Claims

1. Use of a recombinant adeno-associated virus (rAAV) virion comprising a polynucleotide encoding a soluble protein comprising: (a) an IgG-like domain 2 of VEGFR-1 (Flt-1) capable of inhibiting VEGF activity, and (b) a multimerization domain capable of forming a homodimer, in the manufacture of a medicament for treating macular degeneration associated with wet age-related macular degeneration (wet AMD) in a human subject, wherein 1 x 10^8 to 2 x 10^9 rAAV virions are to be delivered to a diseased eye of the subject.

2. Use of a recombinant adeno-associated virus (rAAV) virion comprising a polynucleotide encoding a soluble protein comprising: (a) an IgG-like domain 2 of VEGFR-1 (Flt-1) capable of inhibiting VEGF activity, and (b) a multimerization domain capable of forming a homodimer, in the manufacture of a medicament for treating macular edema associated with wet AMD in a human subject, wherein 1 x 10^8 to 2 x 10^9 rAAV virions are to be delivered to a diseased eye of the subject.

3. The use of claim 1 or claim 2, wherein 1 x 10^8, 1.5 x 10^8, 2 x 10^8, 6 x 10^8, 1 x 10^9, or 2 x 10^9 virions are to be administered to the eye.

4. The use of any one of claims 1-3, wherein the composition further comprises an opthalmalogically acceptable vehicle.

5. The use of any one of claims 1-4, wherein a single intravitreal injection of rAAV virions is to be delivered to the eye.

6. The use of any one of claims 1-5, wherein the soluble protein comprises:

(a) the IgG-like domain 2 of Flt-1;

(b) the multimerization domain, wherein the multimerization domain is derived from an immunoglobulin heavy chain; and

(c) a linker 5-25 amino acid residues in length linking (a) to (b),

wherein when the soluble protein is expressed, a multimer of the soluble protein is produced.

7. The use of claim 6, wherein the multimerization domain comprises the Fc region of an IgG, or an active fragment thereof.

8. The use of any one of claims 6-7, wherein the multimerization domain comprises the CH3 domain of an IgG, or an active fragment thereof.

9. The use of any one of claims 6-8, wherein the multimerization domain is from an IgG1, an IgG2, an IgG3 or an IgG4.

10. The use of claim 9, wherein the multimerization domain is from the constant region of an IgG1 heavy chain.

11. The use of any one of claims 6-10, wherein the linker is selected from the group consisting of:

gly_9 (SEW ID NO:1);

glu_9 (SEQ ID NO:2);

ser_9 (SEQ ID NO:3);

$gly_5cyspro_2cys$ (SEQ ID NO:4);

$(gly_4ser)_3$ (SEQ ID NO:5);

SerCysValProLeuMetArgCysGlyGlyCysCysAsn (SEQ ID NO:6);

ProSerCysValProLeuMetArgCysGlyGlyCysCysAsn (SEQ ID NO:7);

GlyAspLeuIleTyrArgAsnGlnLys (SEQ ID NO:8); and

Gly_9ProSerCysValProLeuMetArgCysGlyGlyCysCysAsn (SEQ ID NO:9).

12. The use of any one of claims 6-11, wherein the soluble protein has the formula X-Y-Z, wherein X comprises the IgG-like domain 2 of Flt-1, wherein Y is Gly_9, and wherein Z is an IgG Fc region or an IgG CH3 region.

13. The use of any one of claims 6-12, wherein the multimerization domain is humanized.

14. The use of any one of claims 6-13, wherein the soluble protein comprises an amino acid sequence selected from the group consisting of (a) the amino acid sequence depicted in Figures 2A-2B (SEQ ID NO: 11); (b) the amino acid sequence depicted in Figure 6 (SEQ ID NO:15); (c) the amino acid sequence depicted in Figure 8 (SEQ ID NO:17); (d) the amino acid sequence depicted in Figure 12 (SEQ ID NO:21); and (e) a variant of (a), (b), (c) or (d) having at least 90% sequence identity thereto.

15. The use of any one of claims 1-14, wherein the rAAV virion is derived from an

AAV serotype selected from AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAVrh8, AAVrh8R, AAV10, AAVrh10, AAV11 or AAV12.

16. The use of claim 15, wherein the rAAV virion is derived from AAV2.