WHAT IS CLAIMED IS:

~~1. A bispecific ribonucleic acid (RNA) aptamer is disclosed comprising Formula I:~~

~~X_1-(aptamer 1)-X_2-(linker)-Y_1-(aptamer 2)-Y_2-invdT~~

~~**Formula I**~~

~~wherein the bispecific RNA aptamer comprises at least one nucleotide sequence shown in Table 1 or at least one nucleotide sequence having at least about 70% identify to a nucleotide sequence shown in Table 1.~~

~~2. The bispecific RNA aptamer of claim 1, wherein aptamer 1 and aptamer 2 each comprise a nucleotide sequence selected from the nucleotide sequences shown in Table 1 or at least one nucleotide sequence having at least about 70% identity to the nucleotide sequences shown in Table 1.~~

~~3. The bispecific RNA aptamer of claims 1-2, wherein the bispecific RNA aptamer has a hydrodynamic radius greater than about 10 nm.~~

~~4. The bispecific RNA aptamer of claims 1-3, wherein aptamer 1 comprises a nucleotide sequence selected from SEQ ID NOS: 1-54 and aptamer 2 comprises a different nucleotide sequence selected from SEQ ID NOS: 1-54.~~

~~5. The bispecific RNA aptamer of claims 1-4, wherein aptamer 1 and aptamer 2 are between about 30 and about 40 nucleotides in length, respectively.~~

~~6. The bispecific RNA aptamer of claim 1, wherein the bispecific RNA aptamer specifically binds to Vascular Endothelial Growth Factor (VEGF) (or an isoform thereof) and Interleukin 8 (IL8).~~

~~7. The bispecific RNA aptamer of claim 6, wherein the bispecific RNA aptamer inhibits the function of VEGF (or an isoform thereof) and IL8 by an amount between about 90% and about 100%.~~

~~8. The bispecific RNA aptamer of claim 7, wherein the bispecific RNA aptamer inhibits the function of VEGF (or an isoform thereof) and IL8 by an amount of about 95% or more.~~

9. The bispecific RNA aptamer of claim 1, wherein the bispecific RNA aptamer binds to VEGF (or the isoform thereof) and IL8 with a binding affinity of between about 250 pM and about 20 pM.

10. The bispecific RNA aptamer of claim 9, wherein the bispecific RNA aptamer binds to VEGF (or the isoform thereof) and IL8 with a binding affinity of between about 500 nM and about 10 pM.

11. The bispecific RNA aptamer of claim 9, wherein the bispecific RNA aptamer binds to VEGF (or the isoform thereof) and IL8 with a binding affinity of between about 750 nM and about 1pM.

12. The bispecific RNA aptamer of claim 9, wherein the bispecific RNA aptamer has a binding affinity selected from about 250 nM, about 300 nM, about 350 nM, about 400 nM, about 450 nM, about 500 nM, about 550 nM, about 600 nM, about 650 nM, about 700 nM, about 750 nM or about 800 nM, about 850 nM, about 900 nM, about 950 nM or about 1 pM.

13. The bispecific RNA aptamer of claim 1, wherein the bispecific RNA aptamer specifically binds to VEGF (or an isoform thereof) and Angiopoietin 2 (Ang2).

14. The bispecific RNA aptamer of claim 13, wherein the bispecific RNA aptamer inhibits the function of VEGF (or the isoform thereof) and Ang2 by an amount between about 90% and about 100%.

15. The bispecific RNA aptamer of claim 13, wherein the bispecific RNA aptamer inhibits the function of VEGF (or the isoform thereof) and Ang2 by an amount of about 95% or more.

16. The bispecific RNA aptamer of claim 13, wherein the bispecific RNA aptamer binds to VEGF (or the isoform thereof) and Ang2 with a binding affinity of between about 250pM and about 10 pM.

17. The bispecific RNA aptamer of claim 16, wherein the bispecific RNA aptamer has a binding affinity between about 500 nM and about 5 pM.

18. The bispecific RNA aptamer of claim 16, wherein the bispecific RNA aptamer has a binding affinity selected from the group consisting of about 250 nM, about 300 nM, about 350 nM, about 400 nM, about 450 nM, about 500 nM, about 550 nM, about 600 nM, about 650 nM, about 700 nM, about 750 nM or about 800 nM, about 850 nM, about 900 nM, about 950 nM or

about 1 pM. In one embodiment, the bispecific RNA aptamer has a binding affinity less than about 10 pM, less than about 5 pM, or less than about 1 pM.

19. The bispecific RNA aptamer of claim 1, wherein the bispecific RNA aptamer specifically binds to IL8 and Ang2.

20. The bispecific RNA aptamer of claim 19, wherein the bispecific RNA aptamer inhibits the function of IL8 and Ang2 by an amount between about 90% and about 100%.

21. The bispecific RNA aptamer of claim 19, wherein the bispecific RNA aptamer inhibits the function of IL8 and Ang2 by an amount of about 95% or more.

22. The bispecific RNA aptamer of claim 19, wherein the bispecific RNA aptamer has a binding affinity of greater than about 10 pM.

23. The bispecific RNA aptamer of claims 1-5, wherein X_1 comprises between 0 – 5 nucleotides, wherein the nucleotides are complementary to the nucleotides of X_2.

24. The bispecific RNA aptamer of claims 1-5, wherein Y_1 comprises between 0 – 5 nucleotides that are complementary to the nucleotides of Y_2.

25. The bispecific RNA aptamer of claims 1-5, wherein the linker is a nucleotide linker comprising between 0 and 20 nucleotides.

26. The bispecific RNA aptamer of claim 25, wherein the nucleotide linker comprises one or more 2' O-methyl (2'OMe) uridine (U) residues.

27. The bispecific RNA aptamer of claim 25, wherein the nucleotide linker comprises five or more 2' O-methyl (2'OMe) uridine (U) residues.

28. The bispecific RNA aptamer of claims 1-5, wherein the linker is a non-nucleotide linker as shown in Table 2.

29. The bispecific RNA aptamer of claims 1-5, wherein the linker is a heterobifunctional linker comprising a thiol reactive moiety (e.g., maleimide) and an amine reactive moiety.

30. The bispecific RNA aptamer of claims 1-29, wherein the bispecific RNA aptamer is modified with polyethylene glycol (PEG).

~~31. The bispecific RNA aptamer of claim 30, wherein the polyethylene glycol is coupled to the bispecific RNA aptamer.~~

~~32. The bispecific RNA aptamer of claim 30, wherein the polyethylene glycol is coupled to a second linker, wherein the second linker is coupled to the bispecific aptamer.~~

~~33. The bispecific RNA aptamer of claims 1-5, wherein an inverted deoxythymidine (invdT) is incorporated at the 3'-end of the bispecific RNA aptamer.~~

~~34. The bispecific RNA aptamer of claims 1-5, wherein the bispecific RNA aptamer is modified with one or more additional therapeutic agents.~~

~~35. The bispecific RNA aptamer of claims 1-5, wherein one or more nucleotides of the bispecific RNA aptamer are chemically modified.~~

~~36. The bispecific RNA aptamer of claim 35, wherein the one or more chemically modified nucleotides are selected from the group consisting of 2'Fluoro (2'F) Guanosine, 2' OMe Guanosine, 2'OMe Adenosine, 2'OMe Cytosine, 2'OMe Uridine and combinations thereof.~~

~~37. The bispecific RNA aptamer of claim 35, wherein the one or more chemical modification(s) result in one or more improved characteristics selected from the group consisting of *in vivo* stability, stability against degradation, binding affinity for its target, and/or improved delivery characteristics in comparison to the same bispecific RNA aptamer having unmodified nucleotides.~~

~~38. The bispecific RNA aptamer of claims 35, wherein the or more chemical modification results in an improvement in *in vivo* stability and wherein the Omen half-life of the non-pegylated bispecific RNA aptamer is greater than about 10 hours or more.~~

~~39. The bispecific RNA aptamer of claim 35, wherein the or more chemical modification results in an improvement in *in vivo* stability and wherein the half-life of the non-pegylated bispecific RNA aptamer is between about 10 and about 100 hours.~~

~~40. The bispecific RNA aptamer of claim 35, wherein the or more chemical modification results in an improvement in *in vivo* stability and wherein the half-life of the non-pegylated bispecific aptamer is between about 300 and about 700 hours.~~

41. The bispecific RNA aptamer of claim 35, wherein the or more chemical modification results in an improvement in in vivo stability and wherein the half-life of the non-pegylated aptamer is between about 400 and about 700 hours.

42. The bispecific RNA aptamer of claim 35, wherein the one or more chemical modifications enhance the affinity and specificity of the binding moiety for the target molecule compared to the bispecific RNA aptamer having a binding moiety with unmodified nucleotides.

43. The bispecific RNA aptamer of claim 35, wherein the one or more chemical modifications provide additional charge, polarizability, hydrophobicity, hydrogen bonding, electrostatic interaction, and functionality to the bispecific aptamer.

44. The bispecific RNA aptamer of claims 1-5, wherein aptamer 1 comprises VEGF Aptamer 285 and aptamer 2 comprises IL8 Aptamer 269.

45. The bispecific RNA aptamer of claims 1-5, wherein aptamer 1 comprises VEGF Aptamer 285 and aptamer 2 comprises IL8 Aptamer 248.

46. The bispecific RNA aptamer of claims 1-5, wherein aptamer 1 comprises VEGF Aptamer 481 and aptamer 2 comprises IL8 Aptamer 269.

47. The bispecific RNA aptamer of claims 1-5, wherein aptamer 1 comprises VEGF Aptamer 481 and aptamer 2 comprises IL8 Aptamer 248.

48. The bispecific RNA aptamer of claims 1-5, wherein aptamer 1 comprises VEGF Aptamer 628 and aptamer 2 comprises IL8 Aptamer 269.

49. The bispecific RNA aptamer of claims 1-5, wherein aptamer 1 comprises VEGF Aptamer 628 and aptamer 2 comprises IL8 Aptamer 248.

50. The bispecific RNA aptamer of claims 44-49, wherein the linker is a non-nucleotide linker.

51. The bispecific RNA aptamer of claims 1-5, wherein the bispecific RNA aptamer is associated with one or more additional molecules selected from the group consisting of antibodies, peptides, proteins, carbohydrates, enzymes, polymers, drugs, small molecules, gold nanoparticles, radiolabels, fluorescent labels, dyes, haptens, other aptamers, or nucleic acids.

~~52. The bispecific RNA aptamer of claim 51, wherein the one or more additional molecules is polyethylene glycol.~~

~~53. The bispecific RNA aptamer of claim 52, wherein the polyethylene glycol is attached directly to the bispecific RNA aptamer or joined to the bispecific RNA aptamer via a second linker.~~

~~54. A pharmaceutical composition comprising the bispecific RNA aptamer of claims 1-53 and a pharmaceutically acceptable carrier.~~

~~55. The pharmaceutical composition of claim 54, formulated for intravitreal administration.~~

~~56. A pre-filled syringe comprising the pharmaceutical composition of claims 54-55.~~

~~57. A method of inhibiting the function of at least one target molecule, comprising contacting the target molecule with the bispecific RNA aptamer of claims 1-53 or the pharmaceutical composition of claims 54-55.~~

~~58. The method of claim 57, wherein the target molecule is selected from the group consisting of VEGF, IL8, Ang2 or a combination thereof.~~

~~59. A method of treating retinal disease or disorder is disclosed comprising administering an effective amount of the bispecific RNA aptamer of claims 1-53 or the pharmaceutical composition of claims 54-55 to a subject in need thereof, thereby treating the retinal disease or disorder.~~

~~60. The method of claim 59, wherein the retinal disease or disorder is the wet form of age-related macular degeneration (wAMD).~~

~~61. The method of claim 59, wherein the retinal disease or disorder is diabetic retinopathy.~~

~~62. The method of claim 61, wherein the diabetic retinopathy is diabetic macular edema.~~

~~63. The method of claim 59, wherein the retinal disease or disorder is retinal vein occlusion.~~

~~64. The method of claim 63, wherein the retinal vein occlusion is branched retinal vein occlusion.~~

~~65. The method of claim 63, wherein the retinal vein occlusion is central retinal vein occlusion.~~

~~66. The method of claim 59, wherein the retinal disease or disorder is retinopathy of prematurity.~~

~~67. The method of claim 59, wherein the retinal disease or disorder is radiation retinopathy.~~

~~68. The method of claims 59-67, wherein the subject in need thereof has been diagnosed with the retinal disease or disorder.~~

69. The method of claims 59-68, wherein the subject in need thereof has been previously treated with one or more anti-VEGF agents, but where the subject has shown a suboptimal response to such treatment.

70. The method of claims 59-67, wherein the subject in need thereof is at risk for the retinal disease or disorder.

71. The method of claims 59-70, wherein the administering comprises intraocular administration.

72. The method of claims 59-70, wherein the administering comprises intravitreal injection.

73. The method of claim 72, wherein the method further comprising providing a kit comprising a syringe that is prefilled with the bispecific RNA aptamer or the pharmaceutical composition.

74. The method of claims 59-73, wherein treatment results in an increase in overall best corrected visual acuity (BCVA) as measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart by at least 3 letters, at least 4 letters, at least 5 letters, at least 6 letters, at least 7 letters, at least 8 letters, at least 9 letters, at least 10 letters, at least 11 letters, at least 12 letters, at least 13 letters, at least 14 letters, at least 15 letters, at least 16 letters, at least 17 letters, at least 18 letters, at least 19 letters, at least 20 letters, or more than 20 letters as compared to an untreated control subject over a defined period of time selected from at least one of 2 weeks, one month, 2 months, 3 months, 6 months, one year, 2 years, or 5 years.

75. The method of claims 59-73, wherein the treatment results in a percentage of patients gaining $\geq$ 15 letters in BCVA from baseline of at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or more as compared to an untreated control subject over a defined period of time selected from at least one of 2 weeks, one month, 2 months, 3 months, 6 months, one year, 2 years, or 5 years.

76. The method of claims 59-73, wherein the treatment results in a percentage of patients gaining $\geq$ 10 letters in BCVA from baseline of at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or more as compared to an untreated control subject over a defined period of time selected from at least one of 2 weeks, one month, 2 months, 3 months, 6 months, one year, 2 years, or 5 years.

77. The method of claims 59-73, wherein treatment results in a percentage of patients gaining ≥ 5 letters in BCVA from baseline of at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or more as compared to an untreated control subject over a defined period of time selected from at least one of 2 weeks, one month, 2 months, 3 months, 6 months, one year, 2 years, or 5 years.

78. The method of claims 59-73, wherein treatment results in a reduction of retinal fluid as measured by fluorescein angiography (FA) and optical coherence tomography (OCT) of at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or more as compared to an untreated control subject over a defined period of time, selected from at least one of 2 weeks, one month, 2 months, 3 months, 6 months, one year, 2 years, or 5 years.

79. The method of claims 59-73, wherein, treatment results in a reduction of retinal thickness as measured by fluorescein angiography (FA) and optical coherence tomography (OCT) of at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or more as compared to an untreated control subject over a defined period of time selected from at least one of 2 weeks, one month, 2 months, 3 months, 6 months, one year, 2 years, or 5 years.

80. The method of claims 59-73, wherein treatment results in a reduction of the total area of choroidal neovascular (CNV) lesions as measured by fluorescein angiography (FA) and optical coherence tomography (OCT) of at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or more as compared to an untreated control subject over a defined period of time selected from at least one of 2 weeks, one month, 2 months, 3 months, 6 months, one year, 2 years, or 5 years.

81. The method of claims 59-73, further comprising co-administering to the subject in need thereof at least one additional therapeutic modality.

82. The method of claim 81, wherein the at least one additional therapeutic modality is a therapeutic agent.

~~83. The method of claim 82, wherein the at least one additional therapeutic agent is selected from Illuvien® and Ozurdex. ®~~

~~84. A method of treating a population of subjects in need thereof is provided, comprising administering an effective amount of the bispecific RNA aptamer of claims 1-53 or the pharmaceutical composition of claims 54-55 to such population.~~

~~85. The method of claim 84, wherein the method results in effective treatment for more than 30%, more than 35%, more than 40%, more than 45%, more than 50%, more than 55%, more than 60%, more than 65%, more than 70%, more than 75%, more than 80%, more than 85%, more than 90% or more than 95% of subjects treated.~~

~~86. The method of claim 85, wherein effective treatment is measured by overall best corrected visual acuity (BCVA) as measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) Chart.~~

~~87. The method of claim 84, wherein the method results in fewer than 30%, fewer than 25%, fewer than 20%, fewer than 15% or fewer than 10% of such subjects maintaining persistent retinal fluid.~~

~~88. A method of making the bispecific RNA aptamer of claims 1-53, comprising carrying out direct chemical synthesis, enzymatic synthesis, chemical synthesis followed by domain chemical conjugation, and/or domain hybridization.~~

~~89. The method of claim 88, comprising carrying out direct chemical synthesis.~~

~~90. The method of claim 88, comprising carrying out enzymatic synthesis.~~

~~91. The method of claim 88, comprising carrying out chemical synthesis followed by domain chemical conjugation.~~

~~92. The method of claim 88, comprising synthesis by domain hybridization.~~

1. A bispecific ribonucleic acid (RNA) aptamer comprising Formula I:

X_1-(aptamer 1)-X_2-(linker)-Y_1-(aptamer 2)-Y_2-invdT

Formula I

wherein aptamer 1 is selected from the group consisting of SEQ ID. Nos.: 1-46 and 67 or at least one nucleotide sequence having at least about 70% identity thereto and wherein aptamer 2 is selected from the group consisting of SEQ ID. Nos: 47-48 or at least one nucleotide sequence

having at least about 70% identity thereto, wherein the order of aptamer 1 and aptamer 2 can be varied.

2. The bispecific RNA aptamer of claim 1, wherein the linker is a nucleotide linker comprising five or more 2' O-methyl (2'OMe) uridine (U) residues.

3. The bispecific RNA aptamer of claim 1, wherein the linker is a non-nucleotide linker selected from the group consisting of 1,3-propanediol, 1,6 hexanediol, 1,12 dodecyldiol, triethylene glycol and hexaethylene glycol.

4. The bispecific RNA aptamer of claim 1, wherein one or more nucleotides of the bispecific RNA aptamer are chemically modified.

5. The bispecific RNA aptamer of claim 4, wherein the one or more chemically modified nucleotides are selected from the group consisting of 2'Fluoro (2'F) Guanosine, 2' OMe Guanosine, 2'OMe Adenosine, 2'OMe Cytosine, 2'OMe Uridine and combinations thereof.

6. The bispecific RNA aptamer of claim 1, wherein the bispecific RNA aptamer specifically binds to Vascular Endothelial Growth Factor (VEGF) or an isoform thereof and Interleukin 8 (IL8).

7. The bispecific RNA aptamer of claim 6, wherein the bispecific RNA aptamer inhibits the function of VEGF or an isoform thereof and IL8 by an amount between about 90% and about 100%.

8. The bispecific RNA aptamer of any one of claims 1-7, wherein the bispecific RNA aptamer is attached directly to polyethylene glycol (PEG).

9. The bispecific RNA aptamer of claim 8, wherein the bispecific RNA aptamer has a hydrodynamic radius greater than about 10 nm.

10. A pharmaceutical composition comprising the bispecific RNA aptamer of any one of claims 1-9 and a pharmaceutically acceptable carrier.

11. The pharmaceutical composition of claim 10, formulated for intravitreal administration.

12. Use of the bispecific RNA aptamer of any one of claims 1-9 or the pharmaceutical composition of claim 10 or 11 in the manufacture of a medicament for treating a retinal disease or disorder in a subject in need thereof.

13. The use of claim 12, wherein the retinal disease or disorder is selected from the group consisting of the wet form of age-related macular degeneration (wAMD), diabetic retinopathy, diabetic macular edema, retinal vein occlusion, retinopathy of prematurity and radiation retinopathy

14. The use of claim 12 or 13, wherein the subject in need thereof has been previously treated with one or more anti-VEGF agents, but where the subject has shown a suboptimal response to such treatment.

15. The use of any one of claims 12-14, wherein the medicament is for intravitreal injection.