WHAT IS CLAIMED IS:

1. A multispecific antibody or antibody fragment comprising at least:

(A) a first antigen-binding region which specifically binds to frizzled class receptor 4 (Fzd4) and comprises a first heavy chain variable domain (VH1) and a first light chain variable domain (VL1),

(B) a second antigen-binding region which specifically binds to low density lipoprotein receptor-related protein 5 and/or 6 (LRP5 and/or LRP6) and comprises at least a second heavy chain variable domain (VH2),

wherein:

(A) the VH1 comprises:

(i) a heavy chain complementarity-determining region 1 (CDRH1) which has an amino acid sequence which:

(i-1) has at least 80% identity to the amino acid sequence of SEQ ID NO: 121 or to the CDRH1 amino acid sequence contained in SEQ ID NO: 181, optionally defined according to Kabat; or

(i-2) comprises or consists of the amino acid sequence of SEQ ID NO: 121, or comprises or consists of the CDRH1 amino acid sequence contained in SEQ ID NO: 181, optionally defined according to Kabat;

(ii) a heavy chain complementarity-determining region 2 (CDRH2) which has an amino acid sequence which:

(ii-1) has at least 90% identity to the amino acid sequence of SEQ ID NO: 141 or to the CDRH2 amino acid sequence contained in SEQ ID NO: 181, optionally defined according to Kabat;

or

(ii-2) comprises or consists of: the amino acid sequence of SEQ ID NO: 141; or comprises or consists of the CDRH2 amino acid sequence contained in SEQ ID NO: 181, optionally defined by Kabat; and

(iii) a heavy chain complementarity-determining region 3 (CDRH3) which has an amino acid sequence which:

(iii-1) has at least 90% identity to the amino acid sequence of SEQ ID NO: 161 or to the CDRH3 amino acid sequence contained in SEQ ID NO: 181, optionally defined by Kabat; or

(iii-2) comprises or consists of the amino acid sequence of SEQ ID NO: 161, or comprises or consists of the CDRH3 amino acid sequence contained in SEQ ID NO: 181, optionally defined by Kabat; and

the VL1 comprises:

(iv) a light chain complementarity-determining region 1 (CDRL1) which has an amino acid sequence which:

(iv-1) has at least 90% identity to the amino acid sequence of SEQ ID NO: 221 or to the CDRL1 amino acid sequence contained in SEQ ID NO: 281, optionally defined by Kabat; or

(iv-2) comprises or consists of the amino acid sequence of SEQ ID NO: 221, or comprises or consists of the CDRL1 amino acid sequence contained in SEQ ID NO: 281, optionally defined according to Kabat;

(v) a light chain complementarity-determining region 2 (CDRL2) which has an amino acid sequence which comprises or consists of:

(v-1) the amino acid sequence of SEQ ID NO: 241; or

(v-2) the CDRL2 amino acid sequence contained in SEQ ID NO: 281, optionally defined according to Kabat; and

(vi) a light chain complementarity-determining region 3 (CDRL3) which has an amino acid sequence which comprises or consists of:

(vi-1) the amino acid sequence of SEQ ID NO: 261; or

(vi-2) the CDRL3 amino acid sequence contained in SEQ ID NO: 281, optionally defined according to Kabat; and

(B) the VH2 comprises:

(i) a CDRH1 which has an amino acid sequence which comprises or consists of:

(i-1) the amino acid sequence of SEQ ID NO: 321; or

(i-2) the CDRH1 amino acid sequence contained in SEQ ID NO: 381, optionally defined according to IMGT or Kabat;

(ii) a CDRH2 which has an amino acid sequence which:

(ii-1) has at least 90% identity to the amino acid sequence of SEQ ID NO: 341 or to the CDRH3 amino acid sequence contained in SEQ ID NO: 381, optionally defined according to IMGT or Kabat;

(ii-2) comprises or consists of the amino acid sequence of SEQ ID NO: 341; or

(ii-3) comprises or consists of the CDRH2 amino acid sequence contained in SEQ ID NO: 381, optionally defined according to IMGT or Kabat; and

(iii) a CDRH3 which has an amino acid sequence which:

(iii-1) has at least 90% identity to the amino acid sequence of SEQ ID NO: 361 or to the CDRH3 amino acid sequence contained in SEQ ID NO: 381, optionally defined according to IMGT or Kabat; or

(iii-2) comprises or consists of the amino acid sequence of any one of SEQ ID NOs: 361 and 363-366, or comprises or consists of the CDRH3 amino acid sequence contained in any one of SEQ ID NOS: 381 and 393-396, optionally defined according to IMGT or Kabat.

2. The multispecific antibody or antibody fragment of claim 1, wherein the VH2 is, comprises, or is comprised in a nanobody.

3. The multispecific antibody or antibody fragment of claim 1 or 2, which is a bispecific antibody or antibody fragment.

4. The multispecific antibody or antibody fragment of any one of claims 1-3, wherein:

(A) the VH1 comprises:

(i) the CDRH1, the CDRH2, and the CDRH3 of the VH1 comprising the amino acid sequence contained in SEQ ID NO: 181, optionally according to Kabat; or

(ii) a CDRH1, a CDRH2, and a CDRH3 comprising the amino acid sequences of SEQ ID NOS: 121, 141, and 161, respectively, and

the VL1 comprises:

(i) the CDRL1, the CDRL2, and the CDRL3 of the VL1 comprising the amino acid sequence contained in SEQ ID NO: 281, optionally according to Kabat, or

(ii) a CDRL1, a CDRL2, and a CDRL3 comprising the amino acid sequences of SEQ ID NOS: 221, 241, and 261, respectively; and

(B) the VH2 comprises:

(i) the CDRH1, the CDRH2, and the CDRH3 of the VH2 comprising the amino acid sequence contained in any one of SEQ ID NOs: 381 and 393-396, optionally according to IMGT or Kabat; or

(ii) a CDRH1, a CDRH2, and a CDRH3 comprising the amino acid sequences of SEQ ID NOS: 321, 341, and 361, respectively, SEQ ID NOS: 321, 341, and 363, respectively, SEQ ID NOS: 321, 341, and 364, respectively, SEQ ID NOS: 321, 341, and 365, or SEQ ID NOS: 321, 341, and 366, respectively.

5. The multispecific antibody or antibody fragment of any one of claims 1-4, wherein:

(A) (i) the VH1 comprises an amino acid sequence which has at least 80% identity to the amino acid sequence of SEQ ID NO: 181; and/or

(ii) the VL1 comprises an amino acid sequence which has at least 80% identity to the amino acid sequence of SEQ ID NO: 281; and/or

(B) the VH2 comprises an amino acid sequence which has at least 80% identity to the amino acid sequence contained in any one of SEQ ID NOS: 381 and 393-396.

6. The multispecific antibody or antibody fragment of any one of claims 1-5, wherein:

(A) the VH1 comprises an amino acid sequence which comprises or consists of the amino acid sequence of SEQ ID NO: 181: and/or

the VL1 comprises an amino acid sequence which comprises or consists of the amino acid sequence of SEQ ID NO: 281; and/or

(B) the VH2 comprises an amino acid sequence which comprises or consists of the amino acid sequence contained in any one of SEQ ID NOS: 381 and 393-396.

7. The multispecific antibody or antibody fragment of any one of claims 1-6, wherein:

(A) the VH1 comprises an amino acid sequence which consists of the amino acid sequence of SEQ ID NO: 181: and

the VL1 comprises an amino acid sequence which consists of the amino acid sequence of SEQ ID NO: 281; and

(B) the VH2 comprises an amino acid sequence which consists of the amino acid sequence contained in any one of SEQ ID NOS: 381 and 393-396.

8. A multispecific antibody according to claim 1, comprising:

(A) a first antigen-binding region which specifically binds to Fzd4 and comprises a VH1 and a VL1,

(B) a second antigen-binding region which specifically binds to LRP5 and/or LRP6 and comprises at least a VH2,

wherein:

(i) the CDRH1, the CDRH2, and the CDRH3 of the VH1 are identical to those of the heavy chain variable domain (VH) having the amino acid sequence of SEQ ID NO: 181;

(ii) the CDRL1, the CDRL2, and the CDRL3 of the VL1 are identical to those of the light chain variable domain (VL) having the amino acid sequence of SEQ ID NO: 281; and

(iii) the CDRH1, the CDRH2, and the CDRH3 of the VH2 are identical to those of the VH having the amino acid sequence of SEQ ID NO: 381.

9. The multispecific antibody of claim 8, wherein:

(i) the VH1 comprises or consists of the amino acid sequence of SEQ ID NO: 181; and

(ii) the VL1 comprises or consists of the amino acid sequence of SEQ ID NO: 281; and

(iii) the VH2 comprises or consists of the amino acid sequence of SEQ ID NO: 381.

10. The multispecific antibody or antibody fragment of any one of claims 1-9, which comprises a fragment crystallizable (Fc) region, optionally wherein the Fc region:

(I) is of an IgG, an IgA, an IgE, an IgD, an IgM, optionally of an IgG1, an IgG4, an IgG2, or an IgG3, further optionally of human, or a variant thereof;

(II) comprises one or more amino acid substitutions that reduce an Fc effector function, optionally wherein the one or more amino acid substitutions are at position(s) selected from the group consisting of positions 234, 235, 236, 237, 265, 297 and 329, according to EU numbering;

(III) comprises at least the following amino acid substitutions according to EU numbering:

(ii-1) L234A, L235A, and P329G;

(ii-2) L234A and L235A;

(ii-3) I253A, H310A, and H435Q; and/or

(ii-4) I253A, H310A, and H435A,

optionally relative to a human IgG1 Fc region and/or to any of SEQ ID NOS: 71-74 (optionally not including the C-terminal K); and/or

(IV) comprises an amino acid sequence which comprises or consists of the amino acid sequence of any one of SEQ ID NOS: 71-74, 81-84, 86-89, 91-94, 96-99, 471-474, 476-479, 481-484, and 486-489 (optionally not including the C-terminal K) or which is at least 80% identical thereto.

11. The multispecific antibody or antibody fragment of any one of claims 1-10, which comprises:

(a) a first polypeptide comprising said VH1; and

(b) a second polypeptide comprising

the following in the order from the N-terminus to the C-terminus:

(b-1) said VH2;

(b-2) optionally a linker, which is optionally a peptide linker, further optionally a flexible linker, optionally wherein the linker:

(i) comprises one or more amino acids, optionally one, two, three, four, five, six, seven, eight, nine, ten, eleven, or twelve amino acids;

(ii) consists of small amino acids consisting of G, S, and/or A;

(iii) comprising an amino acid sequence which comprises or consists of an amino acid sequence selected from the group consisting of SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, G, GG, GGG, GS, SG, GGS, GSG, SGG, GSS, SGS, and SSG; and/or

(iv) comprises or consists of multiple repeats of an amino acid or peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, G, GG, GGG, GS, SG, GGS, GSG, SGG, GSS, SGS, and SSG; and

(b-3) said VL1.

12. The multispecific antibody or antibody fragment of claim 11, wherein:

(a) the first polypeptide;

(i) comprises an amino acid sequence which has at least 80% identity to any one of SEQ ID NOS: 2, 7, 8, 9, 450, 451, 452, and 453 (optionally without the C-terminal K);

and/or

(ii) comprises an amino acid sequence which comprises or consists of the amino acid sequence of any one of SEQ ID NOS: 2, 7, 8, 9, 450, 451, 452, and 453 (optionally without the C-terminal K); and

(b) the second polypeptide:

(i) comprises an amino acid sequence which has at least 80%identity to SEQ ID NO: 1; and/or

(ii) comprising an amino acid sequence which comprises or consists of the amino acid sequence of SEQ ID NO: 1.

13. The multispecific antibody or antibody fragment of claim 11 or 12, wherein:

(a) the first polypeptide comprises an amino acid sequence which comprises or consists of the amino acid sequence of SEQ ID NO: 2, 7, 450, or 451 (optionally without the C-terminal K); and

(b) the second polypeptide comprises an amino acid sequence which comprises or consists of the amino acid sequence of SEQ ID NO: 1.

14. The multispecific antibody or antibody fragment of any one of claims 11-13, which comprises: two of said first polypeptides forming a dimer with each other via one or more disulfide bonds; and two of said second polypeptides, wherein one of the second polypeptides is interacting with one of the first polypeptides via a disulfide bond and the other of the second polypeptides is interacting with the other of the first polypeptides via a disulfide bond.

15. The multispecific antibody or antibody fragment of any one of claims 1-13, which comprises:

(A) two or more Fzd4-binding regions, wherein at least one of said Fzd4-binding regions is, comprises, or is comprised in said first antigen-binding region; and/or
(B) two or more LRP5 and/or LRP6-binding regions, wherein at least one of said LRP5 and/or LRP6-binding regions is, comprises, or is comprised in said second antigen-binding region.

16. The multispecific antibody or antibody fragment of claim 15, wherein:
(I) the ratio of the number of said one or more Fzd4-binding regions and the number of said one or more LRP5 and/or LRP6-binding regions comprised in the multispecific antibody or antibody fragment is selected from the group consisting of 2:1, 1:2, 2:2, 3:1, 1:3, 3:2, 2:3, 3:3, 4:1, 1:4, 4:2, 2:4, 4:3, 3:4, and 4:4 ;
(II) the number of said one or more Fzd4-binding regions and the number of said one or more LRP5 and/or LRP6-binding regions comprised in the multispecific antibody or antibody fragment are: 2 and 1, respectively; 1 and 2, respectively; 2 and 2, respectively; 3 and 1, respectively; 1 and 3, respectively; 3 and 2, respectively; 2 and 3, respectively; 3 and 3, respectively; 4 and 1, respectively; 1 and 4, respectively; 4 and 2, respectively; 2 and 4, respectively; 4 and 3, respectively; 3 and 4, respectively; or 4 and 4 respectively; and/or
(III) the multispecific antibody or antibody fragment comprises:
(a) two identical Fzd4-binding regions, each of which is, comprises, or is comprised in said first antigen-binding region; and one LRP5 and/or LRP6-binding region which is, comprises, or is comprised in said second antigen-binding region;
(b) two Fzd4-binding regions, which are different from each other and (i) at least one of which is, comprises, or is comprised in or (ii) each of which is, comprises, or is comprised in said first antigen-binding region; and one LRP5 and/or LRP6-binding region which is, comprises, or is comprised in said second antigen-binding region;

(c) one Fzd4-binding region which is, comprises, or is comprised in said first antigen-binding region; and two identical LRP5 and/or LRP6-binding regions, each of which is, comprises, or is comprised in said second antigen-binding region;
(d) one Fzd4-binding region which is, comprises, or is comprised in said first antigen-binding region; and two LRP5 and/or LRP6-binding regions, which are different from

each other and (i) at least one of which is, comprises, or is comprised in or (ii) each of which is, comprises, or is comprised in said second antigen-binding region;

(e) two identical Fzd4-binding regions, each of which is, comprises, or is comprised in said first antigen-binding region; and two identical LRP5 and/or LRP6-binding region, each of which is, comprises, or is comprised in said second antigen-binding region;

(f) two Fzd4-binding regions, which are different from each other and (i) at least one of which is, comprises, or is comprised in or (ii) each of which is, comprises, or is comprised in said first antigen-binding region; and two identical LRP5 and/or LRP6-binding region, each of which is, comprises, or is comprised in said second antigen-binding region;

(g) two identical Fzd4-binding regions, each of which is, comprises, or is comprised in said first antigen-binding region; and two LRP5 and/or LRP6-binding regions, which are different from each other and (i) at least one of which is, comprises, or is comprised in or (ii) each of which is, comprises, or is comprised in said second antigen-binding region; and/or

(h) two Fzd4-binding regions, which are different from each other and (i) at least one of which is, comprises, or is comprised in or (ii) each of which is, comprises, or is comprised in said first antigen-binding region; and two LRP5 and/or LRP6-binding region, which are different from each other and (i) at least one of which is, comprises, or is comprised in or (ii) each of which is, comprises, or is comprised in said second antigen-binding region.

17. A nucleic acid or a combination of nucleic acids encoding the multispecific antibody or antibody fragment of any one of claims 1-16, optionally wherein the nucleic acid(s) is/are DNA, cDNA, RNA, mRNA, modified mRNA, or a DNA/RNA hybrid.

18. The nucleic acid or a combination of nucleic acids of claim 17, which encodes the multispecific antibody or antibody fragment of any one of claims 11-14 and comprises:

(a) a first nucleic acid encoding the first polypeptide; and

(b) a second nucleic acid encoding the second polypeptide.

19. A vector or a combination of vectors which comprises the nucleic acid or the combination of nucleic acids of claim 17 or 18, optionally wherein:

(i) the vector(s) comprise(s) one or more promoters operably linked to the nucleic acid(s);

(ii) the vector(s) is/are an expression vector; and/or

(iii) the vector(s) comprise(s) a plasmid, a viral vector (optionally adeno-associated viral, adenoviral, lentiviral, or retroviral), a lipid-based vector, a self-replicating RNA vector, a virus-like particle, a polymer-based vector, and/or a nanoparticle, optionally a lipid-based nanoparticle.

20. The vector or a combination of vectors of claim 19, which encodes the multispecific antibody or antibody fragment of any one of claims 11-14 and comprises:

(a) a first vector comprising a first nucleic acid encoding the first polypeptide; and

(b) a second vector comprising a second nucleic acid encoding the second polypeptide.

21. A host cell, which comprises:

(A) the multispecific antibody or antibody fragment of any one of claims 1-16;

(B) the nucleic acid or the combination of nucleic acids of claim 17 or 18; and/or

(C) the vector or the combination of vectors of claim 19 or 20,

optionally wherein the host cell is:

(i) mammalian, optionally human, non-human primate, monkey, rabbit, rodent, hamster, rat, or mouse; or

(ii) non-mammalian, optionally plant, bacterial, fungal, yeast, protozoa, or insect,

and optionally wherein the host cell is:

(i) a human embryonal kidney (HEK) cell, optionally a HEK293 cell, or a variant thereof, further optionally Expi293F™ cell;

(ii) a CHO (Chinese Hamster Ovary) cell;

(iii) an immune cell or

(iv) a hybridoma.

22. A population of cells, which comprises two or more host cells of claim 21.

23. A pharmaceutical composition, which comprises:

(I) (A) the multispecific antibody or antibody fragment of any one of claims 1-16;

(B) the nucleic acid or the combination of nucleic acids of claim 17 or 18;

(C) the vector or the combination of vectors of claim 19 or 20; and/or

(D) the host cell of claim 21 or the population of cells of claim 22; and

(II) a pharmaceutically acceptable carrier and/or excipient.

24. A substance for use in treating a subject in need of such treatment, wherein the substance comprises an effective amount of:

(A) the multispecific antibody or antibody fragment of any one of claims 1-16;

(B) the nucleic acid or the combination of nucleic acids of claim 17 or 18;

(C) the vector or the combination of vectors of claim 19 or 20;

(D) the host cell of claim 21 or the population of cells of claim 22; and/or

(E) the pharmaceutical composition of claim 23,

optionally wherein:

(a) the subject is

(i) a mammal, optionally a human, a non-human primate, a monkey, a horse, a cow, sheep, a goat, a pig, a dog, a cat, a rabbit, a rodent, a hamster, a rat, or a mouse; or

(ii) a non-mammalian vertebrate, optionally a bird, fish, an amphibian, or a reptile;

(b) the subject comprises or has a risk of developing a disease, disorder, or a condition; and/or

(c) an additional agent, optionally an adjuvant or a therapeutic agent is to be further administered to the subject.

25. A substance for use in treating or preventing a disease, disorder, or a condition in a subject in need of such treatment, wherein the substance comprises an effective amount of:

(A) the multispecific antibody or antibody fragment of any one of claims 1-16;

(B) the nucleic acid or the combination of nucleic acids of claim 17 or 18;

(C) the vector or the combination of vectors of claim 19 or 20;

(D) the host cell of claim 19 or the population of cells of claim 21; and/or

(E) the pharmaceutical composition of claim 22,

optionally wherein:

(a) the subject is

(i) a mammal, optionally a human, a non-human primate, a monkey, a horse, a cow, sheep, a goat, a pig, a dog, a cat, a rabbit, a rodent, a hamster, a rat, or a mouse; or

(ii) a non-mammalian vertebrate, optionally a bird, fish, an amphibian, or a reptile; and/or

(b) an additional agent, optionally an adjuvant or a therapeutic agent is to be further administered to the subject.

26. The substance for use of claim 24 or 25, wherein the disease, disorder, or condition comprises one or more of the following:

(a) a retinopathy, optionally a retinal vascular disease (optionally caused by inhibition of vascular development or excessive angiogenesis) and/or optionally selected from the group consisting of exudative vitreoretinopathy, familiar exudative vitreoretinopathy (FEVR), retinopathy of prematurity, Norrie disease, diabetic retinopathy (DR), diabetic macular edema, diabetic macular ischemia, age-related macular degeneration (AMD) (including wet AMD and dry AMD), retinopathy of prematurity (ROP), osteoporosis-pseudoglioma syndrome (OPPG), retinal vein occlusion, and Coats disease;

(b) a vascular disorder, optionally vascular malformation or vascular insufficiency, further optionally associated with ischemia-induced neovascularization;

(c) a bone disease or bone injury, optionally selected from the group consisting of osteoporosis (including osteoporosis pseudoglioma (OPPG) syndrome and juvenile primary osteoporosis), bone mineral density variability, and cancer-associated osteolysis;

(d) a muscle wasting disease, optionally selected from the group consisting of sarcopenia, cachexia, and muscular dystrophies; and/or

(e) a neural or neurodegenerative disease, optionally selected from the group consisting of stroke, traumatic brain injury, epilepsy, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Friedreich ataxia, Lewy body disease, spinal muscular atrophy, motor neuron disease, multiple sclerosis, Batten disease, and Creutzfeldt-Jakob disease.

27. The substance for use of any one of claims 24-26, wherein:

(I)

(i) the substance is to be administered to one or more of the subject's eyes, optionally intravitreally or via ocular drops;

(ii) the substance is to be locally administered, optionally to the eye, ear, nose (optionally intranasally), skin (optionally transdermally or epicutaneously), mucosa, skin, or vagina, or by inhalation; or

(iii) the substance is to be parenterally administered, optionally by injection (optionally intravenous, intramuscular, subcutaneous, intradermal, intrathecal, intra-arterial, intraarticular, intraosseous, or intraperitoneal administration) or by inhalation; or

(iv) the substance is to be enterally administered, optionally orally, sublingually, buccally, or rectally; and/or

(II) the multispecific antibody or antibody fragment of any one of claims 1-20 is to be administered to one or more of the subject's eyes at about 0.1-100000 ng per eye, about 1-100000 ng per eye, about 1-10000 ng per eye, about 10-10000 ng per eye, about 1-100 ng per eye, about 200-300 ng per eye, about 300-400 ng per eye, about 400-500 ng per eye, about 500-600 ng per eye, about 600-700 ng per eye, about 700-800 ng per eye, about 800-900 ng per eye, about 900-1000 ng per eye, about 1000-2000 ng per eye, about 2000-3000 ng per eye, about 3000-4000 ng per eye, about 4000-5000 ng per eye, about 5000-6000 ng per eye, about 6000-7000 ng per eye, about 7000-8000 ng per eye, about 8000-9000 ng per eye, about 9000-10000 ng per eye, about 10000-20000 ng per eye, about 20000-30000 ng per eye, about 30000-40000 ng per eye, about 40000-50000 ng per eye, about 50000-60000 ng per eye, about 60000-70000 ng per eye, about 70000-80000 ng per eye, about 80000-90000 ng per eye, or about 90000-100000 ng per eye.

28. A method of manufacturing the multispecific antibody or antibody fragment of any one of claims 1-16, comprising:

(a) culturing cells comprising the nucleic acid or the combination of nucleic acids of claim 17 or 18 in a condition that allows for expression of said multispecific antibody or antibody fragment, and

(b) harvesting and purifying the multispecific antibody or antibody fragment from the cell culture from (a).

29. A method of manufacturing the host cell of claim 21 or the population of such cells according to claim 22, comprising introducing the nucleic acid or the combination of nucleic acids of claim 17 or 18 and/or the vector or the combination of vectors of claim 19 or 20 into one or more cells, optionally wherein the introducing occurs *in vitro* or *ex vivo*.

30. The multispecific antibody or antibody fragment of any one of claims 1-16, the nucleic acid or the combination of nucleic acids of claim 17 or 18, the vector or the combination of vectors of claim 19 or 20, the host cell of claim 20, or the population of cells of claim 22, and/or the pharmaceutical composition of claim 23, for use in medicine.

31. The multispecific antibody or antibody fragment of any one of claims 1-16, the nucleic acid or the combination of nucleic acids of claim 17 or 18, the vector or the combination of vectors of claim 19 or 20, the host cell of claim 21, or the population of cells of claim 22, and/or the pharmaceutical composition of claim 23, for use in treating a disease, disorder, or condition, optionally wherein the disease, disorder, or condition comprises one or more of the following:

(a) a retinopathy, optionally a retinal vascular disease (optionally caused by inhibition of vascular development or excessive angiogenesis) and/or optionally selected from the group consisting of exudative vitreoretinopathy, familiar exudative vitreoretionopathy (FEVR), retinopathy of prematurity, Norrie disease, diabetic retinopathy (DR),

diabetic macular edema, diabetic macular ischemia, age-related macular degeneration (AMD) (including wet AMD and dry AMD), retinopathy of prematurity (ROP), osteoporosis-pseudoglioma syndrome (OPPG), retinal vein occlusion, and Coats disease;

(b) a vascular disorder, optionally vascular malformation or vascular insufficiency, further optionally associated with ischemia-induced neovascularization;

(c) a bone disease or bone injury, optionally selected from the group consisting of osteoporosis (including osteoporosis pseudoglioma (OPPG) syndrome and juvenile primary osteoporosis), bone mineral density variability, and cancer-associated osteolysis;

(d) a muscle wasting disease, optionally selected from the group consisting of sarcopenia, cachexia, and muscular dystrophies; and/or

(e) a neural or neurodegenerative disease, optionally selected from the group consisting of stroke, traumatic brain injury, epilepsy, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Friedreich ataxia, Lewy body disease, spinal muscular atrophy, motor neuron disease, multiple sclerosis, Batten disease, and Creutzfeldt-Jakob disease.

32. Use of the multispecific antibody or antibody fragment of any one of claims 1-16, the nucleic acid or the combination of nucleic acids of claim 17 or 18, the vector or the combination of vectors of claim 19 or 20, the host cell of claim 21, or the population of cells of claim 22, and/or the pharmaceutical composition of claim 23 in the manufacture of a medicament for treatment of a disease, disorder, or condition, optionally wherein the disease, disorder, or condition comprises one or more of the following:

(a) a retinopathy, optionally a retinal vascular disease (optionally caused by inhibition of vascular development or excessive angiogenesis) and/or optionally selected from the group consisting of exudative vitreoretinopathy, familiar exudative vitreoretinopathy (FEVR), retinopathy of prematurity, Norrie disease, diabetic retinopathy (DR), diabetic macular edema, diabetic macular ischemia, age-related macular degeneration (AMD) (including wet AMD and dry AMD), retinopathy of prematurity (ROP), osteoporosis-pseudoglioma syndrome (OPPG), retinal vein occlusion, and Coats disease;

(b) a vascular disorder, optionally vascular malformation or vascular insufficiency, further optionally associated with ischemia-induced neovascularization;

(c) a bone disease or bone injury, optionally selected from the group consisting of osteoporosis (including osteoporosis pseudoglioma (OPPG) syndrome and juvenile primary osteoporosis), bone mineral density variability, and cancer-associated osteolysis;

(d) a muscle wasting disease, optionally selected from the group consisting of sarcopenia, cachexia, and muscular dystrophies; and/or

(e) a neural or neurodegenerative disease, optionally selected from the group consisting of stroke, traumatic brain injury, epilepsy, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Friedreich ataxia, Lewy body disease, spinal muscular atrophy, motor neuron disease, multiple sclerosis, Batten disease, and Creutzfeldt-Jakob disease.