We claim:

1. Use of a VEGF receptor fusion protein in the manufacture of a medicament:
- for treating or preventing an angiogenic eye disorder, neovascular age related macular degeneration (nAMD), diabetic retinopathy (DR) and/or diabetic macular edema (DME), in a subject in need thereof,
- for improving best corrected visual acuity in a subject in need thereof with nAMD, DR and/or DME; or
- for promoting retinal drying in a subject with an angiogenic eye disorder, nAMD, DR and/or DME in need thereof;
wherein the medicament is to be administered to an eye of the subject, as one or more doses of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein about once every 8-24, 12-24, 16-24, 20-24, 21-24, 21, 22, 23 or 24 weeks.

2. The use of claim 1, wherein the medicament is for treating or preventing an angiogenic eye disorder, neovascular age related macular degeneration (nAMD), diabetic retinopathy (DR) and/or diabetic macular edema (DME), in a subject in need thereof, wherein the medicament is to be administered to an eye of the subject,
as a single initial dose of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein, followed by
one or more secondary doses of about 8 mg or more of the VEGF receptor fusion protein, followed by
one or more tertiary doses of about 8 mg or more of the VEGF receptor fusion protein;
wherein each secondary dose is to be administered about 2, 3, 4 or 2-4 weeks after the immediately preceding dose; and
wherein each tertiary dose is to be administered about 8-24, 12-24, 16-24, 20-24, 21-24, 21, 22, 23 or 24 weeks after the immediately preceding dose.

3. The use of any one of claims 1-2, wherein the medicament is for treating or preventing an angiogenic eye disorder, neovascular age related macular degeneration (nAMD), diabetic retinopathy (DR) and/or diabetic macular edema (DME), in a subject in need thereof, wherein the medicament is to be administered to an eye of the subject,
as a single initial dose of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein, followed by

two secondary doses of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein, followed by
one or more tertiary doses of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein;
wherein each secondary dose is to be administered about 4 weeks after the immediately preceding dose; and
wherein each tertiary dose is to be administered about 8-24, 12-24, 16-24, 20-24, 21-24, 21, 22, 23 or 24 weeks after the immediately preceding dose.

4. Use of a VEGF receptor fusion protein in the manufacture of a medicament for treating or preventing an angiogenic eye disorder, neovascular age related macular degeneration (nAMD), diabetic retinopathy and/or diabetic macular edema, in a subject in need thereof, wherein the medicament is to be administered to an eye of the subject, as about 3 doses of about 8 mg (±0.8 mg) VEGF receptor fusion protein in a formulation that comprises about 114.3 mg/ml VEGF receptor fusion protein at an interval of about once every 4 weeks; wherein after said 3 doses, the medicament is to be administered as one or more doses of the VEGF receptor fusion protein at an interval which is lengthened up to about 24 weeks.

5. Use of a VEGF receptor fusion protein in the manufacture of a medicament for slowing the clearance of free aflibercept from the ocular compartment after an intravitreal injection relative to the rate of clearance of aflibercept from the ocular compartment after an intravitreal injection of 2 mg or ≤4 mg aflibercept, wherein the VEGF receptor fusion protein is aflibercept, and
the medicament is to be intravitreally injected into an eye of a subject in need thereof,
as a single initial dose of about 8 mg (±0.8 mg) or more of aflibercept, followed by
one or more secondary doses of about 8 mg (±0.8 mg) or more of the aflibercept, followed by
one or more tertiary doses of about 8 mg (±0.8 mg) or more of the aflibercept;
wherein each secondary dose is to be administered about 2 to 4 weeks after the immediately preceding dose; and
wherein each tertiary dose is to be administered about 8-24, 12-24, 16-24, 20-24, 21-24, 21, 22, 23 or 24 weeks after the immediately preceding dose.

6. The use of any one of claims 1-5 wherein the clearance of free aflibercept from the ocular compartment is about 34% slower than that from the ocular compartment after an intravitreal injection of 2 or ≤4 mg aflibercept.

7. The use of any one of claims 1-6 wherein the clearance of free aflibercept from the ocular compartment is about 0.37-0.46 mL/day or 0.41 mL/day after an intravitreal injection of ≥8 mg (±0.8 mg) aflibercept.

8. Use of a VEGF receptor fusion protein in the manufacture of a medicament for increasing the duration of efficacy and/or the time for the amount of free aflibercept to reach the lower limit of quantitation (LLOQ) in the ocular compartment of a subject after an intravitreal injection of aflibercept, relative to the time to reach LLOQ of the amount of free aflibercept in the ocular compartment of a subject after an intravitreal injection of about 2 mg or ≤4 mg aflibercept, wherein the VEGF receptor fusion protein is aflibercept, and the medicament is to be intravitreally injected into an eye of a subject in need thereof,
as a single initial dose of about 8 mg (±0.8 mg) or more of aflibercept, followed by
one or more secondary doses of about 8 mg (±0.8 mg) or more of the aflibercept, followed by
one or more tertiary doses of about 8 mg (±0.8 mg) or more of the aflibercept;
wherein each secondary dose is to be administered about 2 to 4 weeks after the immediately preceding dose; and
wherein each tertiary dose is to be administered about 8-24, 12-24, 16-24, 20-24, 21-24, 21, 22, 23 or 24 weeks after the immediately preceding dose.

9. The use of any one of claims 1-8 wherein the duration of efficacy and/or the time for the amount of free aflibercept to reach the lower limit of quantitation (LLOQ) in the ocular compartment of a subject after said intravitreal injection of aflibercept is increased by about 5 or 6 weeks, relative to the time to reach LLOQ of the amount of free aflibercept in the ocular compartment of a subject after an intravitreal injection of about 2 or ≤4 mg aflibercept.

10. The use of any one of claims 1-9 wherein the time for the amount of free aflibercept to reach the lower limit of quantitation (LLOQ) in the ocular compartment of a subject after said intravitreal injection of aflibercept is increased by more than about 1, 2, 1.2 or 1.3 weeks relative to the time to reach LLOQ of free aflibercept in the ocular compartment of a subject after an intravitreal injection of about 2 or ≤4 mg aflibercept.

11 The use of any one of claims 1-10 wherein the time for the amount for free aflibercept to reach the lower limit of quantitation (LLOQ) in the ocular compartment of a subject after said intravitreal injection of ≥8 mg (±0.8 mg) aflibercept is about 15 weeks.

12. The use of any one of claims 1-11 wherein the time for the amount of free aflibercept to reach the lower limit of quantitation (LLOQ) in the ocular compartment of a subject after said intravitreal injection of ≥8 mg (±0.8 mg) aflibercept is greater than about 8, 8.7, 8.71, 9, 9.2, 9.21 or 10 weeks.

13. Use of a VEGF receptor fusion protein in the manufacture of a medicament for increasing the time for free aflibercept to reach the lower limit of quantitation (LLOQ) in the plasma of a subject after an intravitreal injection of aflibercept relative to the time to reach LLOQ of free aflibercept in the plasma of a subject after an intravitreal injection of about 2 or ≤4 mg aflibercept, wherein the VEGF receptor fusion protein is aflibercept, and the medicament is to be intravitreally injected into an eye of a subject in need thereof,
as a single initial dose of about 8 mg (±0.8 mg) or more of aflibercept, followed by
one or more secondary doses of about 8 mg (±0.8 mg) or more of the aflibercept, followed by
one or more tertiary doses of about 8 mg (±0.8 mg) or more of the aflibercept;
wherein each secondary dose is to be administered about 2 to 4 weeks after the immediately preceding dose; and
wherein each tertiary dose is to be administered about 8-24, 12-24, 16-24, 20-24, 21-24, 21, 22, 23 or 24 weeks after the immediately preceding dose.

14. The use of claim 13 wherein said LLOQ of free aflibercept measured in plasma is about 0.0156 mg/L.

15. The use of any one of claims 1-14 wherein the time for free aflibercept to reach the lower limit of quantitation (LLOQ) in the plasma of a subject after said intravitreal injection of aflibercept is increased by about 2 weeks relative to the time to reach LLOQ of free aflibercept in the plasma of a subject after an intravitreal injection of about 2 mg aflibercept.

16. The use of any one of claims 1-15 wherein the time for free aflibercept to reach the lower limit of quantitation (LLOQ) in the plasma of a subject after said intravitreal injection of ≥8 mg (±0.8 mg) aflibercept is about 3, 3.5, 3.8 or 4 weeks.

17. The use of any one of claims 1-16 wherein the time for free aflibercept to reach the lower limit of quantitation (LLOQ) in the plasma of a subject after said intravitreal injection of ≥8 mg (±0.8 mg) aflibercept is greater than about 1.5 or 1.6 weeks.

18. The use of any one of claims 5-17 wherein ≤4mg is about 2 mg or 2-4 mg.

19. The use of any one of claims 13-18 wherein the subject suffers from an angiogenic eye disorder, neovascular age related macular degeneration, diabetic retinopathy and/or diabetic macular edema.

20. The use of any one of claims 1-19 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation comprising histidine-based buffer.

21. The use of any one of claims 1-20 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation comprising arginine.

22.The use of any one of claims 1-21 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation having a pH of about 5.8.

23.The use of any one of claims 1-22 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation comprising a sugar or polyol.

24.The use of any one of claims 1-23 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation comprising a sucrose.

25.The use of any one of claims 1-24 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation wherein the aflibercept has less than about 3.5% high molecular weight species immediately after manufacture and purification and/or less than or equal to about 6% high molecular weight species after storage for about 24 months at about 2-8°C.

26. The use of any one of claims 1-25 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation comprising an aqueous pharmaceutical formulation comprising: at least about 100 mg/ml of a VEGF receptor fusion protein comprising two polypeptides that each

comprises an immunoglobin-like (Ig) domain 2 of VEGFR1, an Ig domain 3 of VEGFR2, and a multimerizing component; about 10-100 mM L-arginine; sucrose; a histidine-based buffer; and a surfactant; wherein the formulation has a pH of about 5.0 to about 6.8; wherein the VEGF receptor fusion protein has less than about 3.5% high molecular weight species immediately after manufacture and purification and/or less than or equal to about 6% high molecular weight species after storage for about 24 months at about 2-8°C.

27. Use of a VEGF receptor fusion protein in the manufacture of a medicament:
- for treating or preventing an angiogenic eye disorder, neovascular age related macular degeneration (nAMD), diabetic retinopathy (DR) and/or diabetic macular edema (DME), in a subject in need thereof,
- for improving best corrected visual acuity in a subject in need thereof with nAMD, DR and/or DME; or
- for promoting retinal drying in a subject with an angiogenic eye disorder, nAMD, DR and/or DME in need thereof;
wherein the medicament is to be administered to an eye of the subject,
as a single initial dose of about 8 mg (±0.8 mg) or more of a VEGF receptor fusion protein, followed by
one or more secondary doses of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein, followed by
one or more tertiary doses of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein;
wherein each secondary dose is to be administered about 2, 3, 4 or 2-4 weeks after the immediately preceding dose; and
each tertiary dose is to be administered about 8-23, 20, 21, 22, or 23 weeks after the immediately preceding dose, wherein if the subject exhibits:
1. <5 letter loss in BCVA;
2. CRT <300 μm or <320 μm;
3. No fluid at the central subfield on OCT; and/or
4. No new onset foveal hemorrhage or foveal neovascularization;
lengthening the interval between tertiary doses by one or more weeks.

28. The use of claim 27 wherein the interval between tertiary doses was lengthened one or more times prior.

29. The use of claim 27-28 wherein the interval between tertiary doses was lengthened one or more times prior,
to 24 weeks;
or, from:
8 weeks to 12, 16 or 20 weeks;
12 weeks to 16 or 20; and/or
16 weeks to 20 weeks.

30. The use of any one of claims 27-29 wherein lengthening the interval between tertiary doses by one or more weeks is lengthening the interval between tertiary doses by one or more 4 week increments.

31. The use of any one of claims 27-30 wherein said 8-23 weeks is 8, 12, 16 or 20 weeks.

32. The use of claim 31 wherein said 8-23 weeks is 20 weeks.

33. The use of any one of claims 27-32 wherein said interval between tertiary doses is lengthened if the subject exhibits
1. <5 letter loss in BCVA; and
2. CRT <300 μm or <320 μm.

34. The use of claim 33 wherein the subject has DR and/or DME.

35. The use of any one of claims 27-32 wherein said interval between tertiary doses is lengthened if the subject exhibits
1. BCVA loss <5 letters; and
2. No fluid at the central subfield; and
3. No new onset foveal hemorrhage or foveal neovascularization.

36. The use of claim 35 wherein the subject has nAMD.

37. The use of any one of claims 27-36 wherein said:

- <5 letter loss in BCVA is <5 letter loss in BCVA from week 12 from treatment initiation;

- CRT <300 μm or <320 μm is from SD-OCT;
- CRT <300 μm is from Cirrus SD-OCT;
- CRT <320 μm is from Spectralis SD-OCT; and/or
- No fluid at the central subfield is on OCT.

38. Use of a VEGF receptor fusion protein in the manufacture of a medicament:
- for treating or preventing an angiogenic eye disorder, neovascular age related macular degeneration (nAMD), diabetic retinopathy (DR) and/or diabetic macular edema (DME), in a subject in need thereof,
- for improving best corrected visual acuity in a subject in need thereof with nAMD, DR and/or DME; or
- for promoting retinal drying in a subject with an angiogenic eye disorder, nAMD, DR and/or DME in need thereof;
wherein the medicament is to be administered to an eye of the subject,
as a single initial dose of about 8 mg (±0.8 mg) or more of a VEGF receptor fusion protein, followed by
one or more secondary doses of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein, followed by
one or more tertiary doses of about 8 mg (±0.8 mg) or more of the VEGF receptor fusion protein;
wherein each secondary dose is to be administered about 2 to 4 weeks after the immediately preceding dose; and
wherein each tertiary dose is to be administered about 8-24, 12-24, 16-24, 20-24, 21-24, 21, 22, 23 or 24 weeks after the immediately preceding dose wherein if the subject exhibits

1. BCVA loss >5 or >10 letters;
2. >25 μm or >50 μm increase in central retinal thickness (CRT);
3. new foveal hemorrhage;
4. new foveal neovascularization; and/or
5. persistent or worsening DME

shortening the interval between tertiary doses by one or more weeks.

39. The use of claim 38 wherein shortening the interval between tertiary doses by one or more weeks is shortening the interval between tertiary doses by one or more 4 week increments.

40. The use of any one of claims 38-39 wherein said interval between tertiary doses is shortened if the subject exhibits
1. >10 letter loss in BCVA in association with persistent or worsening DME; and
2. >50 μm increase in CRT.

41. The use of claim 40 wherein the subject has DR and/or DME.

42. The use of any one of claims 38-39 wherein said interval between tertiary doses is lengthened if the subject exhibits
1. BCVA loss >5 letters, and
2. >25 μm increase in central retinal thickness (CRT) or new foveal hemorrhage or new foveal neovascularization.

43. The use of claim 42 wherein the subject has nAMD.

44. The use of any one of claims 38-43 wherein said:

- >10 letter loss in BCVA, in association with persistent or worsening DME is >10 letter loss in BCVA from week 12 from treatment initiation or 4 weeks after the last secondary dose, in association with persistent or worsening DME;
- >50 μm increase in CRT is from week 12 from treatment initiation
- BCVA loss >5 letters is from week 12 from treatment initiation, and
- >25 μm increase in central retinal thickness (CRT) or new foveal hemorrhage or new foveal neovascularization is >25 μm increase in central retinal thickness (CRT) from week 12 from treatment initiation or new foveal hemorrhage or new foveal neovascularization.

45. The use of any one or claims 1-44 wherein by week 96 from treatment initiation, the subject exhibits one or more of:

- A BCVA improvement of about 6, 7, 8 or 9 letters;
- A BCVA improvement of 39, 40, 41, 42, 43, 44, 45, 46 or 47 letters;
- Does not lose 5 or more, 10 or more or 15 or more letters BCVA;
- A BCVA of about 65, 66, 67, 68, 69, 70, 71, 72 or 73 letters;
- gains 5 or more, 10 or more or 15 or more letters BCVA;
- 2 or more step improvement in DRSS;

- A decrease in CRT of about 149, 152, 155; 156; 157; 158; 159; 160; 161; 162; 163; 164; 165; 166; 167; 168; 169; 170; 171; 172; 173; 174; 175; 176; 177; 178; 179; 180; 181; 182; 183; 184; 185, 194 micrometers;
- Between week 48 and week 96 of treatment, further improvement or maintenance of BCVA improvement from baseline ± 1 or 2 letters;
- Between week 48 and week 96 of treatment, maintenance of BCVA or about 66 ± 2 letters;
- Between week 48 and week 96 of treatment, maintenance of a fluid-free retinal center subfield;
- A CRT of about 267; 268; 269; 270; 271; 272; 273; 274; 275; 276; 277; 278; 279; 280; 281; 282; 283; 284; 285; 286; 287; 288; 289; 290; 291; 292; 293; 294; 295; 296; 297; 298; 299; 300; 301; 302; 303; or 304 micrometers;
- Between week 48 and week 96 of treatment further reduction or maintenance of central subfield thickness or central retinal thickness reduction from baseline ± 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12; micrometers;
- No IRF;
- No SRF;
- No IRF and no SRF;
- No significant change in intraocular pressure;
- No significant change in systolic blood pressure; and/or
- No significant change in diastolic blood pressure.

46. The use of claim 45 wherein the subject has DR and/or DME.

47. The use of any one or claims 1-46 wherein by week 96 from treatment initiation, the subject exhibits one or more of:

- A BCVA improvement of about 5, 6 or 7 letters;
- A BCVA improvement of 43, 44, 45, 46, 47 or 48 letters;
- A BCVA of 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93 or 94 letters;
- Does not lose 5 or more, 10 or more or 15 or more letters BCVA;
- gains 5 or more, 10 or more or 15 or more letters BCVA;
- 2 or more step improvement in DRSS;

- A decrease in CRT of about 12; 13; 14; 15; 16; 17; 18; 19; 20; 21; 22; 23; 24; 25; 26; 27; 28; 29; 30; 31; 32; 33; 34; 35; 36; 37; 38; 39; 40; 41; 42; 43; 44; 45; 46; 47; 48; 49; 50; 51; 52; 53; 54; 55; 56; 57; 58; 59; 60; 61; 62; 63; 64; 65; 66; 67; 68; 69; 70; 71; 72; 73; 74; 75; 76; 77; 78; 79; 80; 81; 82; 83; 84; 85; 86; 87; 88; 89; 90; 91; 92; 93; 94; 95; 96; 97; 98; 99; 100; 101; 102; 103; 104; 105; 106; 107; 108; 109; 110; 111; 112; 113; 114; 115; 116; 117; 118; 119; 120; 121; 122; 123; 124; 125; 126; 127; 128; 129; 130; 131; 132; 133; 134; 135; 136; 137; 138; 139; 140; 141; 142; 143; 144; 145; 146; 147; 148; 149; 150; 151; 152; 153; 154; 155; 156; 157; 158; 159; 160; 161; 162; 163; 164; 165; 166; 167; 168; 169; 170; 171; 172; 173; 174; 175; 176; 177; 178; 179; 180; 181; 182; 183; 184; 185; 186; 187; 188; 189; 190; 191; 192; 193; 194; 195; 196; 197; 198; 199; 200; 201; 202; 203; 204; 205; 206; 207; 208; 209; 210; 211; 212; 213; 214; 215; 216; 217; 218; 219; 220; 221; 222; 223; 224; 225; 226; 227; 228; 229; 230; 231; 232; 233; 234; 235; 236; 237; 238; 239; 240; 241; 242; 243; 244; 245; 246; 247; 248; 249; 250; 251; 252; 253; 254; 255; 256; 257; 258; 259; 260; 261; 262; 263; 264; 265; 266; 267; 268; 269; 270; 271; 272; 273; 274; 275; 276; 277; 278; 279; 280; 281; 282; 283; 284; 285; 286; 287; 288; 289; 290; 291; 292; 293; or 294 micrometers;
- A CRT of about 156; 157; 158; 159; 160; 161; 162; 163; 164; 165; 166; 167; 168; 169; 170; 171; 172; 173; 174; 175; 176; 177; 178; 179; 180; 181; 182; 183; 184; 185; 186; 187; 188; 189; 190; 191; 192; 193; 194; 195; 196; 197; 198; 199; 200; 201; 202; 203; 204; 205; 206; 207; 208; 209; 210; 211; 212; 213; 214; 215; 216; 217; 218; 219; 220; 221; 222; 223; 224; 225; 226; 227; 228; 229; 230; 231; 232; 233; 234; 235; 236; 237; 238; 239; 240; 241; 242; 243; 244; 245; 246; 247; 248; 249; 250; 251; 252; 253; 254; 255; 256; 257; 258; 259; 260; 261; 262; 263; 264; 265; 266; 267; 268; 269; 270; 271; 272; 273; 274; 275; 276; 277; 278; 279; 280; 281; 282; 283; 284; 285; or 286 micrometers;
- A choroidal neovascularization size decrease of about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 mm^2;
- A choroidal neovascularization size of about 0, 1, 2 or 3 mm^2;
- No leakage observed on fluorescein angiography;
- Total lesion size of about 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 mm^2;
- Decrease in total lesion size of about 0, 0.1, 0.2 or 0.3 mm^2;
- A NEI-VFQ-25 total score of about 80;
- A NEI-VFQ-25 total score change from baseline of about 2 or 3;
- No IRF;
- No SRF;

- No IRF and no SRF;
- No significant change in pre-dose intraocular pressure;
- No significant change in systolic blood pressure; and/or
- No significant change in diastolic blood pressure.

48. The use of claim 47 wherein the subject has nAMD.

49. The use of any one of claims 1-48 wherein a subject having any one or more of
ocular or periocular infection;
active intraocular inflammation; and/or
hypersensitivity;
is excluded from administration of VEGF receptor fusion protein to the eye.

50. The use of claim 49, wherein
the subject is to be evaluated for:
ocular or periocular infection;
active intraocular inflammation; and/or
hypersensitivity;
and the subject is to be excluded from said administration if any one or more if found in the subject.

51. The use of any one of claims 49-50, wherein the subject is to be monitored during said treatment or prevention for conjunctival hemorrhage, cataract, vitreous detachment, vitreous floaters, corneal epithelium defect and/or increased intraocular pressure.

52. The use of any one of claims 1-51 wherein, prior to each administration, providing
• one single-dose glass vial having a protective plastic cap and a stopper containing an aqueous formulation comprising 8 mg (±0.8 mg) VEGF receptor fusion protein in about 70 microliters;
• one 18-gauge x 1½-inch, 5-micron, filter needle that includes a tip and a bevel;
• one 30-gauge x ½-inch injection needle; and
• one 1-mL Luer lock syringe having a graduation line marking for 70 microliters of volume;
packaged together; then

(1) visually inspecting the aqueous formulation in the vial and, if particulates, cloudiness, or discoloration are visible, then using another vial of aqueous formulation containing the VEGF receptor fusion protein;
(2) removing the protective plastic cap from the vial; and
(3) cleaning the top of the vial with an alcohol wipe; then
using aseptic technique:
(4) removing the 18-gauge x 1½-inch, 5-micron, filter needle and the 1 mL syringe from their packaging;
(5) attaching the filter needle to the syringe by twisting it onto the Luer lock syringe tip;
(6) pushing the filter needle into the center of the vial stopper until the needle is completely inserted into the vial and the tip touches the bottom or a bottom edge of the vial;
(7) withdrawing all of the VEGF receptor fusion protein vial contents into the syringe, keeping the vial in an upright position, slightly inclined, while ensuring the bevel of the filter needle is submerged into the liquid;
(8) continuing to tilt the vial during withdrawal keeping the bevel of the filter needle submerged in the formulation;
(9) drawing the plunger rod sufficiently back when emptying the vial in order to completely empty the filter needle;
(10) removing the filter needle from the syringe and disposing of the filter needle;
(11) removing the 30-gauge x ½-inch injection needle from its packaging and attaching the injection needle to the syringe by firmly twisting the injection needle onto the Luer lock syringe tip;
(12) holding the syringe with the needle pointing up, and checking the syringe for bubbles, wherein if there are bubbles, gently tapping the syringe with a finger until the bubbles rise to the top; and
(13) slowly depressing the plunger so that the plunger tip aligns with the graduation line that marks 70 microliters on the syringe.

53. The use of any one of claims 1-52 wherein injection of VEGF receptor fusion protein is to be performed under controlled aseptic conditions, which comprise surgical hand disinfection and the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent) and anesthesia and a topical broad–spectrum microbicide are to be administered prior to the injection.

54. The use of any one of claims 1-53, wherein the VEGF receptor fusion protein comprises amino acids 27-457 of the amino acid sequence set forth in SEQ ID NO: 2.

55. The use of any one of claims 1-53, wherein the VEGF receptor fusion protein is selected from the group consisting of: aflibercept and conbercept.

56. The use of any one of claims 1-53, wherein the VEGF receptor fusion protein:
(i) comprises two polypeptides that comprise (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO: 2; (2) a VEGFR2 component comprising amino acids 130-231 of SEQ ID NO: 2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO: 2;
(ii) comprises two polypeptides that comprise an immunoglobin-like (Ig) domain 2 of VEGFR1, an Ig domain 3 of a VEGFR2, and a multimerizing component;
(iii) comprises two polypeptides that comprise an immunoglobin-like (Ig) domain 2 of VEGFR1, an Ig domain 3 of VEGFR2, an Ig domain 4 of VEGFR2 and a multimerizing component; or
(iv) comprises two VEGFR1R2-FcΔC1(a) polypeptides encoded by the nucleic acid sequence of SEQ ID NO: 1.

57. The use of claim 1-53, wherein the VEGF receptor fusion protein comprises two polypeptides that comprise an immunoglobin-like (Ig) domain 2 of VEGFR1, an Ig domain 3 of a VEGFR2, and a multimerizing component.

58. The use of any one of claims 1-57, wherein the VEGF receptor fusion protein is in an aqueous pharmaceutical formulation selected from the group consisting of A-KKKK.

59. The use of any one of claims 1-58 wherein said VEGF receptor fusion protein is in an aqueous pharmaceutical formulation comprising about 114.3 mg/ml VEGF receptor fusion protein.

60. The use of any one of claims 1-59, wherein the medicament containing the VEGF receptor fusion protein is to be administered to both eyes of the subject.

61. The use of any one of claims 1-60, wherein the VEGF receptor fusion protein is to be administered from a syringe or pre-filled syringe.

62. The use of claim 61, wherein the syringe or pre-filled syringe is glass or plastic, and/or sterile.

63. The use of any one of claims 1-62 wherein the VEGF receptor fusion protein is to be intravitreally injected with a 30 gauge × ½-inch sterile injection needle.

64. The use of any one of claims 1-63 wherein the subject has previously received one or more doses of 2 mg VEGF receptor fusion protein.

65. The use of any one of claims 1-64 wherein one or more further doses of VEGF receptor fusion protein are to be administered.

66. The use of any one of claims 5-26, 64 or 65 wherein 2 mg VEGF receptor fusion protein is in an aqueous pharmaceutical formulation comprising 40 mg/ml VEGF receptor fusion protein.

67. The use of claim 5-26 or 64-66 wherein 2 mg of VEGF receptor fusion protein is in a pharmaceutical formulation comprising:
40 mg/ml VEGF receptor fusion protein, 10 mM sodium phosphate, 40 mM NaCl, 0.03% polysorbate 20 and 5% sucrose, with a pH of 6.2.

68 The use of any one of claims 1-67 wherein ≥8 mg (±0.8 mg) of VEGF receptor fusion protein is in an aqueous pharmaceutical formulation that comprises a sugar or polyol.

69. The use of any one of claims 1-68 wherein ≥8 mg (±0.8 mg) VEGF receptor fusion protein in an aqueous pharmaceutical formulation that comprises sucrose.

70. The use of any one of claims 1-69 wherein ≥8 mg (±0.8 mg) of a VEGF receptor fusion protein is in an aqueous pharmaceutical formulation that has a pH of about 5.8.

71. The use of any one of claims 1-70 wherein ≥8 mg (±0.8 mg) of a VEGF receptor fusion protein is in an aqueous pharmaceutical formulation comprising about 103-126 mg/ml VEGF receptor fusion protein, histidine-based buffer and arginine.

72. The use of any one of claims 1-71 wherein ≥8 mg (±0.8 mg) of a VEGF receptor fusion protein is an aqueous pharmaceutical formulation comprising about 114.3 mg/ml VEGF receptor fusion protein, histidine-based buffer and arginine.

73. The use of any one of claims 1-72 wherein the ≥8 mg (±0.8 mg) aflibercept is in an aqueous pharmaceutical formulation wherein the aflibercept has less than about 3.5% high molecular weight species immediately after manufacture and purification and/or less than or equal to about 6% high molecular weight species after storage for about 24 months at about 2-8° C.

74. The use of any one of claims 1-73 wherein the ≥8 mg VEGF receptor fusion protein is in an aqueous pharmaceutical formulation comprising:
at least about 100 mg/ml of a VEGF receptor fusion protein;
about 10-100 mM L-arginine;
sucrose;
a histidine-based buffer; and
a surfactant;
wherein the formulation has a pH of about 5.0 to about 6.8; wherein the VEGF receptor fusion protein has less than about 3.5% high molecular weight species immediately after manufacture and purification and/or less than or equal to about 6% high molecular weight species after storage for about 24 months at about 2-8°C.

75. The use of claim 1-74 wherein ≥ about 8 mg (±0.8 mg) of VEGF receptor fusion protein is in an aqueous pharmaceutical formulation comprising

- ≥100 mg/ml VEGF receptor fusion protein, histidine-based buffer and L-arginine;
- 140 mg/ml aflibercept; 20 mM histidine-based buffer; 5 % sucrose; 0.03 % polysorbate 20; 10 mM L-arginine; pH 5.8;
- 150 ± 15 mg/ml aflibercept, 10 mM phosphate-based buffer, 8 ± 0.8% (w/v) sucrose, 0.02-0.04% (w/v) polysorbate 20 and 50 mM L-arginine, pH 5.9-6.5;
- 103-126 mg/ml aflibercept, 10 ± 1 mM histidine-based buffer, 5 ± 0.5% (w/v) sucrose, 0.02-0.04% (w/v) polysorbate 20, and 50 ± 5 mM L-arginine, pH 5.5-6.1;
- 140 mg/ml aflibercept, 10 mM histidine-based buffer, 2.5 % (w/v) sucrose, 2.0 % (w/v) proline, 0.03 % (w/v) polysorbate 20 and 50 mM L-arginine, pH 5.8;
- 114.3 mg/ml aflibercept, 10 mM histidine-based buffer, 5% (w/v) sucrose, 0.03% (w/v) polysorbate 20 and 50 mM L-arginine, pH 5.8;

- ≥100 mg/ml aflibercept, histidine-based buffer and L-arginine;
- ≥100 mg/ml aflibercept at about pH 5.8, wherein the formulation forms <3% HMW aggregates after incubation at 5°C for 2 months;
- About 114.3 mg/mL aflibercept; 10 mM – 50 mM histidine-based buffer, sugar, non-ionic surfactant, L-Arginine, pH 5.8; or
- About 114.3 mg/mL aflibercept; 10 mM His/His-HCl-based buffer, 5% sucrose, 0.03% polysorbate-20, 50 mM L-Arginine, pH 5.8.

76. The use of any one of claims 1-75 wherein the ≥8 mg (±0.8 mg) of VEGF receptor fusion protein is to be administered in a volume of about 100 μl or less, about 75 μl or less; about 70 μl or less; or about 50 μl; 51 μl; 52 μl; 53 μl; 54 μl; 55 μl; 56 μl; 57 μl; 58 μl; 59 μl; 60 μl; 61 μl; 62 μl; 63 μl; 64 μl; 65 μl; 66 μl; 67 μl; 68 μl; 69 μl; 70 μl; 71 μl; 72 μl; 73 μl; 74 μl; 75 μl; 76 μl; 77 μl; 78 μl; 79 μl; 80 μl; 81 μl; 82 μl; 83 μl; 84 μl; 85 μl; 86 μl; 87 μl; 88 μl; 89 μl; 90 μl; 91 μl; 92 μl; 93 μl; 94 μl; 95 μl; 96 μl; 97 μl; 98 μl; 99 μl; or 100 μl.

77. The use of claim 76 wherein said VEGF receptor fusion protein is to be administered in a volume of about 70 ± 4 or 5 microliters.

78. The use of any one of claims 1-77 wherein the intervals between doses are adjusted (increased/maintained/reduced) based on visual and/or anatomic outcomes.

79. The use of any one of claims 1-78, wherein the medicament is to be administered in one or more periods of *pro re nata* (PRN), capped PRN or treat and extend (T&E) dosing.

80. The use of any one of claims 1-79 wherein the VEGF receptor fusion protein is aflibercept.

81. The use of any one of claims 1-80 wherein the subject is to be treated for at least 96 weeks.

82. The use of any one of claims 1-81 wherein the VEGF receptor fusion protein is to be administered by intraocular or intravitreal injection.