

WHAT IS CLAIMED

1. A bispecific antibody or antigen-binding portion thereof, comprising a PD-L1 antigen-binding moiety associated with a VEGF antigen-binding moiety, wherein:

the PD-L1 antigen-binding moiety comprises:

a complementarity determining region (CDR) 1 comprising SEQ ID NO: 1, a CDR2 comprising SEQ ID NO: 2, and a CDR3 comprising SEQ ID NO: 3; and

the VEGF antigen-binding moiety comprises:

a heavy chain complementarity determining region (HCDR) 1 comprising SEQ ID NO: 4, a HCDR2 comprising SEQ ID NO: 5, a HCDR3 comprising SEQ ID NO: 6, a light chain complementarity determining region (LCDR) 1 comprising SEQ ID NO: 7, a LCDR2 comprising SEQ ID NO: 8, and a LCDR3 comprising SEQ ID NO: 9.

2. The bispecific antibody or antigen-binding portion thereof of claim 1, wherein the PD-L1 antigen-binding moiety comprises:

a variable domain comprising the amino acid sequence of SEQ ID NO: 10 or an amino acid sequence at least 85%, 90%, or 95% identical to SEQ ID NO: 10.

3. The bispecific antibody or antigen-binding portion thereof of claim 1 or 2, wherein the VEGF antigen-binding moiety comprises:

a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 11 or an amino acid sequence at least 85%, 90%, or 95% identical to SEQ ID NO: 11; and

a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence at least 85%, 90%, or 95% identical to SEQ ID NO: 12.

4. The bispecific antibody or antigen-binding portion thereof of any of the preceding claims, wherein the PD-L1 antigen-binding moiety is fused to the N terminal of the VEGF antigen-binding moiety.

5. The bispecific antibody or antigen-binding portion thereof of any of the preceding claims, wherein the PD-L1 antigen-binding moiety is from a single-domain antibody (sdAb), such as a VHH antibody.

6. The bispecific antibody or antigen-binding portion thereof of claim 5, wherein the VHH is derived from a camelid animal, comprising an alpaca or a llama.

7. The bispecific antibody or antigen-binding portion thereof of claim 5 or 6, wherein the PD-L1 antigen-binding moiety is operably linked to the N terminal of the light chain or heavy chain of

the VEGF antigen-binding moiety, optionally via a linker.

8. The bispecific antibody or antigen-binding portion thereof of claim 7, wherein the linker comprises or consists of 1 to 4 copies of GGGGS (G4S).

9. The bispecific antibody or antigen-binding portion thereof of any of the preceding claims, comprising a heavy chain and a light chain, wherein:

the heavy chain comprises domains operably linked as in VH-CH1-hinge-Fc, wherein the VH-CH1 is from the VEGF antigen binding moiety; and

the light chain comprises domains operably linked as in VHH-VL-CL, wherein the VHH is from the PD-L1 antigen binding moiety and the VL-CL is from the VEGF antigen binding moiety.

10. The bispecific antibody or antigen-binding portion thereof of claim 9, wherein the Fc region is a human IgG Fc region, preferably a human IgG1 Fc region.

11. The bispecific antibody or antigen-binding portion thereof of any of the preceding claims, wherein the heavy chain comprises SEQ ID NO: 13, and the light chain comprises SEQ ID NO: 14.

12. The bispecific antibody or antigen-binding portion thereof of any of the preceding claims, wherein the bispecific antibody is a humanized antibody.

13. An isolated nucleic acid molecule, comprising a nucleic acid sequence encoding the bispecific antibody or the antigen-binding portion thereof of any of claims 1-12.

14. A vector comprising the nucleic acid molecule of claim 13.

15. A host cell comprising the nucleic acid molecule of claim 13 or the vector of claim 14.

16. A pharmaceutical composition comprising the bispecific antibody or the antigen-binding portion thereof of any of claims 1-12 and a pharmaceutically acceptable carrier.

17. A method for producing the bispecific antibody or the antigen-binding portion thereof of any of claims 1-12, comprising the steps of:

- expressing the antibody or the antigen-binding portion thereof of any of claims 1-12 in the host cell of claim 15; and
- isolating the antibody or antigen-binding portion thereof from the host cell.

18. The bispecific antibody or the antigen-binding portion thereof as defined in any of claims 1-12 or the pharmaceutical composition of claim 16 for use in preventing or treating cancer in a subject.

19. The bispecific antibody or the antigen-binding portion thereof or pharmaceutical composition for use of claim 18, wherein the cancer is selected from colon cancer, colorectal

cancer, breast cancer, lung cancer, cervical cancer, renal cancer, glioblastoma, ovarian cancer, pancreatic cancer, prostate cancer, esophageal cancer, gastric cancer, lymphoma, melanoma, liver cancer, and head and neck cancer.

20. The bispecific antibody or the antigen-binding portion thereof for use of claim 18 or claim 19, wherein the bispecific antibody or antigen-binding portion thereof is in combination with a chemotherapeutic agent, radiation and/or other agents for use in cancer immunotherapy.

21. The bispecific antibody or antigen-binding portion thereof of any of claims 1-12 for use

- i) in the modulation of PD-L1/VEGF related immune responses;
- ii) in enhancing T cell proliferation and cytokine production; and/or
- iii) in stimulating an immune response or function, such as boosting the immune response against cancer cells.

22. The bispecific antibody or antigen-binding portion thereof as defined in any of claims 1-12 for use in diagnosing, treating or preventing cancers.

23. A kit comprising the bispecific antibody or antigen-binding portion thereof of any of claims 1-12.