CLAIMS

1. Use of a recombinant adeno-associated virus (rAAV) virion comprising a polynucleotide encoding a soluble protein comprising: (a) at least one domain 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 composition for treating macular degeneration in a human subject by delivering up to about 2×10^8 rAAV virions to the eye.

2. Use of a recombinant adeno-associated virus (rAAV) virion comprising a polynucleotide encoding a soluble protein comprising: (a) at least one domain 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 composition for treating macular edema in a human subject by delivering up to about 2×10^8 rAAV virions to the eye.

3. The use of claim 1 or 2, wherein about 1×10^7, about 2×10^7, about 5×10^7, about 6×10^7, about 1×10^8, about 1.5×10^8, or about 2×10^8 rAAV virions are to be administered to the eye.

4. Use of a recombinant adeno-associated virus (rAAV) virion comprising a polynucleotide encoding a soluble protein comprising: (a) at least one domain 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 composition for treating macular degeneration in a human subject by delivering less than about 2×10^8 rAAV virions to the eye.

5. Use of a recombinant adeno-associated virus (rAAV) virion comprising a polynucleotide encoding a soluble protein comprising: (a) at least one domain 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 composition for treating macular edema in a human subject by delivering less than about 2×10^8 rAAV virions to the eye.

6. The use of any one of claims 1-5, wherein the composition further comprises an opthalmalogically acceptable vehicle.

7. The use of any one of claims 1-6, wherein a single intravitreal injection of rAAV virions is delivered to the eye.

8. The use of any one of claims 1-7, wherein the soluble protein comprises:

(a) the at least one domain 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.

9. The use of any one of claims 1-8, wherein the at least one domain of Flt-1 comprises the IgG-like domain 2 of Flt- 1.

10. The use of claim 8 or 9, wherein the multimerization domain comprises the Fc region of an IgG, or an active fragment thereof.

11. The use of any one of claims 8-10, wherein the multimerization domain comprises the CH3 domain of an IgG, or an active fragment thereof.

12. The use of any one of claims 8-11, wherein the multimerization domain is from an IgG1, an IgG2, an IgG3 or an IgG4.

13. The use of claim 12, wherein the multimerization domain is from the constant region of an IgG1 heavy chain.

14. The use of any one of claims 8-13 wherein the linker is selected from the group consisting of:

gly_9 (SEQ 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).

15. The use of any one of claims 8-14, 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.

16. The use of any one of claims 8-15, wherein the multimerization domain is humanized.

17. The use of any one of claims 8-16, 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) an active variant of (a), (b), (c) or (d) having at least 90% sequence identity thereto.

18. The use of any one of claims 1, 3, 4 or 6-17, wherein the macular degeneration is age-related macular degeneration (AMD).

19. The use of claim 18, wherein the macular degeneration is wet AMD.

20. The use of any one of claims 1-19, 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.

21. The use of claim 20, wherein the rAAV virion is derived from AAV2.