CLAIMS

What is claimed is:

1. Use of a non-replicating recombinant adeno-associated virus-8 (rAAV8) vector in the manufacture of a medicament for ~~A method of~~ treating ~~a human subject diagnosed with~~ neovascular age-related macular degeneration (nAMD), wherein the rAAV8 vector comprises an expression cassette encoding an ~~comprising delivering to the retina of said human subject a therapeutically effective amount of~~ anti-human vascular endothelial growth factor (hVEGF) antigen-binding fragment, wherein said expression cassette is flanked by AAV2 inverted terminal repeats (ITRs), and wherein the cassette comprises: ~~produced by human retinal cells.~~

(i) a CB7 promoter consisting of a chicken β-actin promoter and a CMV enhancer;

(ii) a chicken β-actin intron;

(iii) a nucleotide sequence encoding:

an IL-2 signal peptide;

a heavy chain of the anti-hVEGF antigen-binding fragment comprising the amino acid sequence of SEQ ID NO: 2;

a self-cleaving furin (F)/F2A linker;

a second IL-2 signal peptide;

a light chain of the anti-hVEGF antigen-binding fragment comprising the amino acid sequence of SEQ ID NO: 1; and

a rabbit β-globin poly A signal; and

wherein a therapeutically effective dose of the rAAV8 vector is to be administered to a human subject,

wherein the therapeutically effective dose of the rAAV8 vector is a dose sufficient to maintain a concentration of the anti-hVEGF antigen-binding fragment of at least 0.330 µg/mL in the Vitreous humour or 0.110 µg/mL in the Aqueous humour for three months.

~~2. A method of treating a human subject diagnosed with nAMD, comprising delivering to the retina of said human subject a therapeutically effective amount of anti-hVEGF antigen-binding fragment produced by human photoreceptor cells.~~

~~3. The method of claims 1 or 2, in which the antigen-binding fragment is a Fab.~~

~~4. The method of claims 1 or 2, in which the antigen-binding fragment is a $F(ab')_2$.~~

~~5. The method of claims 1 or 2, in which the antigen-binding fragment is a single-chain variable domain (scFv).~~

~~6. The method of claim 1 or 2, in which the antigen-binding fragment comprises a heavy chain comprising the amino acid sequence of SEQ ID NO. 1 or SEQ ID NO. 3, and a light chain comprising the amino acid sequence of SEQ ID NO. 2, or SEQ ID NO. 4.~~

~~7. The method of claims 1 or 2, wherein the antigen-binding fragment comprises light chain CDRs 1-3 of SEQ ID NOs: 14-16 and heavy chain CDRs 1-3 of SEQ ID NOs:17-19 or SEQ ID NOs: 20, 18, and 21.~~

2. The use of claim 1, wherein treatment efficacy is measured by Best-Corrected Visual Acuity (BCVA).

3. The use of claim 1, wherein treatment efficacy is measured by physical changes to the eye by SD-Optical Coherence Tomography.

4. The use of claim 1, wherein treatment efficacy is measured by signs of vision loss, infection, or inflammation.

5. The use of claim 1, wherein the rAAV8 vector is used in combination with intravitreal injections of one or more anti-hVEGF agents.

6. The use of claim 5, wherein the one or more anti-hVEGF agents are ranibizumab, bevacizumab, aflibercept, and/or pegaptanib.

7. Use of a non-replicating recombinant adeno-associated virus-8 (rAAV8) vector in the manufacture of a medicament for treating neovascular age-related macular degeneration (nAMD), wherein the rAAV8 vector comprises an expression cassette encoding an anti-human

vascular endothelial growth factor (hVEGF) antigen-binding fragment, wherein said expression cassette is flanked by AAV2 inverted terminal repeats (ITRs), and wherein the expression cassette comprises:

(i) a CB7 promoter consisting of a chicken β-actin promoter and a CMV enhancer;

(ii) a chicken β-actin intron;

(iii) a nucleotide sequence encoding:

an IL-2 signal peptide;

a heavy chain of the anti-hVEGF antigen-binding fragment comprising the amino acid sequence of SEQ ID NO: 2;

a self-cleaving furin (F)/F2A linker;

a second IL-2 signal peptide;

a light chain of the anti-hVEGF antigen-binding fragment comprising the amino acid sequence of SEQ ID NO: 1; and

(iv) a rabbit β-globin poly A signal; and

wherein a therapeutically effective dose of the rAAV8 vector is to be administered to a human subject,

wherein the therapeutically effective dose of the rAAV8 vector is a dose sufficient to slow or arrest the progression of retinal degeneration and to slow or prevent loss of vision with minimal intervention or invasive procedures.

8. The use of claim 7, wherein treatment efficacy is measured by Best-Corrected Visual Acuity (BCVA).

9. The use of claim 7, wherein treatment efficacy is measured by physical changes to the eye by SD-Optical Coherence Tomography.

10. The use of claim 7, wherein treatment efficacy is measured by signs of vision loss, infection, or inflammation.

11. The use of claim 7, wherein the rAAV8 vector is used in combination with intravitreal injections of one or more anti-hVEGF agents.

12. The use of claim 11, wherein the one or more anti-hVEGF agents are ranibizumab, bevacizumab, aflibercept, and/or pegaptanib.