

What is claimed is:

1. A stable liquid formulation comprising:
aflibercept; and
an antibody that binds specifically to human angiopoietin-2 (hAng-2)
wherein the antibody comprises three heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) wherein
HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 3,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 4,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 5, and
three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 6,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 7, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 8.
2. The formulation of claim 1, wherein the antibody comprises
a heavy chain variable region (HCVR) comprising the amino acid sequence set forth in SEQ ID NO: 1; and
a light chain variable region (LCVR) comprising the amino acid sequence set forth in SEQ ID NO: 2.
3. The formulation of claim 2, wherein the antibody is nesvacumab; and wherein the formulation further comprises:
 - (i) a sodium phosphate buffer at pH of 6.2 ± 0.3 ;
 - (ii) polysorbate 20;
 - (iii) sodium chloride; and
 - (iv) sucrose.
4. The formulation of claim 3, wherein the aflibercept concentration is 40 mg/mL $\pm$ 1.5 mg/mL.

5. The formulation of claim 3, wherein the nesvacumab concentration is 10 – 120 mg/mL.

6. The formulation of claim 5, wherein the nesvacumab concentration is selected from the group consisting of 10 mg/mL, 20 mg/mL, 60 mg/mL, and 120 mg/mL.

7. The formulation of claim 3, comprising

5 – 100 mg/mL aflibercept;
10 – 120 mg/mL nesvacumab;
5 – 50 mM sodium phosphate, pH 6.2;
0.01 – 0.1% (w/v) polysorbate 20;
10 – 50 mM sodium chloride; and
1 – 20% (w/v) sucrose.

8. The formulation of claim 7, comprising:

40 mg/mL $\pm$ 6.0 mg/mL aflibercept,
10 mg/mL $\pm$ 1.5 mg/mL nesvacumab,
10 mM $\pm$ 1.5 mM sodium phosphate, pH 6.2 $\pm$ 0.3,
0.03% w/v $\pm$ 0.0045% polysorbate 20,
40 mM $\pm$ 6.0 mM sodium chloride, and
5% w/v $\pm$ 1.5% sucrose.

9. The formulation of claim 7, comprising

40 mg/mL $\pm$ 6.0 mg/mL aflibercept,
20 mg/mL $\pm$ 3.0 mg/mL nesvacumab,
10 mM $\pm$ 1.5 mM sodium phosphate, pH 6.2 $\pm$ 0.3,
0.03% w/v $\pm$ 0.0045% polysorbate 20,
40 mM $\pm$ 6.0 mM sodium chloride, and

5% w/v $\pm$ 1.5% sucrose.

10. The formulation of claim 7, comprising

40 mg/mL $\pm$ 6.0 mg/mL aflibercept,
60 mg/mL $\pm$ 9.0 mg/mL nesvacumab,
10 mM $\pm$ 1.5 mM sodium phosphate, pH 6.2 $\pm$ 0.3,
0.03% w/v $\pm$ 0.0045% polysorbate 20,
40 mM $\pm$ 6.0 mM sodium chloride, and
5% w/v $\pm$ 1.5% sucrose.

11. The formulation of claim 7, comprising

40 mg/mL $\pm$ 6.0 mg/mL aflibercept,
120 mg/mL $\pm$ 18.0 mg/mL nesvacumab,
10 mM $\pm$ 1.5 mM, pH 6.2 $\pm$ 0.3 sodium phosphate,
0.03% w/v $\pm$ 0.0045% polysorbate 20,
40 mM $\pm$ 6.0 mM sodium chloride, and
5% w/v $\pm$ 1.5% sucrose.

12. Use of the formulation of claim 1 in the manufacture of a medicament for treating a vascular eye disease or disorder in a subject.

13. The use of claim 12, wherein 2 mg aflibercept and 6 mg of the antibody in the formulation is to be intravitreally administered to the subject in need thereof.

14. The use of claim 12 wherein:
the aflibercept concentration is 40 mg/mL $\pm$ 6.0 mg/mL,
the antibody concentration is 120 mg/mL $\pm$ 18.0 mg/mL or 60 mg/mL $\pm$ 9.0 mg/mL,
wherein the antibody is nesvacumab,

the sodium phosphate concentration is $10 \text{ mM} \pm 1.5 \text{ mM}$, $\text{pH } 6.2 \pm 0.3$,
the polysorbate 20 concentration is $0.03\% \text{ w/v} \pm 0.0045\%$,
the sodium chloride concentration is $40 \text{ mM} \pm 6.0 \text{ mM}$, and
the sucrose concentration is $5\% \text{ w/v} \pm 1.5\%$,
in said formulation.

15. The use of claim 14, wherein the formulation is to be administered to the subject every 4 weeks.

16. The use of claim 14, wherein the eye disease or disorder is selected from the group consisting of diabetic retinopathy, diabetic macular edema, age-related macular degeneration, retinal neovascularization, central retinal vein occlusion, branched retinal vein occlusion, polypoidal choroidal vasculopathy, and choroidal neovascularization.

17. The use of claim 16, wherein the eye disease or disorder is age-related macular degeneration.

18. The use of claim 16, wherein the eye disease or disorder is diabetic macular edema.

19. The use of claim 16, wherein the eye disease or disorder is diabetic retinopathy.

20. The use of claim 16, wherein the eye disease or disorder is central retinal vein occlusion.

21. Use of the formulation of claim 1 in the manufacture of a medicament for inhibiting retinal angiogenesis, inhibiting retinal neovascularization, inhibiting vascular leak and/or suppressing vascular leak in a subject.

22. The use of claim 21 wherein:
the aflibercept concentration is $40 \text{ mg/mL} \pm 6.0 \text{ mg/mL}$,

the antibody concentration is $120 \text{ mg/mL} \pm 18.0 \text{ mg/mL}$ or $60 \text{ mg/mL} \pm 9.0 \text{ mg/mL}$,
wherein the antibody is nesvacumab,
the sodium phosphate concentration is $10 \text{ mM} \pm 1.5 \text{ mM}$, pH 6.2 ± 0.3 ,
the polysorbate 20 concentration is $0.03\% \text{ w/v} \pm 0.0045\%$,
the sodium chloride concentration is $40 \text{ mM} \pm 6.0 \text{ mM}$, and
the sucrose concentration is $5\% \text{ w/v} \pm 1.5\%$,
in said formulation.

23. The use of claim 22, wherein the retinal angiogenesis is associated with an eye disease or disorder selected from the group consisting of diabetic retinopathy, diabetic macular edema, age-related macular degeneration, retinal neovascularization, central retinal vein occlusion, branched retinal vein occlusion, polypoidal choroidal vasculopathy, and choroidal neovascularization.

24. The use of claim 23, wherein the eye disease or disorder is age-related macular degeneration.

25. The use of claim 23, wherein the eye disease or disorder is diabetic macular edema.

26. The use of claim 23, wherein the eye disease or disorder is diabetic retinopathy.

27. The use of claim 23, wherein the eye disease or disorder is central retinal vein occlusion.

28. The use of claim 22, wherein the pharmaceutical formulation is to be administered to the subject every 4 weeks.