

WHAT IS CLAIMED IS:

1. A method of treating retinal degeneration caused by mutations in a nicotinamide mononucleotide adenylyltransferase 1 (*NMNAT1*) gene in a human subject, the method comprising delivering to the eye of the subject a therapeutically effective
5 amount of an Adeno-associated virus (AAV) vector comprising a sequence encoding human NMNAT1, operably linked to a promoter that drives expression in retinal cells, preferably in photoreceptors.
2. The method of claim 1 wherein the promoter is a CAG, CASI, CMV, RHO, or rhodopsin kinase (GRK1) promotor.
- 10 3. The method of claim 2, wherein the NMNAT1-encoding sequence is at least 80% identical to a wild type (SEQ ID NO:2) or codon optimized (SEQ ID NO:1) sequence.
4. The method of claims 1-3, wherein the vector is delivered via sub-retinal injection.
5. A method of increasing expression of NMNAT1 in the eye of a human subject, the
15 method comprising delivering to the eye of the subject a therapeutically effective amount of an Adeno-associated virus type 2 (AAV2) vector comprising a sequence encoding human NMNAT1, operably linked to a promoter that drives expression in the retina, preferably in photoreceptor cells.
6. The method of claim 5, wherein the promoter is a CAG, CASI, CMV, RHO, or
20 rhodopsin kinase (GRK1)promotor.
7. The method of claim 5, wherein the NMNAT1 sequence is codon optimized.
8. The method of claims 5-7, wherein the vector is delivered via sub-retinal injection.
9. An Adeno-associated virus type 2 (AAV2) vector comprising a sequence encoding human NMNAT1, operably linked to a promotor that drives expression in the retina,
25 preferably in the photoreceptor cells.

10. The vector of claim 9, wherein the promotor is a CAG, CASI, CMV, RHO, or rhodopsin kinase (GRK1) promotor.
11. The vector of claim 9, wherein the NMNAT1 sequence is codon optimized.
12. A pharmaceutical composition comprising the vector of claims 9-11, formulated for
5 delivery via sub-retinal injection.
13. The vector of claims 9-11, for use in treating retinal degeneration caused by mutations in NMNAT1 in the eye of a human subject.
14. The vector of claims 9-11, for use in increasing expression of NMNAT1 in the eye of a human subject.
- 10 15. The pharmaceutical composition of claim 12, for use in treating retinal degeneration caused by mutations in NMNAT1 in the eye of a human subject.
16. The pharmaceutical composition of claim 12, for use in increasing expression of NMNAT1 in the eye of a human subject.