CLAIMS

1. Use of a composition for the manufacture of a medicament for treating an ocular genetic disease by localized administration to a subject's eye, in which the composition comprises a CRISPR-Cas system comprising:

A. a polynucleotide encoding a CRISPR-Cas system guide comprising: (a) a guide sequence capable of hybridizing to an ocular genetic disease target sequence, (b) a tracr mate sequence, and (c) a tracr sequence, in which (a), (b), and (c) are arranged in a 5' to 3' orientation; and

B. a polynucleotide encoding a Cas9;

in which each of A and B are formulated for delivery together in a delivery vehicle, the vehicle being an adeno-associated viral (AAV) vector, in which the AAV is AAV1, AAV2, or AAV5; and capable, when administered together to the subject's eye, of forming a CRISPR-Cas complex comprising the Cas9 and the CRISPR-Cas system guide.

2. Use according to Claim 1, in which the CRISPR-Cas system guide is a chimeric RNA (chiRNA).

3. Use according to Claim 1 or 2, in which the ocular genetic disease is a retinal disease.

4. Use according to Claim 3, in which the retinal disease is a hereditary disease.

5. Use according to any preceding claim, in which the Cas9 is a nuclease directing cleavage of both DNA strands at the location of the target sequence, or in which the Cas9 is a nickase directing cleavage of one DNA strand at the location of the target sequence.

6. Use according to any preceding claim, in which the Cas9 is complexed with the CRISPRCas system guide.

7. Use according to Claim 6, in which the tracr mate sequence hybridizes to the tracr sequence, and the guide sequence directs sequence-specific binding of a CRISPR complex to the target sequence.

8. Use according to any preceding claim, in which the ocular genetic disease is selected from Stargardt disease, Bardet-Biedl Syndrome, Best disease, blue cone monochromacy,

choroidermia, cone-rod dystrophy, congenital stationary night blindness, enhanced S-cone syndrome, juvenile X-linked retinoschisis, Leber congenital amaurosis (LCA), Malattia leventinesse, Norrie disease or X-linked familial exudative vitreoretinopathy, Pattern dystrophy, Sorsby dystrophy, Usher syndrome, retinitis pigmentosa, achromatopsia or macular dystrophies or macular degeneration, and age-related macular degeneration.

9. Use according to Claim 8, in which the ocular genetic disease is Leber congenital amaurosis (LCA), Usher syndrome, or retinitis pigmentosa.

10. Use according to any preceding claim, in which the Cas9 is a *Streptococcus pyogenes* Cas9 (SpCas9), a *Staphylococcus aureus* Cas9 (SaCas9), or a *Streptococcus thermophilus* Cas9 (StCas9).

11. Use according to any preceding claim, in which the CRISPR-Cas system is a multiplexed system comprising two or more CRISPR-Cas system guides with different guide sequences.

12. Use according to any preceding claim, in which the Cas9 comprises one or more nuclear localization sequences.

13. Use according to any preceding claim, in which the Cas9 comprises one or more mutations, and in which the Cas9 is fused to a heterologous protein domain.

14. Use according to any preceding claim, in which the composition further comprises a recombination template.

15. Use according to any preceding claim, in which the composition is formulated for subretinal injection.