

What is claimed is:

1. An anti-ANG2 heavy-chain single-domain antibody, comprising a heavy chain variable region, wherein the heavy chain variable region comprises or consists of a sequence shown in SEQ ID NO: 4 or a sequence having at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity with the sequence shown in SEQ ID NO: 4 and having ANG2 binding activity ,

wherein, according to an IMGT numbering system, the heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 selected from a group consisting of:

HCDR1 shown in SEQ ID NO: 40, HCDR2 shown in SEQ ID NO: 41 and HCDR3 shown in SEQ ID NO: 42.

2. The anti-ANG2 heavy-chain single-domain antibody according to claim 1, wherein ANG2 is selected from human ANG2, rabbit ANG2 or monkey ANG2.

3. A recombinant protein, comprising the anti-ANG2 heavy-chain single-domain antibody according to any one of claims 1 to 2, preferably, the recombinant protein further comprises a bioactive substance, for example, a toxin having enzymatic activity or an active fragment (for example, abrin, ricin A, pseudomonas exotoxin or diphtheria toxin) of the toxin, a tumor necrosis factor or an interferon (for example, IFN- γ), a biological response modifier (for example, lymphokines IL-2, IL-2, IL2-6, IL-10 and GM-CSF) and an Fc fragment (for example, from an Fc region of IgG (for example, an IgG1, IgG2, IgG3 or IgG4 subtype), IgA1, IgA2, IgD, IgE or IgM, for example, from an Fc region of human, rabbit or monkey IgG, IgA1, IgD, IgE or IgM), preferably, the anti-ANG2 heavy-chain single-domain antibody and the Fc fragment are linked by a linker peptide, preferably, the linker peptide is GGGGSGGGGSGGGGS (SEQ ID NO: 47), preferably, the Fc fragment is a human IgG1 heavy chain constant region, more preferably an Fc fragment shown in GenBank No. AK303185.1, more preferably, the recombinant protein comprises or consists of a sequence shown in SEQ ID NO: 14.

4. A multi-specific antibody, preferably a bispecific antibody, comprising the anti-ANG2 heavy-chain single-domain antibody according to any one of claims 1 to 2, preferably, a structure of the bispecific antibody comprises a light chain and a heavy chain, wherein the light chain and the heavy chain are paired to form an interchain disulfide bond, and two heavy chains are paired to form an interchain disulfide bond, wherein the heavy chain is (VH)-(CH1)-(hinge region)-(Fc)-(linker peptide)-(VHH), and the light chain is (VL)-(light chain constant region).

5. The multi-specific antibody according to claim 4, wherein VHH is the anti-ANG2 heavy-chain single-domain antibody according to any one of claims 1 to 2, VH and VL are heavy chain and light chain variable regions of a second antibody, preferably, an antigen targeted by the second antibody is selected from an immune cell surface antigen, a tumor antigen, a virus, a bacterium, an endotoxin, a cytokine or a combination thereof; more

- preferably, the antigen targeted by the second antibody is selected from PD-L1, PD-1, VEGFA, IL-10, IL-10R, BCMA, VEGF, TGF- β , CTLA-4, LAG-3, TIGIT, CEA, CD38, SLAMF7, B7-H3, Her2, EpCAM, CD19, CD20, CD30, CD33, CD47, CD52, CD133, EGFR, GD2, GD3, GM2, RANKL, CD3 and/or CD16a, preferably, the antigen targeted by the second antibody is
- 5 VEGF, more preferably, the second antibody is selected from an anti-VEGF antibody, the anti-VEGF antibody comprises HCDR1, HCDR2 and HCDR3 contained in a heavy chain variable region shown in SEQ ID NO: 24 (preferably, according to an IMGT numbering system, the anti-VEGF antibody comprises HCDR1 shown in SEQ ID NO: 50, HCDR2 shown in SEQ ID NO: 51 and HCDR3 shown in SEQ ID NO: 53) and LCDR1, LCDR2 and LCDR3 contained
- 10 in a light chain variable region shown in SEQ ID NO: 27 (preferably, according to the IMGT numbering system, the anti-VEGF antibody comprises LCDR1 shown in SEQ ID NO: 54, LCDR2 shown in SEQ ID NO: 58 and LCDR3 shown in SEQ ID NO: 59), more preferably, a heavy chain variable region of the anti-VEGF antibody comprises or consists of a sequence shown in SEQ ID NO: 24 or a sequence having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%,
- 15 95%, 96%, 97%, 98% or 99% identity with the sequence shown in SEQ ID NO: 24, and a light chain variable region of the anti-VEGF antibody comprises or consists of a sequence shown in SEQ ID NO: 27 or a sequence having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity with the sequence shown in SEQ ID NO: 27.
6. The multi-specific antibody according to claim 4 or 5, wherein a sequence of CH1 is shown
- 20 in SEQ ID NO: 25, a sequence of the hinge region is shown in SEQ ID NO: 26, a sequence of the Fc constant region is shown in SEQ ID NO: 29, a sequence of the linker peptide is shown in SEQ ID NO: 30 or 47, and a sequence of the light chain constant region is shown in SEQ ID NO: 28.
7. A polynucleotide, encoding the anti-ANG2 heavy-chain single-domain antibody according to
- 25 any one of claims 1 to 2, the recombinant protein according to claim 3 or the multi-specific antibody according to any one of claims 4 to 6.
8. A vector, comprising the polynucleotide according to claim 7.
9. A host cell, comprising the vector according to claim 8.
10. A conjugate, comprising the anti-ANG2 heavy-chain single-domain antibody according to
- 30 any one of claims 1 to 2, the recombinant protein according to claim 3, or the multi-specific antibody according to any one of claims 4 to 6, and a conjugated moiety, wherein the conjugated moiety is a purification tag (for example, a His tag), a detectable label, a drug, a toxin, a cytokine, an enzyme or a combination thereof; preferably, the conjugated moiety is a radioisotope, a fluorescent substance, a chemiluminescent substance, a colored substance, a
- 35 chemotherapeutic agent, a biological toxin, polyethylene glycol or an enzyme.
11. A kit, comprising the anti-ANG2 heavy-chain single-domain antibody according to any one

of claims 1 to 2, the recombinant protein according to claim 3, the multi-specific antibody according to any one of claims 4 to 6 or the conjugate according to claim 10; preferably, the kit further comprises an anti-ANG2 heavy-chain single-domain antibody, a recombinant protein or a multi-specific antibody specifically recognizing the anti-ANG2 heavy-chain single-domain antibody according to any one of claims 1 to 2, the recombinant protein according to claim 3, the multi-specific antibody according to any one of claims 4 to 6 or the conjugate according to claim 10; optionally, the anti-ANG2 heavy-chain single-domain antibody, the recombinant protein or the multi-specific antibody further comprises a detectable label, for example, a radioisotope, a fluorescent substance, a chemiluminescent substance, a colored substance or an enzyme; preferably, the kit is used for detecting the presence or a level of ANG2 in a sample; or the kit comprises: (1) the anti-ANG2 heavy-chain single-domain antibody according to any one of claims 1 to 2, the recombinant protein according to claim 3, the multi-specific antibody according to any one of claims 4 to 6 or the conjugate according to claim 10, and (2) an antibody or an antigen-binding fragment of the antibody that targets another antigen, and/or a cytotoxic agent, and/or a chemotherapeutic drug, and optionally, an instruction for use.

12. A pharmaceutical composition, comprising the anti-ANG2 heavy-chain single-domain antibody according to any one of claims 1 to 2, the recombinant protein according to claim 3, the multi-specific antibody according to any one of claims 4 to 6 or the conjugate according to claim 10, optionally, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier and/or an excipient, preferably, the pharmaceutical composition is in a form suitable for administration through subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

13. Use of the anti-ANG2 heavy-chain single-domain antibody according to any one of claims 1 to 2, the recombinant protein according to claim 3, the multi-specific antibody according to any one of claims 4 to 6 or the conjugate according to claim 10 in the manufacture of a medicament for treating fundus neovascular disease, and/or a tumor.