CLAIMS

What is claimed is:

1. A pharmaceutical composition, comprising:

an anti-VEGF fusion protein A, wherein the fusion protein A is a dimer comprising two fusion polypeptides as set forth in SEQ ID NO: 1; and

a protein fragment B, wherein the protein fragment B is a dimer comprising two fusion polypeptides as set forth in SEQ ID NO: 1 and SEQ ID NO: 2, respectively, and wherein a content of the protein fragment B in the pharmaceutical composition ranges from 0.01% to 7%, and preferably, from 0.01% to 5.4%, and more preferably, from 0.01% to 4.6%.

2. The pharmaceutical composition according to claim 1, wherein the content of the protein fragment B in the pharmaceutical composition ranges from 0.6% to 7%, preferably, from 0.6% to 5.4%, and more preferably, from 0.6% to 4.6% or from 1.3% to 5.4%; and even more preferably, from 1.3% to 4.6%.

3. The pharmaceutical composition according to claim 1, wherein a content of the fusion protein A in the pharmaceutical composition ranges from 77% to 98%, and preferably, from 80% to 98%.

4. The pharmaceutical composition according to claim 3, wherein the content of the fusion protein A in the pharmaceutical composition ranges from 77% to 87%, and preferably, from 80% to 87%.

5. The pharmaceutical composition according to claim 1, wherein a concentration of the fusion protein A in the pharmaceutical composition ranges from 1 mg/mL to 200 mg/mL, preferably, from 10 mg/mL to 150 mg/mL, and more preferably, from 10 mg/mL to 120 mg/mL.

6. The pharmaceutical composition according to claim 1, wherein a pH value of the pharmaceutical composition ranges from 6.8 to 8.7, preferably, from 7.5 to 8.7, and more preferably 7.7±0.2.

7. The pharmaceutical composition according to any one of claims 1 to 6, further comprising:

a buffer;

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an osmotic pressure adjuster;

a surfactant; and

amino acid,

wherein a pH value of the pharmaceutical composition ranges from 6.8 to 8.7.

8. The pharmaceutical composition according to claim 6, comprising:

1 mg/mL to 200 mg/mL of the fusion protein A;

5 mM to 300 mM of a buffer, wherein the buffer is selected from one or more of Tris-HCl, citric acid, phosphate, histidine, glutamic acid, succinate, tromethamine, or an acetate buffer;

10 mM to 500 mM of amino acid, wherein the amino acid is selected from one or more of lysine, arginine, histidine, ornithine, isoleucine, leucine, alanine, glycine, glutamic acid, or aspartic acid;

0% to 30% of an osmotic pressure adjuster, wherein the osmotic pressure adjuster is selected from one or more of sucrose, trehalose, mannitol, glycerol, propylene glycol, or sorbitol; and

0% to 0.1% of a surfactant, wherein the surfactant is selected from one or more of polyethylene glycol, Tween 20, Tween 80, P188, propylene glycol, or dimethyl sulfoxide,

wherein the pH value of the pharmaceutical composition ranges from 6.8 to 8.7.

9. The pharmaceutical composition according to claim 7, comprising:

1 mg/mL to 200 mg/mL of the fusion protein A;

5 mM to 300 mM of the buffer, wherein the buffer is selected from one or more of citric acid, phosphate, arginine, glutamic acid, or tromethamine;

10 mM to 300 mM of the amino acid, wherein the amino acid is selected from one or more of glutamic acid, arginine, or histidine;

0% to 30% of the osmotic pressure adjuster, wherein the osmotic pressure adjuster is selected from one or more of sucrose, trehalose, mannitol, or sorbitol; and

0% to 0.1% of the surfactant, wherein the surfactant is selected from one or more of Tween 20, Tween 80, or P188,

wherein the pH value of the pharmaceutical composition ranges from 6.8 to 8.7.

10. The pharmaceutical composition according to claim 8, comprising:

10 mg/mL to 150 mg/mL of the fusion protein A;

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10 mM to 250 mM of a citrate buffer;

100 mM to 250 mM of arginine or histidine;

5% to 20% of sucrose or trehalose; and

0% to 0.1% of Tween 20, Tween 80, or P188,

wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7.

11. The pharmaceutical composition according to claim 1, comprising:

10 mg/mL to 120 mg/mL of the fusion protein A, 10 mM of a citrate buffer, 100 mM of arginine, 5% of sucrose, and 0.05% of Tween 20, wherein a pH value of the pharmaceutical composition ranges from 7.5 to 8.7; or

10 mg/mL to 120 mg/mL of the fusion protein A, 100 mM of the citrate buffer, 250 mM of arginine, 20% of sucrose, and 0.1% of Tween 20, wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7; or

10 mg/mL to 120 mg/mL of the fusion protein A, 250 mM of the citrate buffer, 100 mM of histidine, 8% of sucrose, and 0.1% of Tween 20, wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7; or

10 mg/mL to 120 mg/mL of the fusion protein A, 10 mM of the citrate buffer, 250 mM of arginine, 20% of sucrose, and 0.1% of Tween 20, wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7; or

10 mg/mL to 120 mg/mL of the fusion protein A, 10 mM of tromethamine, 100 mM of arginine, and 5% of sucrose, wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7; or

10 mg/mL to 120 mg/mL of the fusion protein A, 290 mM of glutamic acid, 290 mM of arginine, and 78 mM of NaOH, wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7; or

10 mg/mL to 120 mg/mL of the fusion protein A, 5 mM of phosphate, and preferably, 5 mM of sodium dihydrogen phosphate, 100 mM of arginine, 10% of trehalose, and 0.01% of P188, wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7; or

10 mg/mL to 120 mg/mL of the fusion protein A, 10 mM of the citrate buffer, 100 mM of arginine, and 5% of trehalose, wherein the pH value of the pharmaceutical composition ranges from 7.5 to 8.7.

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12. The pharmaceutical composition according to claim 1, wherein a content of the fusion protein A or the content of the protein fragment B is determined by gel electrophoresis (SDS-PAGE).

13. A container or delivery device, comprising the pharmaceutical composition according to any one of claims 1 to 12,

preferably, the container is a vial or a syringe; or the delivery device is a pre-filled injection device.

14. A lyophilized preparation, prepared by lyophilizing the pharmaceutical composition according to any one of claims 1 to 12.

15. Use of the pharmaceutical composition according to any one of claims 1 to 12 in the manufacture of a medicament for treating an ocular disease, wherein the ocular disease is an ocular neovascular disease,

preferably, the ocular neovascular disease is selected from a retinal neovascular ocular disease, a choroidal neovascular ocular disease, an iris neovascular ocular disease, or a corneal neovascular ocular disease,

more preferably, the ocular neovascular disease is selected from age-related macular degeneration, macular edema, macular edema secondary to retinal vein occlusion, retinal vein occlusion, macular edema caused by central retinal vein occlusion, macular edema caused by branch retinal vein occlusion, diabetic macular edema, diabetic retinopathy, polypoidal choroidal vasculopathy, choroidal neovascularization secondary to degenerative myopia, or retinopathy of prematurity, and

even more preferably, the ocular neovascular disease is selected from age-related macular degeneration, diabetic macular edema, or diabetic retinopathy.

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