claim 27, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 12 or the complement thereof.

32. The AAV vector or composition of claim 27, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 26 or the complement thereof.
33. The AAV vector of claim 3, or the ~~composition-use~~ 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
34. The AAV vector or ~~composition-use~~ of claim 33, wherein said EF1- α comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 2, or the complement thereof.
35. The AAV vector or ~~composition-use~~ of claim 33, wherein said CMV enhancer comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 11, or the complement thereof.
36. The AAV vector of claim 3, or the ~~composition-use~~ of claim 6, wherein said chimeric intron comprises a nucleic acid sequence at least 80% identical to a nucleic acid selected from the group consisting of SEQ ID NOs: 5 and 27, or the complement thereof.
37. The AAV vector of claim 3, or the ~~composition-use~~ of claim 6, wherein said WPRE comprises a nucleic acid sequence at least 80% identical to a nucleic acid selected from the group consisting of SEQ ID NOs: 7 and 29, or the complement thereof.
38. The AAV vector of claim 3, or the ~~composition-use~~ of claim 6, wherein said ~~polyadenylation polyadenylated~~-signal is selected from the group consisting of SV40 polyadenylation signal, a hGH polyadenylation signal, and a bGH polyadenylation signal.

39. The AAV vector or ~~composition~~use of claim 38, wherein said SV40 ~~polyadenylation polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 8, or the complement thereof.
40. The AAV vector or ~~composition~~use of claim 38, wherein said hGH ~~polyadenylation polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 17, or the complement thereof.
41. The AAV vector or ~~composition~~use of claim 38, wherein said bGH ~~polyadenylation polyadenylated~~ signal comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 30, or the complement thereof.
42. The AAV vector of claim 3, or the ~~composition~~use of claim 6, wherein said AAV vector further comprises a nucleic acid sequence encoding an AAV protein sequence.
43. The AAV vector of any one of claims 0-3, or the ~~composition~~use of any one of claims 4-6, wherein said AAV vector comprises AAV serotype 2 inverted terminal repeats (ITRs).
44. The AAV vector of any one of claims 0-3, or the ~~composition~~use of any one of claims 4-6, wherein said AAV vector comprises AAV serotype 5 inverted terminal repeats (ITRs).
45. The AAV vector of any one of claims 0-3, or the ~~composition~~use of any one of claims 4-6, wherein said AAV vector comprises AAV serotype 9 inverted terminal repeats (ITRs).
46. The AAV vector of any one of claims 0-3, or the 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.

47. The AAV vector of any one of claims 0-3, or the ~~composition~~use 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.
48. The ~~composition~~use of claim 6, wherein said subject in need thereof is a mammal.
49. The ~~composition~~use of claim 48, wherein said mammal is a human.
50. The ~~composition~~use of claim 48, wherein said mammal is a non-human primate.
51. The ~~composition~~use of claim 6, wherein said subject in need thereof has a neurological condition.
52. The ~~composition~~use of claim 13-~~or 51~~, wherein said neurological condition comprises an injury to the central nervous system (CNS) or peripheral nervous system.
53. The ~~composition~~use of claim 13-~~or 51~~, wherein said wherein said neurological condition comprises an injury to the CNS.
54. The ~~composition~~use of claim 13-~~or 51~~, 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.

55. The ~~composition~~use of claim 13-~~or 51~~, wherein said neurological condition is Alzheimer's Disease.
56. The ~~composition~~use of claim 13-~~or 51~~, wherein said neurological condition is Parkinson's Disease.
57. The ~~composition~~use of claim 13-~~or 51~~, wherein said neurological condition is ALS.
58. The ~~composition~~use of claim 13-~~or 51~~, wherein said neurological condition is Huntington's Disease.
59. The ~~composition~~use of claim 13-~~or 51~~, wherein said neurological condition is a stroke.
60. The ~~composition~~use of claim 59, wherein said stroke is an ischemic stroke.
61. The ~~composition~~use of claim 59, wherein said stroke is a hemorrhagic stroke.
62. The ~~composition~~use of claim 51, wherein said composition is capable of converting at least one glial cell to a neuron.
63. The ~~composition~~use of claim 62, wherein said glial cells are selected from the group consisting of astrocytes and NG2 cells.
64. The ~~composition~~use of claim 62, wherein said glial cells are astrocytes.
65. The ~~composition~~use of claim 62, wherein said astrocytes are reactive astrocytes.
66. The ~~composition~~use of claim 62, wherein said glial cells are GFAP positive.
67. The ~~composition~~use of claim 62, wherein said neurons are functional neurons.
68. The ~~composition~~use of claim 62, 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.

69. The ~~composition~~use of claim 68, wherein said functional neurons are glutamatergic neurons.

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

71. The ~~composition~~use of claim 70, wherein said composition is formulated for local delivery.

72. The ~~composition~~use of claim 70, wherein said composition is formulated for systemic delivery.

73. The ~~composition~~use of any one of claims 70-72, 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.

~~74. A method comprising delivering the composition of claim 6 to said subject in need thereof.~~

~~75. The method of claim 74, wherein said composition is formulated to be delivered to a subject in need thereof.~~

~~76. The method of claim 74, wherein said delivering comprises local administration.~~

~~77. The method of claim 74, wherein said delivering comprises systemic administration.~~

~~78. The method of any one of claims 74-77, 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.~~

~~79.~~74. A composition for use in 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 human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6 and a human distal-less homeobox 2 (hDlx2) sequence comprising the nucleic acid sequence of SEQ ID NO: 13, wherein said hNeuroD1 sequence and said hDlx2 sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 sequence and said hDlx2 sequence are operably linked to 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 26;
- (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 selected from the group consisting of SEQ ID NOs: 5 and 27;

(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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

(e) wherein the composition is to be injected into the living human.

~~80-75.~~ A composition for use in 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 coding sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid sequence of SEQ ID NO: 10 and a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 coding sequence and hDlx2 coding sequence are operably linked to expression control 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 26;

- (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 selected from the group consisting of SEQ ID NOs: 5 and 27;
- (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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30;

(e) wherein the composition is to be injected into the living human.

~~81.76.~~ A composition for use in a method of converting glial cells to neurons in a subject in need thereof, the composition comprising: ~~delivering~~ an adeno-associated virus (AAV) ~~to said subject in need thereof, wherein said AAV comprises comprising~~ a DNA vector construct comprising a neurogenic differentiation 1 (NeuroD1) sequence and a distal-less homeobox 2 (Dlx2) sequence, wherein said NeuroD1 sequence and Dlx2 sequence are separated by a linker sequence, wherein said NeuroD1 sequence and Dlx2 sequence are 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 composition is to be delivered to said subject in need thereof, and wherein said AAV vector is capable of converting at least one glial cell to a neuron in said subject in need thereof.

~~82.77.~~ A composition for use in a method of treating a neurological condition in a subject in need thereof, the composition 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 and distal-less homeobox 2 (Dlx2) sequence, wherein said NeuroD1 sequence and Dlx2 sequence are separated by a linker sequence, wherein said NeuroD1 sequence and said Dlx2 sequence are 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 to said subject in need thereof.

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

~~83.78.~~ The composition method of any one of claims ~~79-8274-77~~, wherein said AAV is selected from the group consisting of AAV serotype 2, AAV serotype 5, and AAV serotype 9.

~~84.79.~~ The composition method of claim ~~8378~~, wherein said AAV is AAV serotype 2.

~~85.80.~~ The composition method of claim ~~8378~~, wherein said AAV is AAV serotype 5.

~~86.81.~~ The composition method of claim ~~8378~~, wherein said AAV is AAV serotype 9.

87.82. The composition method of claims 79-74 or 8075, wherein said functional neurons are glutamatergic neurons, GABAergic neurons, dopaminergic neurons, cholinergic neurons, serotonergic neurons, epinephrinergic neurons, motor neurons, and peptidergic neurons.

88.83. The method composition of claims 81-76 or 8277, wherein said NeuroD1 is human NeuroD1 (hNeuroD1).

89.84. The method composition of claims 81-76 or 82-77 wherein said Dlx2 is human Dlx2 (hDlx2).

90.85. The method composition of claims 81-76 or 8277, 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.

91.86. The method composition of claims 75-76 or 7677, wherein said Dlx2 is selected from the group consisting of a chimpanzee Dlx2, a bonobo Dlx2, an orangutan Dlx2, a gorilla Dlx2, a macaque Dlx2, a marmoset Dlx2, a capuchin Dlx2, a baboon Dlx2, a gibbon Dlx2, and a lemur Dlx2.

92.87. The method composition of claim 8883, wherein said hNeuroD1 comprises an amino acid sequence encoding an amino acid coding sequence at least 80% identical or similar to SEQ ID NO: 10.

93.88. The method composition of claim 8984, said hDlx2 comprises a amino acid sequence encoding an amino acid sequence at least 80% identical or similar to SEQ ID NO: 14.

94.89. The composition method of claim 8883, wherein said hNeuroD1 coding sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 6, or the complement thereof.

95.90. The composition method of claim 8984, said hDlx2 coding sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 13, or the complement thereof.

96.91. The composition method of claims 81-76 or 8277, wherein said GFAP promoter is a human GFAP (hGFAP) promoter.

97.92. The composition method of claims 81-76 or 8277, 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.

98.93. The composition method of any one of claims 79-9774-77, wherein said IRES sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 3, or the complement thereof.

99.94. The composition method of claim 9691, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 4, or the complement thereof.

100.95. The composition method of claim 9691, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 12, or the complement thereof.

101.96. The composition method of claim 9691, wherein said hGFAP promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NOs: 26, or the complement thereof.

102.97. The composition method of claims 81-76 or 8277, wherein said linker is selected from the group consisting of P2A and T2A.

~~103.98.~~ The composition method of claim ~~10297~~, wherein said P2A linker comprises a nucleic acid sequence at least 80% identical to the sequence selected from the group consisting of SEQ ID NO: 15 and 18, or the complement thereof.

~~104.99.~~ The composition method of claim ~~10297~~, wherein said T2A linker comprises a nucleic acid sequence at least 80% identical to the sequence selected from the group consisting of SEQ ID NO: 16 and 19, or the complement thereof.

~~105.100.~~ The composition method of claims ~~81-76~~ or ~~8277~~, 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.

~~106.101.~~ The composition method of claim ~~105100~~, wherein said enhancer from EF1- α promoter comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 2, or the complement thereof.

~~107.102.~~ The composition method of claim ~~105100~~, wherein said CMV enhancer comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 11, or the complement thereof.

~~108.103.~~ The composition method of claims ~~81-76~~ or ~~8277~~, wherein said chimeric intron comprises a nucleic acid sequence at least 80% identical to nucleic acid selected from the group consisting of SEQ ID NOs: 5 and 27, or the complement thereof.

~~109.104.~~ The composition method of claims ~~81-76~~ or ~~8277~~, wherein said WPRE comprises a nucleic acid sequence at least 80% identical to a nucleic acid selected from the group consisting of SEQ ID NOs: 7 and 29, or the complement thereof.

~~110.105.~~ The composition method of claims ~~81-76~~ or ~~8277~~, wherein said polyadenylated polyadenylation signal selected from the group consisting of SV40 polyadenylation signal and a hGH polyadenylation signal

~~111.106.~~ The composition method of claim ~~110105~~, wherein said SV40 polyadenylated polyadenylation signal comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 8, or the complement thereof.

~~112.107.~~ The composition method of claim ~~110105~~, wherein said hGH polyadenylated polyadenylation signal comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 13, or the complement thereof.

~~113.108.~~ The composition method of claims ~~81-76~~ or ~~8277~~, wherein said vector further comprises a nucleic acid sequence encoding an AAV protein sequence.

~~114.109.~~ The composition method of any one of claims ~~79-8274-77~~, wherein said vector comprises AAV serotype 2 inverted terminal repeats (ITRs).

~~115.110.~~ The composition method of any one of claims ~~74-7779-82~~, wherein said vector comprises AAV serotype 5 inverted terminal repeats (ITRs).

~~116.111.~~ The composition method of any one of claims ~~74-7779-82~~, wherein said vector comprises AAV serotype 9 inverted terminal repeats (ITRs).

~~117.112.~~ The composition method of any one of claims ~~74-7779-82~~, wherein said vector comprises at least one ITR nucleic acid sequence at least 80% identical to SEQ ID NO: 1.

~~118.113.~~ The composition method of any one of claims ~~74-77-79-82~~, wherein said vector comprises at least one ITR nucleic acid sequence at least 80% identical to SEQ ID NO: 9.

~~119.114.~~ The composition method of claim ~~8176~~, wherein said converting occurs in the central nervous system (CNS) or peripheral nervous system.

~~120.115.~~ The composition method of claim ~~81-76~~, wherein said converting occurs in the ~~CNS~~central nervous system.

~~121.116.~~ The composition method of claim ~~81-76~~ or ~~8277~~, wherein said subject in need thereof is a mammal.

~~122.117.~~ The composition method of claim ~~121-116~~, wherein said mammal is a human.

~~123.118.~~ The composition method of claim ~~121-116~~, wherein said mammal is a non-human primate.

~~124.119.~~ The composition method of claim ~~81-76~~ or ~~8277~~, wherein said delivering comprises a local administration.

~~125.120.~~ The composition method of claim ~~81-76~~ or ~~8277~~, wherein said delivering comprises systemic administration.

~~126.121.~~ The composition method of claim ~~81-76~~ or ~~8277~~, 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.

~~127.122.~~ The composition method of claim ~~79-74~~ or ~~8075~~, 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.

~~128-123.~~ The composition method of claims ~~81-76~~ or ~~82-77~~, wherein said delivering comprises injecting.

~~129-124.~~ The composition method of any one of claims ~~79-74~~ or ~~75, 80 or 128~~, wherein said injecting is performed at a concentration of between 10^{10} particles/mL and 10^{14} particles/mL.

~~130-125.~~ The composition method of claim ~~129-124~~, wherein said injecting further comprises a flow rate of between 0.1 μ L/minute and 5.0 μ L/minute.

~~131-126.~~ The composition method of claim ~~81-76~~, wherein said at least one glial cell is selected from the group consisting of at least one astrocyte and at least one NG2 cell.

~~132-127.~~ The composition method of claim ~~131-126~~, wherein said at least one glial cell is at least one astrocyte.

~~133-128.~~ The composition method of claim ~~131-126~~ or ~~132-126~~, wherein said at least one astrocyte is a reactive astrocyte.

~~134-129.~~ The composition method of claim ~~81-76~~, wherein said neuron is a functional neuron.

~~135-130.~~ The composition method of any one of claims ~~79, 80 and 134-74~~ or ~~75~~, 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..

~~136-131.~~ The composition method of claim ~~81-76~~, wherein said subject exhibits an improvement of at least one neurological condition symptom as compared to said subject prior to said delivering.

~~137.132.~~ The composition method of claim ~~136~~131, wherein said improvement is measured within 1 year of said delivering.

~~138.133.~~ The composition method of any one of claims ~~79, 80, or 128~~74 or 75, wherein said method comprises directly injecting said AAV into the brain of said subject.

~~139.134.~~ The composition method of any one of claims ~~79-74~~ or ~~80-75~~ wherein said wherein said converting is in the striatum of said brain.

~~140.135.~~ The composition method of any one of claims ~~79, 80, or 128~~74 or 75, wherein said method comprises directly injecting said AAV into the spinal cord of said subject.

~~141.136.~~ The composition method of claim ~~82~~77, wherein said neurological condition comprises an injury to the central nervous system (CNS) or peripheral nervous system.

~~142.137.~~ The composition method of claim ~~82~~77, 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.

~~143.138.~~ The composition method of claim ~~82~~77, wherein said neurological condition is Alzheimer's Disease.

- ~~144.139.~~ The composition method of claim ~~8277~~, wherein said neurological condition is Parkinson's Disease.
- ~~145.140.~~ The composition method of claim ~~8277~~, wherein said neurological condition is ALS.
- ~~146.141.~~ The composition method of claim ~~8277~~, wherein said neurological condition is Huntington's Disease.
- ~~147.142.~~ The composition method of claim ~~8277~~, wherein said neurological condition is a stroke.
- ~~148.143.~~ The composition method of claim ~~147142~~, wherein said stroke is an ischemic stroke.
- ~~149.144.~~ The composition method of claim ~~147142~~, wherein said stroke is a hemorrhagic stroke.
- ~~150.145.~~ The composition method of claim ~~8277~~, wherein said method is capable of converting at least one glial cell into a neuron.
- ~~151.146.~~ The composition method of claim ~~150145~~, wherein said glial cells are selected from the group consisting of astrocytes and NG2 cells.
- ~~152.147.~~ The composition method of claim ~~150145~~, wherein said glial cells are astrocytes.
- ~~153.148.~~ The composition method of claim ~~152147~~, wherein said astrocytes are reactive astrocytes.
- ~~154.149.~~ The composition method of claim ~~150145~~, wherein said glial cells are GFAP positive.
- ~~155.150.~~ The composition method of claim ~~150145~~, wherein said neurons are functional neurons.

~~156.151.~~ The ~~composition method~~ of claim ~~145.140~~, 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.

~~157.152.~~ The ~~composition method~~ of claims ~~79-74~~ or ~~80.75~~, wherein a therapeutically effective dose of said AAV is injected into said subject.

~~158.153.~~ The ~~composition method~~ of claims ~~81-76~~ or ~~82.77~~, wherein a therapeutically effective dose of said AAV is delivered to said subject.

~~159.154.~~ The ~~composition method~~ of claim ~~147 or 148.157~~, wherein said therapeutically effective dose is administered with a pharmaceutically acceptable carrier.

~~160.155.~~ A composition comprising (i) an adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6, and (ii) an adeno-associated virus (AAV) vector comprising a human distal-less homeobox 2 (hDlx2) sequence comprising the nucleic acid sequence of SEQ ID NO: 13; wherein the hNeuroD1 sequence is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) an enhancer from a human elongation factor-1 alpha (EF1- α) promoter comprising the nucleic acid sequence of SEQ ID NO: 2;
- (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or SEQ ID NO: 27;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and

(e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~161,156.~~ A composition comprising (i) an adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6, and (ii) an adeno-associated virus (AAV) vector comprising a human distal-less homeobox 2 (hDlx2) sequence comprising the nucleic acid sequence of SEQ ID NO: 13;

wherein the hNeuroD1 sequence is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) 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 SEQ ID NO: 27;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and
- (e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~162,157.~~ The composition of claim ~~160-155~~ or ~~161,156~~, wherein (ii) comprises an AAV vector comprising the hDlx2 sequence comprising the nucleic acid sequence of SEQ ID NO: 13 operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising a nucleic acid sequence of SEQ ID NO: 26;
- (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 selected from the group consisting of SEQ ID NOs: 5 and 27;
- (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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~163-158.~~ A composition comprising (i) an adeno-associated virus (AAV) vector comprising a nucleic acid sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding sequence of SEQ ID NO: 10, and (ii) an adeno-associated virus (AAV) vector comprising a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14;

wherein the nucleic acid sequence encoding an hNeuroD1 protein is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) an enhancer from a human elongation factor-1 alpha (EF1- α) promoter comprising the nucleic acid sequence of SEQ ID NO: 2;
- (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or SEQ ID NO: 27;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and
- (e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~164~~159. A composition comprising (i) an adeno-associated virus (AAV) vector comprising a nucleic acid sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding sequence of SEQ ID NO: 10, and (ii) an adeno-associated virus (AAV) vector comprising a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14;

wherein the nucleic acid sequencing encoding an hNeuroD1 protein is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) 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 SEQ ID NO: 27;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and
- (e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30

~~165~~160. The composition of claim ~~163-158~~ or ~~164~~159, wherein (ii) comprises an AAV vector comprising a nucleic acid coding sequence encoding the hDlx2 protein, wherein the nucleic acid is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising a nucleic acid sequence of SEQ ID NO: 26;
- (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 selected from the group consisting of SEQ ID NOs: 5 and 27;
- (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 29; 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: 17, or a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~166-161.~~ An adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6 and a human distal-less homeobox 2 (hDlx2) sequence comprising the nucleic acid sequence of SEQ ID NO: 13, wherein said hNeuroD1 sequence and said hDlx2 sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 sequence and said hDlx2 sequence are operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) an enhancer from a human elongation factor-1 alpha (EF1- α) promoter comprising the nucleic acid sequence of SEQ ID NO: 2;
- (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5 or SEQ ID NO: 5;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and

(e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~167~~.162. An adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6 and a human distal-less homeobox 2 (hDlx2) sequence comprising the nucleic acid sequence of SEQ ID NO: 13, wherein said hNeuroD1 sequence and said hDlx2 sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 sequence and said hDlx2 sequence are operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) 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;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and
- (e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~168~~.163. An adeno-associated virus (AAV) vector comprising a nucleic acid sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding sequence of SEQ ID NO: 10 and a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence are separated by

(i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) an enhancer from a human elongation factor-1 alpha (EF1- α) promoter comprising the nucleic acid sequence of SEQ ID NO: 2;
- (c) a chimeric intron comprising the nucleic acid sequence of SEQ ID NO: 5;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and
- (e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

169.164. An adeno-associated virus (AAV) vector comprising a nucleic acid sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding sequence of SEQ ID NO: 10 and a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence are separated by (i) a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18, (ii) a T2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 16 and 19, or (iii) an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 coding

sequence and said hDlx2 coding sequence is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) 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;
- (d) a woodchuck hepatitis virus posttranscriptional regulatory element (WPRE) comprising the nucleic acid sequence of SEQ ID NO: 29; and
- (e) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~170-165.~~ An adeno-associated virus (AAV) vector comprising a human neurogenic differentiation 1 (hNeuroD1) sequence comprising the nucleic acid sequence of SEQ ID NO: 6 and a human distal-less homeobox 2 (hDlx2) sequence comprising the nucleic acid sequence of SEQ ID NO: 13, wherein said hNeuroD1 sequence and said hDlx2 sequence are separated by a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18 or an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 sequence and said hDlx2 sequence are operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) 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; and

(d) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.

~~171.166.~~ An adeno-associated virus (AAV) vector comprising a nucleic acid sequence encoding a human neurogenic differentiation 1 (hNeuroD1) protein comprising the amino acid coding sequence of SEQ ID NO: 10 and a nucleic acid coding sequence encoding a human distal-less homeobox 2 (hDlx2) protein comprising the amino acid sequence of SEQ ID NO: 14, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence are separated by a P2A linker comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 15 and 18 or an internal ribosomal entry site of the encephalomyocarditis virus (IRES) sequence comprising SEQ ID NO: 3, wherein said hNeuroD1 coding sequence and said hDlx2 coding sequence is operably linked to regulatory elements comprising:

- (a) a glial fibrillary acidic protein (GFAP) promoter comprising the nucleic acid sequence of SEQ ID NO: 26;
- (b) 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; and
- (d) a bGH polyadenylation sequence comprising the nucleic acid sequence of SEQ ID NO: 30.