CLAIMS

WHAT IS CLAIMED IS:

1. Use of

a) a first pharmaceutical composition comprising an adeno-associated virus (AAV) comprising a recombinant nucleic acid comprising:

i) a nucleic acid sequence encoding a mitochondrial targeting peptide;

ii) a nucleic acid sequence encoding a mitochondrial protein comprising a nucleic acid sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 6-7 and 9-12; and

iii) a 3'UTR nucleic acid sequence

in the manufacture of a first medicament and use of

b) a second pharmaceutical composition comprising a steroid in the manufacture of a second medicament,

wherein the first and second medicaments are to be used in combinatorial therapy to treat an eye disorder, and wherein the first and second medicaments are to be administered to a patient in need thereof.

2. The use of claim 1, wherein the nucleic acid sequence encoding the mitochondrial protein encodes a polypeptide comprising an amino acid sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 160-162.

3. The use of claim 1, wherein the nucleic acid sequence encoding a mitochondrial targeting peptide encodes a polypeptide comprising an amino acid sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 126-159.

4. The use of claim 1, wherein the nucleic acid sequence encoding a mitochondrial targeting peptide comprises a nucleic acid sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 1-5.

5. The use of claim 1, wherein the 3'UTR nucleic acid sequence comprises a nucleic sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 13, 14, and 111-125.

6. The use of claim 1, wherein the recombinant nucleic acid comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 15-18, 21-32, 35-46, 49-60, 63-74, and 77-84.

7. The use of claim 1, wherein the first pharmaceutical composition is to be administered via intraocular or intravitreal injection.

8. The use of claim 1, wherein about 0.01-0.1 mL of the first pharmaceutical composition is to be administered via intravitreal injection.

9. The use of claim 1, wherein about 0.05 mL of the first pharmaceutical composition is to be administered via intravitreal injection.

10. The use of claim 1, wherein the steroid is a glucocorticoid.

11. The use of claim 10, wherein the glucocorticoid is methylprednisolone or prednisone.

12. The use of claim 1, wherein the steroid is to be administered prior to administration of the first pharmaceutical composition.

13. The use of claim 12, wherein the steroid is methylprednisolone and is to be administered at a daily dosage of about 30 mg/60 kg to about 40 mg/60 kg or about 30 mg to about 40 mg.

14. The use of claim 12, wherein the steroid is prednisone and is to be administered at a daily dosage of about 50 mg/60 kg to about 70 mg/60 kg.

15. The use of claim 1, wherein the steroid is to be administered after the administration of the first pharmaceutical composition.

16. The use of claim 15, wherein the steroid is methylprednisolone and is to be administered at a daily dosage of between about 70 mg/60 kg and 90 mg/60 kg or between about 70 mg and 90 mg.

17. The use of claim 15, wherein the steroid is methylprednisolone and is to be administered for at least two days after the administration of the first pharmaceutical composition, and wherein subsequent doses of methylprednisolone are to be administered daily for at least 7 weeks after the administration of the first pharmaceutical composition and wherein the dosage of the methylprednisolone is decreased on a weekly basis.

18. The use of claim 15, wherein the steroid is predisone and is to be administered at a daily dosage of between about 50 mg/60 kg and 70 mg/ 60 kg or between about 50 mg and about 70 mg.

19. The use of claim 18, wherein the predisone is to be administered for at least seven days after the administration of the first pharmaceutical composition.

20. The use of claim 19, wherein after seven days, the predisone is to be administered at a daily dosage of between about 30 mg/60 kg and about 50 mg/60 kg or between about 30 mg and 50 mg.

21. The use of claim 19, wherein subsequent doses of predisone are to be administered daily for at least 4 days and wherein the dosage of the predisone is decreased on a daily basis.

22. The use of claim 1, wherein the steroid is to be administered prior to and after the administration of the first pharmaceutical composition.

23. The use of claim 22, wherein the steroid is methylprednisolone and is to be administered daily for at least seven days prior to the administration of the first pharmaceutical composition and daily for at least 7 weeks after administration of the first pharmaceutical composition.

24. The use of claim 22, wherein the steroid is prednisone and is to be administered daily for at least two days prior to the administration of the first pharmaceutical composition and daily for at least eleven days after administration of the first pharmaceutical composition.

25. The use of claim 1, further comprising administering sodium creatine phosphate to the patient.

26. The use of claim 1, wherein the eye disorder is Leber's hereditary optic neuropathy (LHON).

27. The use of claim 1, wherein the AAV is AAV2.

28. A method of screening patients for treatment of an eye disorder, the method comprising:

(a) culturing a population of target cells from a serum sample obtained from a patient, with a composition comprising an adeno-associated virus (AAV) comprising a recombinant nucleic acid encoding a detectable label in the presence of the serum sample; and

(b) detecting the expression level of the detectable label in the target cell population after the culturing, wherein the patient is selected for the treatment if the expression level of the detectable label in the target cell population is higher than a pre-determined threshold.

29. Use of:

(a) a first pharmaceutical composition comprising an adeno-associated virus (AAV) comprising a recombinant nucleic acid comprising:

i) a nucleic acid sequence encoding a mitochondrial targeting peptide comprising an amino sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 126-159;

ii) a nucleic acid sequence encoding a mitochondrial protein comprising a nucleic acid sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 6-7 and 9-12; and

iii) a 3'UTR nucleic acid sequence that is at least 90%, at least 95%, at least 97%, at least 99% or 100% identical to a sequence selected from the group consisting of SEQ ID NO: 13, 14, and 111-125 in the manufacture of a first medicament and use of

(b) a second pharmaceutical composition comprising methylprednisolone or prednisone in the manufacture of a second medicament,

wherein the first and second medicaments are to be used in combinatorial therapy to treat Leber's hereditary optic neuropathy (LHON).