pharmaceutical composition comprising a pharmaceutically effective amount of a vector or viral particles (e.g., rAAV) comprising a nucleic acid encoding aflibercept, a functional fragment, or a variant thereof.

[0005] Disclosed herein is a method of treating an eye condition or disease, the method comprising administering a unit dose of a pharmaceutical composition by intravitreal injection to an eye of a primate subject in need thereof, wherein the pharmaceutical composition comprises: (a) a rAAV2 variant comprising an amino acid sequence LGETTRP inserted between positions 587 and 588 of capsid protein VP1, and a nucleic acid sequence encoding a polypeptide having at least 80% homology to aflibercept, a functional fragment, or variant thereof, and (b) a pharmaceutically acceptable excipient. In some cases, the eye condition or disease is neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion, diabetic macular edema (DME), or diabetic retinopathy associated with DME. In some cases, the eye condition or disease is choroidal neovascularization or wet AMD. In some cases, the unit dose comprises between 1E12 to 1E13 vector genomes. In some cases, the unit dose comprises between 2E12 to 6E12 vector genomes. In some cases, the unit dose comprises a volume that is not more than 100 μL. In some cases, the unit dose comprises a volume that is not more than 50 μL. In some cases, the subject is a non-human primate. In some cases, the subject is a human. In some cases, the subject is responsive to aflibercept. In some cases, the subject has been pre-treated with aflibercept. In some cases, the administering by intravitreal injection occurs not more than once in at least 2 years. In some cases, the administering by intravitreal injection occurs not more than once in at least 5 years. In some cases, the administering by intravitreal injection is a one-time administration. In some cases, the pharmaceutical composition is a suspension or a refrigerated suspension. In some cases, the method further comprises agitating the suspension to ensure even distribution of the suspension prior to the administering step. In some cases, the method further comprises warming the pharmaceutical composition to room temperature prior to the administering step.

[0005a] In one aspect, the present disclosure refers to use of a unit dose of a pharmaceutical composition in the manufacture of a medicament for treating an eye condition or disease, wherein the medicament is to be administered by intravitreal injection to an eye of a primate subject in need thereof, wherein the eye condition or disease is neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion, diabetic macular edema (DME), or diabetic retinopathy associated with DME, and wherein the pharmaceutical composition comprises:

(a) a rAAV2 variant comprising an amino acid sequence LGETTRP inserted between positions 587 and 588 of capsid protein VP1, and a nucleic acid sequence encoding a polypeptide having at least 95% homology to aflibercept, and

(b) a pharmaceutically acceptable excipient.

[0006] Disclosed is a pharmaceutical composition comprising a suspension that further comprises a rAAV2 variant comprising an amino acid sequence LGETTRP inserted between positions 587 and 588 of a capsid protein VP1, and a nucleic acid sequence encoding a polypeptide having at least 80% homology to aflibercept, a functional fragment, or variant thereof. In some cases, the nucleic acid sequence comprises a sequence of SEQ ID NO: 2. In some cases, a unit dose of the composition comprises between 1E12 to 1E13 vector genomes. In some cases, a unit dose of the pharmaceutical composition comprises 2E12 to 6E12 vector genomes. In some cases, a kit comprises the suspension pharmaceutical composition and a solution for diluting the pharmaceutical composition. In some cases, the pharmaceutical

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a unit dose of a pharmaceutical composition in the manufacture of a medicament for treating an eye condition or disease, wherein the medicament is to be administered by intravitreal injection to an eye of a primate subject in need thereof, wherein the eye condition or disease is neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion, diabetic macular edema (DME), or diabetic retinopathy associated with DME, and wherein the pharmaceutical composition comprises:

    (a) a rAAV2 variant comprising an amino acid sequence LGETTRP inserted between positions 587 and 588 of capsid protein VP1, and a nucleic acid sequence encoding a polypeptide having at least 95% homology to aflibercept, and
    (b) a pharmaceutically acceptable excipient.
2. The use of claim 1, wherein the nucleic acid sequence encoding a polypeptide having at least 95% homology to aflibercept is under the transcriptional control of a cytomegalovirus (CMV) promoter.
3. The use of claim 1, wherein the eye condition or disease is choroidal neovascularization or wet AMD.
4. The use of any one of claims 1-3, wherein the polypeptide encoded by the nucleic acid comprises a sequence having 100% homology to aflibercept.
5. The use of any one of claims 1-4, wherein the unit dose is between 1E12 to 1E13 vector genomes.
6. The use of any one of claims 1-4, wherein the unit dose is between 2E12 to 6E12 vector genomes.
7. The use of any one of claims 1-4, wherein the unit dose is between 1E9 to 3E13 vector genomes.
8. The use of any one of claims 1-4, wherein the unit dose is between 1E10 to 3E12 vector genomes.
9. The use of any one of claims 1-4, wherein the unit dose is between 1E8 to 3E14 vector genomes.
10. The use of any one of claims 1-9, wherein the unit dose is in a volume that is not more than 100 µL.
11. The use of claim 10, wherein the unit dose is in a volume that is not more than 50 µL.
12. The use of any one of claims 1-11, wherein the subject is a human.
13. The use of any one of claims 1-12, wherein the subject is responsive to aflibercept.

14. The use of any one of claims 1-13, wherein the subject has been pre-treated with aflibercept.
15. The use of any one of claims 1-14, wherein the intravitreal injection occurs not more than once in at least 2 years.
16. The use of claim 15, wherein the intravitreal injection occurs not more than once in at least 5 years.
17. The use of any one of claims 1-14, wherein the intravitreal injection is a one-time administration.
18. The use of any one of claims 1-17, wherein the medicament is a suspension.
19. The use of claim 18, wherein the medicament is agitated to ensure even distribution of the suspension prior to the injection.
20. The use of any one of claims 1-19, wherein the medicament is warmed to room temperature prior to the injection.