

sequence of SEQ ID NO: 90; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 91.

5 As reported herein is an antibody that specifically binds to human PDGF-B, wherein the antibody comprises (a) a HVR-H1 comprising the amino acid sequence of SEQ ID NO: 93, (b) a HVR-H2 comprising the amino acid sequence of SEQ ID NO: 94, and (c) a HVR-H3 comprising the amino acid sequence of SEQ ID NO: 96.

10 The antibody further comprises (d) a HVR-L1 comprising the amino acid sequence of SEQ ID NO: 98; (e) a HVR-L2 comprising the amino acid sequence of SEQ ID NO: 99; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 100.

15 One aspect as reported herein is a bispecific antibody that specifically binds to human PDGF-B and ANG2, wherein the bispecific antibody comprises a binding site specifically binding to human PDGF-B comprising (a) a HVR-H1 comprising the amino acid sequence of SEQ ID NO: 93, (b) a HVR-H2 comprising the amino acid sequence of SEQ ID NO: 94, (c) a HVR-H3 comprising the amino acid sequence of SEQ ID NO: 96, (d) a HVR-L1 comprising the amino acid sequence of SEQ ID NO: 98, (e) a HVR-L2 comprising the amino acid sequence of SEQ ID NO: 99, and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 100.

20 As reported herein is an antibody that specifically binds to human PDGF-B, wherein the antibody comprises (a) a HVR-H1 comprising the amino acid sequence of SEQ ID NO: 102, (b) a HVR-H2 comprising the amino acid sequence of SEQ ID NO: 103, and (c) a HVR-H3 comprising the amino acid sequence of SEQ ID NO: 105.

25 In one embodiment the antibody further comprises (d) a HVR-L1 comprising the amino acid sequence of SEQ ID NO: 107; (e) a HVR-L2 comprising the amino acid sequence of SEQ ID NO: 108; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 109.

30 As reported herein is an antibody comprising a heavy chain variable domain amino acid sequence of sequence of SEQ ID NO: 10 and a light chain variable domain amino acid sequence selected from the group of SEQ ID NO: 40, SEQ ID NO: 44, SEQ ID NO: 48 and SEQ ID NO: 52.

In one embodiment the antibody is a monoclonal antibody.

In one embodiment the antibody is a bispecific antibody.

In one embodiment the antibody specifically binds to human PDGF-B but does not bind to human PDGF-C.

5 In one embodiment the antibody specifically binds to human, rat, mouse and cynomolgus PDGF-B.

In one embodiment the antibody inhibits the biological activity of human PDGF-B by inhibiting the binding of PDGF-B to its receptor.

10 In one embodiment the antibody inhibits the biological activity of human PDGF-B by inhibiting the cell migration.

In one embodiment the antibody inhibits the biological activity of human PDGF-B by inhibiting PDGF-B receptor phosphorylation.

In one embodiment the antibody inhibits the biological activity of human PDGF-B by inhibiting the cell proliferation.

15 As reported herein is an (isolated) nucleic acid encoding the antibody as reported herein.

As reported herein is a host cell comprising the nucleic acid as reported herein.

20 As reported herein is a method of producing an antibody as reported herein comprising culturing the host cell as reported herein to produce the antibody and recovering the antibody from the host cell or the cultivation medium.

As reported herein is a pharmaceutical formulation comprising an antibody as reported herein and optionally a pharmaceutically acceptable carrier. One aspect as reported herein is a pharmaceutical formulation comprising a bispecific antibody as reported herein and optionally a pharmaceutically acceptable carrier

25 In one embodiment the pharmaceutical formulation further comprises an additional therapeutic agent. In one embodiment the additional therapeutic agent is an anti-ANG2 antibody or an anti-VEGF antibody.

As reported herein is the antibody as reported herein for use as a medicament. One aspect as reported herein is the bispecific antibody as reported herein for use as a medicament.

5 As reported herein is the antibody as reported herein for use in treating on ocular vascular disease, preferably for use in treating macular degeneration. One aspect as reported herein is the bispecific antibody as reported herein for use in the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.

The antibody as reported herein for use in inhibiting the interaction between PDGF-B and its receptor.

10 The antibody as reported herein for use in inhibiting cell migration.

The antibody as reported herein for use in inhibiting proliferation.

15 As reported herein is the use of the antibody as reported herein in the manufacture of a medicament. One aspect as reported herein is the use of the bispecific antibody as reported herein in the manufacture of a medicament for the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.

In one embodiment the medicament is for the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.

In one embodiment the medicament is for inhibiting the interaction between PDGF-B and its receptor.

20 As reported herein is a method of treating an individual having on ocular vascular disease, preferably macular degeneration, comprising administering to the individual an effective amount of the antibody as reported herein.

25 As reported herein is a method of inhibiting the interaction between PDGF-B and its receptor in an individual comprising administering to the individual an effective amount of the antibody as reported herein to inhibiting the interaction between PDGF-B and its receptor.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

I. DEFINITIONS

5 An “acceptor human framework” for the purposes herein is a framework comprising the amino acid sequence of a light chain variable domain (VL) framework or a heavy chain variable domain (VH) framework derived from a human immunoglobulin framework or a human consensus framework, as defined below. An acceptor human framework “derived from” a human immunoglobulin framework or a human consensus framework may comprise the same amino acid

Patent Claims

1. A bispecific antibody that specifically binds to human PDGF-B and ANG2, wherein the bispecific antibody comprises a binding site specifically binding to human PDGF-B comprising (a) a HVR-H1 comprising the amino acid sequence of SEQ ID NO: 93, (b) a HVR-H2 comprising the amino acid sequence of SEQ ID NO: 94, (c) a HVR-H3 comprising the amino acid sequence of SEQ ID NO: 96, (d) a HVR-L1 comprising the amino acid sequence of SEQ ID NO: 98, (e) a HVR-L2 comprising the amino acid sequence of SEQ ID NO: 99, and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 100.
2. The bispecific antibody according to claim 1 wherein the bispecific antibody comprises a heavy chain variable domain that has the amino acid sequence of SEQ ID NO: 92 and a light chain variable domain that has the amino acid sequence of SEQ ID NO: 97.
3. The bispecific antibody according to claim 1, wherein the bispecific antibody comprises
 - a) a first light chain and a first heavy chain of an antibody specifically binding to a first antigen, and
 - b) a second light chain and a second heavy chain of an antibody specifically binding to a second antigen, wherein the constant domains CL and CH1 of the second light chain and the second heavy chain are replaced by each other,

wherein the first antigen or the second antigen is human PDGF-B.

4. The bispecific antibody according to claim 3, wherein the bispecific antibody is a bivalent antibody.
5. The bispecific antibody according to claim 3 or 4 comprising CH3 domains that are altered to increase the heterodimerization of both heavy chains containing these two CH3 domains, wherein one CH3 domain comprises a T366W mutation and the other CH3 domain comprises T366S, L368A, Y407V mutations, wherein all numberings are according to the Kabat EU index.
- 10 6. The bispecific antibody according to claim 3 or 4 comprising CH3 domains that are altered to increase the heterodimerization of both heavy chains containing these two CH3 domains, wherein one CH3 domain comprises Y349C and T366W mutations and the other CH3 domain comprises E356C, T366S, L368A and Y407V mutations, wherein all
15 numberings are according to the Kabat EU index.
7. The bispecific antibody according to any one of claims 1 to 6, wherein the bispecific antibody is of the human subclass IgG1 or the human subclass IgG4.
8. The bispecific antibody according to any one of claims 1 to 7, wherein the
20 bispecific antibody blocks the biological activity of human PDGF-B by inhibiting the binding of human PDGF-B to human PDGF receptor.
9. A pharmaceutical formulation comprising a bispecific antibody according to any one of claims 1 to 8 and optionally a pharmaceutically acceptable carrier.
- 25 10. The pharmaceutical formulation according to claim 9, further comprising an additional therapeutic agent selected from an anti-ANG2 antibody and an anti-VEGF antibody.

11. The bispecific antibody according to any one of claims 1 to 8 for use as a medicament.
12. The bispecific antibody according to any one of claims 1 to 8 for use in the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.

13. Use of the bispecific antibody according to any one of claims 1 to 8 in the manufacture of a medicament for the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.