

ensure product stability, yet storage at -80°C impacts supply chain and distribution.

Crystallization of water during slow freezing can result in concentration of excipients which can impact the stability of biologics. Phase separation or pH shifts may also occur which can impact the stability of biologics. For the commercialization of any pharmaceutical product, it would be advantageous to identify formulations that offer stability for extended periods of time. It would be further advantageous to identify formulations that are stable under frozen storage at -20°C to account for freezer temperature excursions, variability, or temporary storage (up to 18 months) in a -20°C freezer, refrigerated conditions to allow for short-term storage (up to 12 months at 2-8°C) at the clinic before dosing, at room temperature to allow for manufacturing and labelling, or under multiple free-thaw cycles to allow for thawing of drug substance and drug product for filling and labelling operations.

2. SUMMARY OF THE INVENTION

[0006] The disclosure provides a pharmaceutical composition comprising a recombinant adeno-associated virus (AAV), buffering agent, ionic salt, sucrose, and surfactant such as poloxamer 188. Sucrose is provided at a concentration that prevents crystallization of the composition and maintains a pH between 6 and 9 during frozen and liquid states.

[0006a] In one aspect, provided herein is a pharmaceutical composition comprising: (a) a recombinant adeno-associated virus (AAV), (b) potassium chloride, (c) potassium phosphate monobasic, (d) sodium chloride, (e) sodium phosphate dibasic anhydrous, (f) sucrose, and (g) poloxamer 188, polysorbate 20, or polysorbate 80.

[0006b] In one aspect, provided herein is a use of the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment or prevention of a disease in a subject wherein the medicament is to be administered to the subject.

[0006c] In one aspect, provided herein is a use of the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment of a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR) wherein the medicament is to be administered to a subject.

[0006d] In one aspect, provided herein is a use of the pharmaceutical composition as described

herein in the manufacture of a medicament for the treatment of a subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), mucopolysaccharidosis type I (MPS I), mucopolysaccharidosis type II (MPS II), familial hypercholesterolemia (FH), homozygous familial hypercholesterolemia (HoFH), coronary artery disease, cerebrovascular disease, Duchenne muscular dystrophy, Limb Girdle muscular dystrophy, Becker muscular dystrophy and sporadic inclusion body myositis, or kallikrein-related disease wherein the medicament is to be administered to a subject.

[0006e] In one aspect, provided herein is a use of the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment of a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR), the use comprising preparing the pharmaceutical composition as described herein, storing the pharmaceutical composition at -80 °C for a first period of time; (ii) thawing the pharmaceutical composition; and (iii) after thawing, storing the pharmaceutical composition at 4 °C for a second period of time.

[0006f] In one aspect, provided herein is a stable liquid pharmaceutical composition comprising: (a) a recombinant adeno-associated virus (rAAV), (b) a buffering agent comprising ionic salt and having an ionic strength between 60 mM and 150 mM, (c) sucrose, and (d) surfactant.

[0006g] In one aspect, provided herein is a stable liquid formulation comprising the pharmaceutical composition as described herein.

[0006h] In one aspect, provided herein is a single unit dosage form comprising (a) 3.2×10^{11} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4 and 0.001% P188 in a volume of about 0.95 mL in a Cyclo Olefin Polymer (COP) vial, or (b) 3.2×10^{11} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4 and 0.001% P188 in a volume of at least 0.8 mL in a COP vial, or (c) 3.2×10^{11} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of about 0.95 mL in a COP vial, or (d) 3.2×10^{11} GC/mL of Construct II, 0.2 g/L potassium

chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of at least 0.8 mL in a COP vial.

[0006i] In one aspect, provided herein is a single unit dosage form comprising (a) 6.5×10^{11} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4 and 0.001% P188 in a volume of about 0.95 mL in a COP vial, or (b) 6.5×10^{11} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, and 0.001% P188 in a volume of at least 0.8 mL in a COP vial, or (c) 6.5×10^{11} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of about 0.95 mL in a COP vial, or (d) 6.5×10^{11} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of at least 0.8 mL in a COP vial.

[0006j] In one aspect, provided herein is a single unit dosage form comprising (a) 2.5×10^{12} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, and 0.001% P188 in a volume of about 0.6 mL in a COP vial, or (b) 2.5×10^{12} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, and 0.001% P188 in a volume of at least 0.5 mL in a COP vial.

[0006k] In one aspect, provided herein is a single unit dosage form comprising (a) 3×10^{13} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of about 0.6 mL in a COP vial, or (b) 3×10^{13} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride,

1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of at least 0.5 mL in a COP vial.

[0006l] In one aspect, provided herein is a pre-filled syringe containing the single unit dosage form as described herein.

[0006m] In one aspect, provided herein is a kit comprising the pre-filled syringe as described herein.

[0006n] In one aspect, provided herein is a kit comprising one or more containers and instructions for use, wherein the one or more containers comprise the pharmaceutical composition as described herein.

[0006l] In one aspect, provided herein is the pharmaceutical composition as described herein for use in therapy.

[0007] In some embodiments, the AAV comprises components from one or more adeno-associated virus serotypes selected from the group consisting of AAV1, AAV2, AAV2tYF, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, and AAVrh10, AAV.rh20, AAV.rh39, AAV.Rh74, AAV.RHM4-1, AAV.hu37, AAV.Anc80, AAV.Anc80L65, rAAV.7m8, AAV.PHP.B, AAV.PHP.eB, AAV2.5, AAV2tYF, AAV3B, AAV.LK03, AAV.HSC1, AAV.HSC2, AAV.HSC3, AAV.HSC4, AAV.HSC5, AAV.HSC6, AAV.HSC7, AAV.HSC8, AAV.HSC9, AAV.HSC10, AAV.HSC11, AAV.HSC12, AAV.HSC13, AAV.HSC14, AAV.HSC15, or AAV.HSC16. In some embodiments, the rAAV comprises a capsid protein of the AAV8 or AAV9 serotype.

[0008] In some embodiments, the pharmaceutical composition further comprises an amino acid.

[0009] In some embodiments, the disclosure provides a pharmaceutical composition comprises a recombinant adeno-associated virus (AAV), ionic salt excipient or buffering agent, sucrose, and poloxamer 188. In some embodiments, the ionic salt excipient or buffering agent

WHAT IS CLAIMED:

1. A pharmaceutical composition comprising:
 - (a) a recombinant adeno-associated virus (AAV),
 - (b) potassium chloride,
 - (c) potassium phosphate monobasic,
 - (d) sodium chloride,
 - (e) sodium phosphate dibasic anhydrous,
 - (f) sucrose, and
 - (g) poloxamer 188, polysorbate 20, or polysorbate 80.
2. The pharmaceutical composition of claim 1, wherein the recombinant AAV comprises components from one or more adeno-associated virus serotypes selected from the group consisting of AAV1, AAV2, AAV2tYF, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAVrh10, AAV.rh20, AAV.rh39, AAV.Rh74, AAV.RHM4-1, AAV.hu37, AAV.Anc80, AAV.Anc80L65, rAAV.7m8, AAV.PHP.B, AAV.PHP.eB, AAV2.5, AAV2tYF, AAV3B, AAV.LK03, AAV.HSC1, AAV.HSC2, AAV.HSC3, AAV.HSC4, AAV.HSC5, AAV.HSC6, AAV.HSC7, AAV.HSC8, AAV.HSC9, AAV.HSC10, AAV.HSC11, AAV.HSC12, AAV.HSC13, AAV.HSC14, AAV.HSC15, and AAV.HSC16.
3. The pharmaceutical composition of any one of claims 1-2, wherein the recombinant AAV is AAV8.
4. The pharmaceutical composition of any one of claims 1-2, wherein the recombinant AAV is AAV9.
5. The pharmaceutical composition of any one of claims 1-4, wherein the pharmaceutical composition further comprises one or more amino acids.
6. The pharmaceutical composition of any one of claims 1-5, wherein the ionic strength of the pharmaceutical composition is in a range from about 60 mM to about 115 mM.
7. The pharmaceutical composition of claim 4, wherein the ionic strength of the pharmaceutical composition is in a range from about 30 mM to about 100 mM

8. The pharmaceutical composition of any one of claims 1-3, wherein the pharmaceutical composition comprises
- (a) potassium chloride at a concentration of 0.2 g/L,
 - (b) potassium phosphate monobasic at a concentration of 0.2 g/L,
 - (c) sodium chloride at a concentration of 5.84 g/L, and
 - (d) sodium phosphate dibasic anhydrous at a concentration of 1.15 g/L.
9. The pharmaceutical composition of any one of claims 1-8, wherein the pharmaceutical composition comprises sucrose at a concentration in a range from 3% (weight/volume, 30 g/L) to 18% (weight/volume, 180 g/L).
10. The pharmaceutical composition of any one of claims 1-8, wherein the pharmaceutical composition comprises sucrose at a concentration of 4% (weight/volume, 40 g/L).
11. The pharmaceutical composition of any one of claims 1-10, wherein the pharmaceutical composition comprises poloxamer 188, polysorbate 20, or polysorbate 80; and wherein the poloxamer 188, polysorbate 20, or polysorbate 80 is at a concentration in a range from 0.0005% (weight/volume, 0.005 g/L) to 0.05% (weight/volume, 0.5 g/L).
12. The pharmaceutical composition of any one of claims 1-10, wherein the pharmaceutical composition comprises poloxamer 188, polysorbate 20, or polysorbate 80; and wherein the poloxamer 188, polysorbate 20, or polysorbate 80 is at a concentration of 0.001% (weight/volume, 0.01 g/L).
13. The pharmaceutical composition of any one of claims 1-12, wherein the pH of the pharmaceutical composition is in a range from about 6.0 to about 9.0.
14. The pharmaceutical composition of any one of claims 1-12, wherein the pH of the pharmaceutical composition is about 7.4.
15. The pharmaceutical composition of any one of claims 1-14, wherein the osmolality of the pharmaceutical composition is in a range from about 200 mOsm/L to about 660 mOsm/L.
16. The pharmaceutical composition of any one of claims 1-15, wherein the pharmaceutical composition is in:

(a) a hydrophobically-coated glass vial; or

~~16.~~

(b) ~~The pharmaceutical composition of any one of claims 1-15, wherein the pharmaceutical composition is in~~ a Cyclo Olefin Polymer (COP) vial; or

~~17.~~

(c) ~~The pharmaceutical composition of any one of claims 1-15, wherein the pharmaceutical composition is in~~ a Daikyo Crystal Zenith® (CZ) vial; or

~~18.~~

~~19.~~(d) ~~The pharmaceutical composition of any one of claims 1-15, wherein the pharmaceutical composition is in~~ a TopLyo coated vial.

~~20.~~17. The pharmaceutical composition of any one of claims 1-17~~19~~, wherein the pharmaceutical composition consists of:

- (a) the recombinant AAV,
 - (b) potassium chloride at a concentration of 0.2 g/L,
 - (c) potassium phosphate monobasic at a concentration of 0.2 g/L,
 - (d) sodium chloride at a concentration of 5.84 g/L,
 - (e) sodium phosphate dibasic anhydrous at a concentration of 1.15 g/L,
 - (f) sucrose at a concentration of 4% weight/volume (40 g/L),
 - (g) poloxamer 188, polysorbate 20, or polysorbate 80 at a concentration of 0.001% weight/volume (0.01 g/L), and
 - (h) water, and
- wherein the recombinant AAV is AAV8.

~~21.~~18. The pharmaceutical composition of any one of claims 1-17, wherein the vector genome concentration (VGC) of the pharmaceutical composition is about 3×10^9 GC/mL, about 1×10^{10} GC/mL, about 1.2×10^{10} GC/mL, about 1.6×10^{10} GC/mL, about 4×10^{10} GC/mL, about 6×10^{10} GC/mL, about 2×10^{11} GC/mL, about 2.4×10^{11} GC/mL, about 2.5×10^{11} GC/mL, about 3×10^{11} GC/mL, about 3.2×10^{11} GC/mL, about 6.2×10^{11} GC/mL, about 6.5×10^{11} GC/mL, about 1×10^{12} GC/mL, about 3×10^{12} GC/mL, about 2×10^{13} GC/mL or about 3×10^{13} GC/mL

19. The pharmaceutical composition of any one of claims 1-18, wherein the recombinant AAV

is:

- (a) at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable to freeze/thaw cycles than the same recombinant AAV in a reference pharmaceutical composition; and/or

~~22.~~

- (b) ~~The pharmaceutical composition of any one of claims 1-22, wherein the recombinant AAV is~~ at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same recombinant AAV in a reference pharmaceutical composition when stored at -20°C for a period of time, wherein the period of time is about 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months; and/or

~~23.~~

- ~~24. The pharmaceutical composition of any one of claims 1-23, wherein the recombinant AAV is~~ at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same recombinant AAV in a reference pharmaceutical composition when stored at -80°C for a period of time, wherein the period of time is about 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months; and/or;

- (c) ~~The pharmaceutical composition of any one of claims 1-24, wherein the recombinant AAV is~~

~~25.~~ at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same recombinant AAV in a reference pharmaceutical composition when stored at room temperature for a period of time, wherein the period of time is about 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months; and/or ;

- (d) ~~The pharmaceutical composition of any one of claims 1-25, wherein, the recombinant AAV is~~

~~26.~~(e) at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same recombinant AAV in a reference pharmaceutical composition when (i) stored at -80 °C for a first period of time; (ii) subsequently thawed; and (iii) after thawing, stored at 4 °C for a second period of time.

20. The pharmaceutical composition of claim ~~19~~26, wherein:

~~27.~~the first period of time is about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months; and/or:-

(a) ~~The pharmaceutical composition of claim 26, wherein~~

~~28.~~(b) the second period of time is about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months.

21. The pharmaceutical composition of any one of claims 1-19, wherein:

~~29.~~the vector genome concentration of the recombinant AAV after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the recombinant AAV before being stored at -80°C for said period of time:-

(a) ~~The pharmaceutical composition of any one of claims 1-22, wherein; and/or~~

~~30.~~the vector genome concentration of the recombinant AAV after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the recombinant AAV before being stored at -20°C for said period of time:-

(b) ~~The pharmaceutical composition of any one of claims 1-22, wherein; and/or~~

~~31.~~(c) the vector genome concentration of the recombinant AAV after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the recombinant AAV before being stored at 4°C for said period of time.

22. The pharmaceutical composition of any one of claims 1-19, wherein:

~~32.~~in the vitro potency of the recombinant AAV after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the recombinant AAV before being stored at -80°C for said period of time; and/or:-

(a) ~~The pharmaceutical composition of any one of claims 1-22, wherein the~~

~~33.~~the in vitro potency of the recombinant AAV after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the recombinant AAV before being stored at -20°C for said period of time; and/or :

(b) ~~The pharmaceutical composition of any one of claims 1-22, wherein the in~~

~~34.~~(c) the in vitro potency of the recombinant AAV after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the recombinant AAV before being stored at 4°C for said period of time.

23. The pharmaceutical composition of any one of claims 1-19, wherein

~~35.~~the size distribution of the recombinant AAV after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the recombinant AAV before being stored at -80°C for said period of time; and/or :

(a) ~~The pharmaceutical composition of any one of claims 1-22, wherein the~~

~~36.~~the size distribution of the recombinant AAV after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the recombinant AAV before being stored at -20°C for said period of time; and/or :

(b) ~~The pharmaceutical composition of any one of claims 1-22, wherein the size~~

~~37.~~(c) the size distribution of the recombinant AAV after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the recombinant AAV before being stored at 4°C for said period of time.

~~38.~~24. The pharmaceutical composition of any one of claims 21 to ~~23~~37, wherein the period of time is about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

25. The pharmaceutical composition of any one of claims 1-18, wherein

~~39.~~the stability of recombinant AAV is determined by the infectivity of recombinant AAV; and/or :

(a) ~~The pharmaceutical composition of any one of claims 1-21, wherein the~~

(b) the stability of recombinant AAV is determined by the levels of aggregation of recombinant AAV; and/or

~~40.~~

~~41.(c) —The pharmaceutical composition of any one of claims 1-21, wherein~~ the stability of recombinant AAV is determined by the levels of free DNA released by the recombinant AAV particles.

26. The pharmaceutical composition of any one of claims 1-25~~41~~, wherein:

(a) the pharmaceutical composition is a liquid composition; ~~or~~

~~42.~~

(b) ~~The pharmaceutical composition of any one of claims 1-41, wherein~~ the pharmaceutical composition is a frozen composition; ~~or~~

~~43.~~

(c) ~~The pharmaceutical composition of any one of claims 1-41, wherein~~ the pharmaceutical composition is a lyophilized composition; ~~or~~

~~44.(d) the pharmaceutical composition is~~ a reconstituted lyophilized composition.

27. The pharmaceutical composition of any one of claims 1-26~~44~~, wherein

(a) the pharmaceutical composition has a property that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасlеral depot procedure; ~~and/or~~

~~45.~~

(b) ~~The pharmaceutical composition of any one of claims 1-44,~~ the pharmaceutical composition has a desired density that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасlеral depot procedure; ~~and/or~~

~~46.~~

~~47.(c) —The pharmaceutical composition of any one of claims 1-44,~~ the pharmaceutical composition has a desired osmolality that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасlеral depot procedure.

~~48.28.~~ The pharmaceutical composition of claim ~~27~~~~47~~, wherein the osmolality is 160-230 mOsm/kg H₂O.

~~49.~~29. The pharmaceutical composition of claim ~~-27~~47, wherein the osmolality is less than 600 mOsm/kg H₂O.

~~50.~~30. The pharmaceutical composition of any one of claims 1-26~~44~~, the pharmaceutical composition has a desired viscosity that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасcleral depot procedure.

~~51.~~31. The pharmaceutical composition of any one of claims 1-26~~44~~, the pharmaceutical composition is suitable for administration to the eye.

~~52.~~32. The pharmaceutical composition of claims 27, the pharmaceutical composition is suitable for suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасcleral depot procedure.

~~53.~~33. The pharmaceutical composition of any one of claims 1-32, wherein the pharmaceutical composition is capable of being stored at 4°C for 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months after having previously been stored at -80°C for about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, about 24 months.

~~54.~~34. ~~A method of treating or preventing a disease in a subject, comprising administering to the subject~~ Use of the pharmaceutical composition of any one of claims 1-33 in the manufacture of a medicament for the treatment or prevention of a disease in a subject wherein the medicament is to be administered to the subject.

~~55.~~35. ~~A method of treating a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR) comprising administering to the subject~~ Use of the pharmaceutical composition of any one of any one of claims 1-33 in the manufacture of a medicament for the treatment of a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR) wherein the medicament is to be administered to a subject.

~~56.36. A method of treating a subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), mucopolysaccharidosis type I (MPS I), mucopolysaccharidosis type II (MPS II), familial hypercholesterolemia (FH), homozygous familial hypercholesterolemia (HoFH), coronary artery disease, cerebrovascular disease, Duchenne muscular dystrophy, Limb Girdle muscular dystrophy, Becker muscular dystrophy and sporadic inclusion body myositis, or kallikrein-related disease comprising administering to the subject~~ Use of the pharmaceutical composition of any one of claims 1-33 in the manufacture of a medicament for the treatment of a subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), mucopolysaccharidosis type I (MPS I), mucopolysaccharidosis type II (MPS II), familial hypercholesterolemia (FH), homozygous familial hypercholesterolemia (HoFH), coronary artery disease, cerebrovascular disease, Duchenne muscular dystrophy, Limb Girdle muscular dystrophy, Becker muscular dystrophy and sporadic inclusion body myositis, or kallikrein-related disease wherein the medicament is to be administered to a subject.

~~57.37. The method-use~~ of any one of claims 34-36, wherein the pharmaceutical composition is to be administered by intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасlеral depot procedure.

~~58.38. The method-use~~ of any one of claims 34-37, wherein the subject is a human subject.

~~59.39. Use of the pharmaceutical composition of any one of claims 1-33 in the manufacture of a medicament for the treatment of~~ A method of treating a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR), the use~~method~~ comprising preparing the pharmaceutical composition of any one of claims 1 to 33, storing the pharmaceutical composition at -80 °C for a first period of time; (ii) thawing the pharmaceutical composition; and (iii) after thawing, storing the pharmaceutical composition at 4 °C for a second period of time.

~~60.40. The method-use~~ of claim 39, wherein the first period of time is about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

~~61.~~41. The ~~method~~use of claim 39, wherein the second period of time is about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months.

~~62.~~42. A kit comprising one or more containers and instructions for use, wherein the one or more containers comprise the pharmaceutical composition of any one of claims 1- 33.

~~63.~~43. The kit of claim 42, wherein at least one of the one or more containers is made from hydrophobically-coated glass vial.

44. The kit of claim 42~~;~~, wherein

(a) at least one of the one or more containers is made from Daikyo Crystal Zenith® (CZ) vial~~;~~, or

~~64.~~

(b) ~~The kit of claim 62, wherein~~ at least one of the one or more containers is made from TopLyo coated vial~~;~~, or

~~65.~~

~~66.~~(c) ~~The kit of claim 62, wherein~~ at least one of the one or more containers is made from Cyclo Olefin Polymer (COP).

~~67.~~45. A pharmaceutical composition comprising:

(a) a Construct II encoding an anti-human vascular endothelial growth factor (hVEGF) antibody,

(b) potassium chloride,

(c) potassium phosphate monobasic,

(d) sodium chloride,

(e) sodium phosphate dibasic anhydrous,

(f) sucrose, and

(g) poloxamer 188, polysorbate 20, or polysorbate 80, and

wherein the anti-hVEGF antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4, and a light chain comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3.

~~68~~.46. The pharmaceutical composition of claim 45, wherein the ionic strength of the pharmaceutical composition is in a range from about 60 mM to about 100 mM.

~~69~~.47. The pharmaceutical composition of any one of claims 45-46, wherein the pharmaceutical composition comprises:

- (a) potassium chloride at a concentration of 0.2 g/L,
- (b) potassium phosphate monobasic at a concentration of 0.2 g/L,
- (c) sodium chloride at a concentration of 5.84 g/L, and
- (d) sodium phosphate dibasic anhydrous at a concentration of 1.15 g/L.

~~70~~.48. The pharmaceutical composition of any one of claims 45-47, wherein the pharmaceutical composition comprises sucrose at a concentration in a range from 3% (weight/volume, 30 g/L) to 18% (weight/volume, 180 g/L).

~~71~~.49. The pharmaceutical composition of any one of claims 45-47, wherein the pharmaceutical composition comprises sucrose at a concentration of 4% (weight/volume, 40 g/L).

~~72~~.50. The pharmaceutical composition of any one of claims 45-49, wherein the pharmaceutical composition comprises poloxamer 188, polysorbate 20, or polysorbate 80; and wherein the poloxamer 188, polysorbate 20, or polysorbate 80 is at a concentration in a range from 0.0005% (weight/volume, 0.005 g/L) to 0.05% (weight/volume, 0.5 g/L).

~~73~~.51. The pharmaceutical composition of any one of claims 45-49, wherein the pharmaceutical composition comprises poloxamer 188, polysorbate 20, or polysorbate 80 at a concentration of 0.001% (weight/volume, 0.01 g/L).

~~74~~.52. The pharmaceutical composition of any one of claims 45-51, wherein the pH of the pharmaceutical composition is in a range from about 6.0 to about 9.0.

~~75~~.53. The pharmaceutical composition of any one of claims 45-51, wherein the pH of the pharmaceutical composition is about 7.4.

~~76~~.54. The pharmaceutical composition of any one of claims 45-53, wherein the osmolality of the pharmaceutical composition is in a range from about 200 mOsm/L to about 660 mOsm/L.
The pharmaceutical composition of any one of claims 45-54, wherein the Construct II comprises

the capsid from AAV8.

55. The pharmaceutical composition of any one of claims 45-54, wherein the Construct II is:

(a) -at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable to freeze/thaw cycles than the same Construct II in a reference pharmaceutical composition-; and/or

~~77.~~

~~78. The pharmaceutical composition of any one of claims 67-77, wherein the Construct II is at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same Construct II in a reference pharmaceutical composition when stored at – 20 °C for a period of time, wherein the period of time is about 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months-; and/or -~~

(b) ~~-The pharmaceutical composition of any one of claims 67-77, wherein the Construct II is~~

(c) at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same Construct II in a reference pharmaceutical composition when stored at – 80 °C for a period of time, wherein the period of time is about 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months-; and/or

~~79.~~

(d) ~~-The pharmaceutical composition of any one of claims 67-77, wherein the Construct II is at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same Construct II in a reference pharmaceutical composition when stored at room temperature for a period of time, wherein the period of time is about 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months-~~

~~80.~~

~~81.~~(c) ~~The pharmaceutical composition of any one of claims 67-77, wherein, the recombinant AAV is~~ at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%,

50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable than the same Construct II in a reference pharmaceutical composition when (i) stored at -80 °C for a first period of time; (ii) subsequently thawed; and (iii) after thawing, stored at 4 °C for a second period of time.

~~82.~~56. The pharmaceutical composition of claim-~~55~~~~81~~, wherein the first period of time is about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

~~83.~~57. The pharmaceutical composition of claim-~~55~~~~81~~, wherein the second period of time is about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months.

58. The pharmaceutical composition of any one of claims 45-55~~79~~, wherein

(a) the vector genome concentration of the Construct II after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the Construct II before being stored at -80°C for said period of time-; and/or

~~84.~~

(b) ~~The pharmaceutical composition of any one of claims 67-79, wherein~~ the vector genome concentration of the Construct II after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the Construct II before being stored at -20°C for said period of time-; and/or

~~85.~~

~~86.~~(c) ~~The pharmaceutical composition of any one of claims 67-79, wherein~~ the vector genome concentration of the Construct II after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the Construct II before being stored at 4°C for said period of time.

59. The pharmaceutical composition of any one of claims 45-55~~79~~, wherein

(a) the in vitro potency of the Construct II after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the Construct II before being stored at -80°C for said period of time-; and/or

~~87.~~

(b) ~~The pharmaceutical composition of any one of claims 67-79, wherein~~ the in vitro potency of the Construct II after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the Construct II before being stored at -20°C for said period of time-; and/or

88.

~~89.(c) The pharmaceutical composition of any one of claims 67-79, wherein t~~he in vitro potency of the Construct II after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the Construct II before being stored at 4°C for said period of time.

60. The pharmaceutical composition of any one of claims 45-55~~79~~, wherein

(a) the size distribution of the Construct II after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the Construct II before being stored at -80°C for said period of time~~;~~ and/or

~~90.~~

(b) ~~The pharmaceutical composition of any one of claims 67-79, wherein~~ the size distribution of the Construct II after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the Construct II before being stored at -20°C for said period of time~~;~~ and/or

~~91.~~

~~92.(c) The pharmaceutical composition of any one of claims 67-79, wherein~~ the size distribution of the Construct II after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the Construct II before being stored at 4°C for said period of time.

~~93.61.~~ The pharmaceutical composition of any one of claims 58 to ~~60~~92, wherein the period of time is about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

62. The pharmaceutical composition of any one of claims 55-57, wherein

(a) the stability of the Construct II is determined by the infectivity of recombinant AAV~~;~~ or

~~94.~~

(b) ~~The pharmaceutical composition of any one of claims 77-83, wherein~~ the stability of the Construct II is determined by the levels of aggregation of recombinant AAV~~;~~ or

~~95.~~

~~96.(c)~~ ~~The pharmaceutical composition of any one of claims 77-83, wherein~~ the stability of the Construct II is determined by the levels of free DNA released by the recombinant AAV particles.

~~63.~~ The pharmaceutical composition of any one of claims 45-62~~96~~, wherein

~~(a)~~ the pharmaceutical composition is in a hydrophobically-coated glass vial~~-, or~~

~~97.~~

~~(b)~~ ~~The pharmaceutical composition of any one of claims 67-96, wherein~~ the pharmaceutical composition is in a Cyclo Olefin Polymer (COP) vial~~-, or~~

~~98.~~

~~(c)~~ ~~The pharmaceutical composition of any one of claims 67-96, wherein~~ the pharmaceutical composition is in a Daikyo Crystal Zenith® (CZ) vial~~-, or~~

~~99.~~

~~100.(d)~~ ~~The pharmaceutical composition of any one of claims 67-96, wherein~~ the pharmaceutical composition is in a TopLyo coated vial.

~~101.64.~~ The pharmaceutical composition of any one of claims 45-63~~100~~, wherein the pharmaceutical composition consists of:

(a) the Construct II encoding an anti-human vascular endothelial growth factor (hVEGF) antibody,

(b) potassium chloride at a concentration of 0.2 g/L,

(c) potassium phosphate monobasic at a concentration of 0.2 g/L,

(d) sodium chloride at a concentration of 5.84 g/L,

(e) sodium phosphate dibasic anhydrous at a concentration of 1.15 g/L,

(f) sucrose at a concentration of 4% weight/volume (40 g/L),

(g) poloxamer 188, polysorbate 20, or polysorbate 80 at a concentration of 0.001% weight/volume (0.01 g/L), and

(h) water, and

wherein the anti-hVEGF antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4, and a light chain comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3.

~~102.65.~~ The pharmaceutical composition of claim 64, wherein the vector genome concentration

(VGC) of the pharmaceutical composition is about 3×10^9 GC/mL, about 1×10^{10} GC/mL, about 1.2×10^{10} GC/mL, about 1.6×10^{10} GC/mL, about 4×10^{10} GC/mL, about 6×10^{10} GC/mL, about 2×10^{11} GC/mL, about 2.4×10^{11} GC/mL, about 2.5×10^{11} GC/mL, about 3×10^{11} GC/mL, about 3.2×10^{11} GC/mL, about 6.2×10^{11} GC/mL, about 6.5×10^{11} GC/mL, about 1×10^{12} GC/mL, about 3×10^{12} GC/mL, about 2×10^{13} GC/mL. or about 3×10^{13} GC/mL.

66. The pharmaceutical composition of any one of claims 45-65, wherein

(a) the pharmaceutical composition has a property that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасcleral depot procedure; and/or

~~103.~~

(b) ~~The pharmaceutical composition of any one of claims 67-102,~~ the pharmaceutical composition has a desired density that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасcleral depot procedure; and/or

~~104.~~

~~105.~~ (c) ~~The pharmaceutical composition of any one of claims 67-102,~~ the pharmaceutical composition has a desired osmolality that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасcleral depot procedure.

~~106.~~ 67. The pharmaceutical composition of claim ~~66~~105 wherein the osmolality is 160-230 mOsm/kg H₂O.

~~107.~~ 68. The pharmaceutical composition of claim ~~66~~105, wherein the osmolality is less than 600 mOsm/kg H₂O.

~~108.~~ 69. The pharmaceutical composition of any one of claims 45-65, the pharmaceutical composition has a desired viscosity that is suitable for intravenous administration, subcutaneous administration, intramuscular injection, suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасcleral depot procedure.

70. The pharmaceutical composition of any one of claims 45-69, wherein

(a) the pharmaceutical composition is a liquid composition., or

~~109.~~

(b) ~~The pharmaceutical composition of any one of claims 67-108, wherein the~~
pharmaceutical composition is a frozen composition., or

~~110.~~

(c) ~~The pharmaceutical composition of any one of claims 67-108, wherein the~~
pharmaceutical composition is a lyophilized composition., or

~~111.~~ (d) the pharmaceutical composition is a reconstituted lyophilized composition.

~~112.~~ 71. The pharmaceutical composition of any one of claims 45-70~~111~~, wherein the pharmaceutical composition is capable of being stored at 4°C for 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months after having previously been stored at -80°C for about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, about 24 months.

~~113.~~ 72. ~~A method of treating a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR) comprising administering to the subject~~ Use of the pharmaceutical composition of any one of claims 45-70~~111~~ in the manufacture of a medicament for the treatment of a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR) wherein the medicament is to be administered to a subject.

~~114.~~ 73. The ~~method-use~~ of claim 72, wherein the pharmaceutical composition is to be administered by suprachoroidal injection, subretinal injection via transvitreal approach, subretinal administration via the suprachoroidal space, or a posterior juxtасcleral depot procedure.

~~115.~~ 74. The ~~method-use~~ of claim 72 or 73, wherein the subject is a human subject.

~~116.~~ 75. Use of the pharmaceutical composition of any one of claims 45-70~~111~~ in the manufacture of a medicament for the treatment of ~~A method of treating~~ a subject diagnosed with

nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR), the ~~method~~use comprising preparing the pharmaceutical composition of any one of claims 45-69, storing the pharmaceutical composition at -80 °C for a first period of time; (ii) thawing the pharmaceutical composition; and (iii) after thawing, storing the pharmaceutical composition at 4 °C for a second period of time.

~~117~~76. The ~~use~~method of claim ~~119~~78, wherein the first period of time is about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

~~118~~77. The ~~method~~use of claim ~~119~~78, wherein the second period of time is about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months.

~~119~~78. A kit comprising one or more containers and instructions for use, wherein the one or more containers comprise the pharmaceutical composition of any one of claims 45-65.

~~120~~79. The kit of claim 78, wherein at least one of the one or more containers is made from Cyclo Olefin Polymer (COP).

~~121~~80. A stable liquid pharmaceutical composition comprising:

- (a) a recombinant adeno-associated virus (rAAV),
- (b) a buffering agent comprising ionic salt and having an ionic strength between 60 mM and 150 mM,
- (d) sucrose, and
- (e) surfactant.

~~122~~81. The composition of claim 80, wherein the rAAV comprises AAV1, AAV2, AAV2tYF, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAVrh10, AAV.rh20, AAV.rh39, AAV.Rh74, AAV.RHM4-1, AAV.hu37, AAV.Anc80, AAV.Anc80L65, rAAV.7m8, AAV.PHP.B, AAV.PHP.eB, AAV2.5, AAV2tYF, AAV3B, AAV.LK03, AAV.HSC1, AAV.HSC2, AAV.HSC3, AAV.HSC4, AAV.HSC5, AAV.HSC6, AAV.HSC7, AAV.HSC8, AAV.HSC9, AAV.HSC10, AAV.HSC11, AAV.HSC12, AAV.HSC13, AAV.HSC14, AAV.HSC15, or AAV.HSC16.

~~123~~82. The composition of claim 80 or 81, wherein the composition comprises 3-16% sucrose.

~~124~~83. The composition of any one of claims 80-82, wherein the buffering agent maintains pH between about pH 6 to about pH 9 over the temperature range of - 20 °C to room temperature.

~~125~~84. The composition of any one of claims 80-83, wherein the composition comprises 4-6% sucrose.

~~126~~85. The composition of any one of claims 80-84, wherein the buffering agent has an ionic strength no greater than about 150 mM, about 145 mM, about 140 mM, about 135 mM, about 130 mM, about 125 mM, about 120 mM, about 115 mM, or about 110 mM.

~~127~~86. The composition of any one of claims 80-85, wherein the buffering agent has an ionic strength between about 60 mM and about 115 mM.

~~128~~87. The composition of any one of claims 80-86, wherein the buffering agent has an ionic strength between about 60 mM and about 110 mM.

~~129~~88. The composition of any one of claims 80-87, wherein the composition comprises between 60 mM and 100 mM NaCl.

~~130~~89. The composition of any one of claims 80-88, wherein the composition comprises 4-6% sucrose.

~~131~~90. The composition of any one of claims 80-89, wherein the composition is frozen to a temperature of about - 20 °C.

~~132~~91. The composition of any one of claims 80-90, wherein the frozen composition maintains pH between about pH 6 to about pH 9.

~~133~~92. The composition of any one of claims 80-91, wherein the buffering agent comprises one or more components selected from the group consisting of potassium phosphate monobasic, potassium phosphate, sodium chloride, sodium phosphate dibasic anhydrous, sodium phosphate hexahydrate, sodium phosphate monobasic monohydrate, sodium phosphate hexahydrate, sodium phosphate monobasic monohydrate, tromethamine, tris(hydroxymethyl)aminomethane

hydrochloride (Tris-HCl), amino acid, histidine, histidine hydrochloride (histidine-HCl), sodium succinate, sodium citrate, sodium acetate, and (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) (HEPES), sodium sulfate, magnesium sulfate, magnesium chloride 6-hydrate, calcium sulfate, potassium chloride, calcium chloride, and calcium citrate.

~~134.~~93. The composition of any one of claims 80-91, wherein the buffering agent comprises potassium chloride, potassium phosphate monobasic, sodium chloride, sodium phosphate dibasic anhydrous.

~~135.~~94. The composition of any one of claims 80-91, wherein the buffering agent comprises sodium chloride, and Tris hydrochloride.

~~136.~~95. The composition of any one of claims 80-92, wherein the surfactant is poloxamer 188, polysorbate 20, or polysorbate 80.

~~137.~~96. The composition of any one of claims 80-92, wherein the surfactant is poloxamer 188, polysorbate 20, or polysorbate 80; and wherein the poloxamer 188, polysorbate 20, or polysorbate 80 is at a concentration in a range from 0.0005% (weight/volume, 0.005 g/L) to 0.05% (weight/volume, 0.5 g/L).

~~138.~~97. The composition of any one of claims 80-92, wherein the surfactant is poloxamer 188, polysorbate 20, or polysorbate 80; and wherein the poloxamer 188, polysorbate 20, or polysorbate 80 is at a concentration of 0.001% (weight/volume, 0.01 g/L).

~~139.~~98. The composition of any one of claims 80-97, wherein the liquid pharmaceutical composition is further lyophilized.

~~140.~~99. The composition of any one of claims 80-97, wherein the liquid pharmaceutical composition is a reconstituted lyophilized powder.

100. The pharmaceutical composition of any one of claims 80-99, wherein

(a) the vector genome concentration of the recombinant AAV after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the recombinant AAV before being stored at -80°C for said period of time; ~~and/or~~

~~141.~~

- ~~(b) The pharmaceutical composition of any one of claims 121-140, wherein~~ the vector genome concentration of the recombinant AAV after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the recombinant AAV before being stored at -20°C for said period of time; and/or

~~142.~~

- ~~143.(c) The pharmaceutical composition of any one of claims 121-140, wherein~~ the vector genome concentration of the recombinant AAV after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the recombinant AAV before being stored at 4°C for said period of time.

101. The pharmaceutical composition of any one of claims 80-99, wherein

- (a) the in vitro potency of the recombinant AAV after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the recombinant AAV before being stored at -80°C for said period of time; and/or

~~144.~~

- ~~(b) The pharmaceutical composition of any one of claims 121-140, wherein~~ the in vitro potency of the recombinant AAV after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the recombinant AAV before being stored at -20°C for said period of time; and/or

~~145.~~

- ~~146.(c) The pharmaceutical composition of any one of claims 121-140, wherein the~~ in vitro potency of the recombinant AAV after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the recombinant AAV before being stored at 4°C for said period of time.

102. The pharmaceutical composition of any one of claims 80-99, wherein

- (a) the size distribution of the recombinant AAV after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the recombinant AAV before being stored at -80°C for said period of time; and/or

~~147.~~

- ~~(b) The pharmaceutical composition of any one of claims 121-140, wherein~~ the size distribution of the recombinant AAV after being stored at -20°C for a period of time is at

least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the recombinant AAV before being stored at -20°C for said period of time; and/or

~~148.~~

~~149.(c) The pharmaceutical composition of any one of claims 121-140, wherein~~ the size distribution of the recombinant AAV after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the recombinant AAV before being stored at 4°C for said period of time.

~~150.~~103. The pharmaceutical composition of any one of claims 100-102~~149~~, wherein the period of time is about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

~~151.~~104. The pharmaceutical composition of any one of claims 80-99, wherein the pharmaceutical composition is capable of being stored at 4°C for 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months after having previously been stored at -80°C for about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, about 24 months.

~~152.~~105. ~~A method of treating a disease of interest comprising administering to the subject~~Use of the pharmaceutical composition of any one of claims 80-99 in the manufacture of a medicament for treating a disease of interest, wherein the rAAV encodes a transgene that treats, or otherwise ameliorates, prevents or slows the progression of the disease of interest.

~~153.~~106. Use of the pharmaceutical composition of any one of claims 80-99 in the manufacture of a medicament for treatment of ~~A method of treating~~ a subject diagnosed with nAMD (wet AMD), dry AMD, retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR), the ~~method-use~~ comprising preparing the pharmaceutical composition of any one of claims 80-99, storing the pharmaceutical composition at -80 °C for a first period of time; (ii) thawing the pharmaceutical composition; and (iii) after thawing, storing the pharmaceutical composition at 4 °C for a second period of time.

~~154.~~107. The ~~use~~~~method~~~~composition~~ of claim 106 wherein the first period of time is about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

~~155.~~108. The ~~method~~~~use~~ of claim 106, wherein the second period of time is about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months.

~~156.~~109. A kit comprising one or more containers and instructions for use, wherein the one or more containers comprise the pharmaceutical composition of any one of claims 80-99.

~~157.~~110. A stable liquid formulation comprising the pharmaceutical composition of any one of claims 1-33, 45-70~~111~~ and 80-99.

111. A single unit dosage form comprising

(a) 3.2 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4 and 0.001% P188 in a volume of about 0.95 mL in a Cyclo Olefin Polymer (COP) vial, or

~~158.~~

(b) ~~—A single unit dosage form comprising~~ 3.2 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4 and 0.001% P188 in a volume of at least 0.8 mL in a COP vial, or

~~159.~~

(c) ~~—A single unit dosage form comprising~~ 3.2 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of about 0.95 mL in a COP vial, or

~~160.~~

~~161.~~(d) ~~—A single unit dosage form comprising~~ 3.2 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of at least 0.8 mL in a COP vial.

112. A single unit dosage form comprising

- (a) 6.5 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4 and 0.001% P188 in a volume of about 0.95 mL in a COP vial, [or](#)

~~162.~~

- (b) ~~A single unit dosage form comprising~~ 6.5 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, and 0.001% P188 in a volume of at least 0.8 mL in a COP vial, [or](#)

~~163.~~

- (c) ~~A single unit dosage form comprising~~ 6.5 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of about 0.95 mL in a COP vial, [or](#)

~~164.~~

- ~~165.~~ (d) ~~A single unit dosage form comprising~~ 6.5 x 10¹¹ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of at least 0.8 mL in a COP vial.

113. A single unit dosage form comprising

- (a) 2.5 x 10¹² GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, and 0.001% P188 in a volume of about 0.6 mL in a COP vial, [or](#)

~~166.~~

- ~~167.~~ (b) ~~A single unit dosage form comprising~~ 2.5 x 10¹² GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, and 0.001% P188 in a volume of at least 0.5 mL in a COP vial.

114. A single unit dosage form comprising

- (a) 3 x 10¹³ GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of about 0.6 mL in a COP vial, [or](#)

~~168.~~

~~169.(b) A single unit dosage form comprising~~ 3×10^{13} GC/mL of Construct II, 0.2 g/L potassium chloride, 0.2 g/L potassium phosphate monobasic, 8.01 g/L sodium chloride, 1.15 g/L sodium phosphate dibasic anhydrous, pH 7.4, 4% sucrose and 0.001% P188 in a volume of at least 0.5 mL in a COP vial.

115. The single unit dosage form of any one of claims 111-114~~169~~, which is:

(a) capable of being stored at 4°C for 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months; and/or

~~170.~~

(b) ~~The single unit dosage form of any one of claims 158-169, which is~~ capable of being stored at -80°C for about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, about 24 months; and/or

~~171.~~

~~172.(c) The single unit dosage form of any one of claims 158-169, which is~~ capable of being stored at 4°C for 1 weeks, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months after having previously been stored at -80°C for about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, about 24 months.

116. The single unit dosage form of any one of claims 111-114~~169~~, wherein

(a) the vector genome concentration of the Construct II after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the Construct II before being stored at -80°C for said period of time; and/or

~~173.~~

(b) ~~The single unit dosage form of any one of claims 158-169, wherein~~ the vector genome concentration of the Construct II after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the Construct II before being stored at -20°C for said period of time; and/or

~~174.~~

~~175.(c) The single unit dosage form of any one of claims 158-169, wherein~~ the vector genome concentration of the Construct II after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the vector genome concentration of the Construct II before being stored at 4°C for said period of time.

117. The single unit dosage form of any one of claims 111-114~~169~~, wherein

(a) the in vitro potency of the Construct II after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the Construct II before being stored at -80°C for said period of time; [and/or](#)

~~176.~~

(b) ~~The single unit dosage form of any one of claims 158-169, wherein~~ the in vitro potency of the Construct II after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the Construct II before being stored at -20°C for said period of time; [and/or](#)

~~177.~~

~~178.~~(c) ~~The single unit dosage form of any one of claims 158-169, wherein~~ the in vitro potency of the Construct II after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% of the in vitro potency of the Construct II before being stored at 4°C for said period of time.

~~118.~~ The single unit dosage form of any one of claims 111-114~~169~~, wherein

(a) the size distribution of the Construct II after being stored at -80°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the Construct II before being stored at -80°C for said period of time; [and/or](#)

~~179.~~

(b) ~~The single unit dosage form of any one of claims 158-169, wherein~~ the size distribution of the Construct II after being stored at -20°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the Construct II before being stored at -20°C for said period of time; [and/or](#)

~~180.~~

~~181.~~(c) ~~The single unit dosage form of any one of claims 158-169, wherein~~ the size distribution of the Construct II after being stored at 4°C for a period of time is at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the size distribution of the Construct II before being stored at 4°C for said period of time.

~~182.~~~~119.~~ The single unit dosage form of any one of claims 116-118~~181~~, wherein the period of time is about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, about 15 months, about 18 months, or about 24 months.

~~183.~~~~120.~~ A pre-filled syringe containing the single unit dosage form of any one of claims 111-120.

~~184.~~ A kit comprising the pre-filled syringe of claim 120.

121.

122. The pharmaceutical composition of any one of claims 1-33, 45-70, or 80-99 for use in therapy.