

CLAIMS

What is claimed is:

1. Use of a pharmaceutical composition in the manufacture of a medicament for treating or preventing an ischemic optic neuropathy in a subject in need thereof,

wherein the pharmaceutical composition comprises one or more polynucleotides encoding octamer-binding transcription factor 4 (OCT4), sex determining region Y-box 2 (SOX2), and Kruppel-like factor 4 (KLF4), but not a Myc protein is to be administered to the subject.
2. The use of claim 1, wherein the use increases the survival and/or function of neurons of an eye of the subject as compared to a reference.
3. The use of claim 1 or 2, wherein the use increases the survival and/or function of retinal ganglion cells (RGCs) of an eye of the subject as compared to a reference.
4. The use of claim 3, wherein the RGC function is measured by electroretinogram (pERG).
5. The use of any one of claims 1-4, wherein the use restores visual function in the subject.
6. The use of any one of claims 1-5, wherein the pharmaceutical composition does not comprise a polynucleotide encoding Nanog.
7. The use of any one of claims 1-6, wherein the pharmaceutical composition is to be administered to one or both eyes of the subject.
8. The use of any one of claims 1-7, wherein a first eye of the subject is affected by the ischemic optic neuropathy and the pharmaceutical composition to be

administered is to a second eye that is not affected by the ischemic optic neuropathy to prevent ischemic optic neuropathy.

9. The use of any one of claims **1** to **8**, wherein the pharmaceutical composition comprises a viral vector comprising the one or more polynucleotides encoding OCT4, SOX2, and KLF4, optionally wherein the viral vector comprises a lentivirus, retrovirus, adenovirus, alphavirus, vaccinia virus, herpes virus, or adeno-associated virus (AAV) vector.
10. The use of claim **9**, wherein the viral vector comprises an adeno-associated virus (AAV) vector.
11. The use of claim **10**, wherein the AAV vector is an AAV serotype 2 (AAV2), AAV8, AAV9, or AAV.PHP.b vector.
12. The use of any one of claims 1-8, wherein the pharmaceutical composition comprises a lipid comprising the one or more polynucleotides encoding OCT4, SOX2, and KLF4.
13. The use of any one of claims 1-12, wherein a single polynucleotide encodes the OCT4, SOX2, and KLF4.
14. The use of any one of claims 1-13, wherein a single multicistronic polynucleotide encodes the OCT4, SOX2, and KLF4.
15. The use of claim of any one of claims 1-14, wherein one or more polynucleotides encoding OCT4, SOX2, and KLF4 are operably linked with at least one promoter.
16. The use of any one of claims 1-15, wherein the use does not induce a pluripotent state in a cell, tissue, or organ of the subject.
17. The use of any one of claims 1-16, wherein the OCT4, SOX2, and KLF4 are the only transcription factors encoded by the pharmaceutical composition.

- 18 The use of any one of claims 1-17, wherein the pharmaceutical composition does not induce expression of Nanog in one or more cells, tissues, or organs.
19. The use of any one of claims 1-18, wherein:
- i) the OCT4 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 2;
 - ii) the SOX2 comprises an amino acid sequence having at least 90%, identity to SEQ ID NO: 4, and/or
 - iii) the KLF4 comprises an amino acid sequence having at least 90%, identity to SEQ ID NO: 6.
20. The use of any one of claims 1-18, wherein:
- i) the OCT4 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 2;
 - ii) the SOX2 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 4; and/or
 - iii) the KLF4 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 6.
21. The use of any one of claims 1-18, wherein:
- i) the OCT4 comprises the amino acid sequence of SEQ ID NO: 2;
 - ii) the SOX2 comprises the amino acid sequence of SEQ ID NO: 4; and/or
 - iii) the KLF4 comprises the amino acid sequence of SEQ ID NO: 6.