CLAIMS

WHAT IS CLAIMED IS:

1. A multispecific antibody that binds to PDL1 and VEGF, comprising:

i) a first antigen-binding moiety comprising a single domain anti-PDL1 antibody that comprises a heavy chain variable region comprising:

a) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 1, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 2, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 3;

b) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 6, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 7, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 8;

c) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 11, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 12, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 13;

d) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 16, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 17, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 18;

e) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 21, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 22, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 23;

f) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 26, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 27, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 28;

g) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 31, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 32, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 33;

h) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 36, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 37, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 38;

i) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 41, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 42, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 43;

j) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 46, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 47, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 48;

k) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 51, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 52, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 53;

l) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 56, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 57, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 58;

m) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 61, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 62, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 63; or

n) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 66, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 67, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 68 ; and

ii) a second antigen-binding moiety comprising an anti-VEGF antibody that binds to VEGF comprises a heavy chain variable region (VH) comprising (1) a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 71, (2) a CDR- H2 comprising the amino acid sequence set forth in SEQ ID NO: 72, and (3) a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 73; and a light chain variable region (VL) comprising (1) a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 74, (2) a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 75, and (3) a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 76.

2. The multispecific antibody of claim 1, wherein the single domain antibody comprises a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 46, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 47, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 48.

3. The multispecific antibody of claim 1 or 2, wherein the single domain antibody comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 9, 14, 19, 24, 29, 34, 39, 44, 49, 54, 59, 64 or 69.

4. The multispecific antibody of any one of claims 1-3, wherein the single domain antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 49.

5. The multispecific antibody of any one of claims 1-4, wherein the second antigen-binding moiety comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 77, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 78.

6. The multispecific antibody of any one of claims 1-6, wherein the anti-VEGF antibody of the second antigen-binding moiety comprises an Fc region selected from the group consisting of the Fc regions of IgG1, IgG2, IgG3 and IgG4.

7. The multispecific antibody of any one of claims 1-6, wherein the Fc region comprises an IgG1 Fc region.

8. The multispecific antibody of any one of claims 1-7, wherein the multispecific antibody comprises a full-length immunoglobulin, a single-chain Fv (scFv) fragment, a Fab fragment, a Fab' fragment, a F(ab')2, an Fv fragment, a disulfide stabilized Fv fragment (dsFv), a (dsFv)2, a VHH, a VHH-Fc fusion, a Fv-Fc fusion, a scFv-Fc fusion, a scFv-Fv fusion, a diabody, a tribody, a tetrabody or any combination thereof.

9. The multispecific antibody of any one of claims 1-8, comprising:

i) a first antigen-binding moiety comprising a single domain anti-PDL1 antibody that comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 49; and

ii) a second antigen-binding moiety comprising an anti-VEGF antibody comprising a heavy chain variable region (VH) comprising the amino acid sequence set forth in SEQ ID NO: 77; and a light chain variable region (VL) comprising the amino acid sequence set forth in SEQ ID NO: 78.

10. The multispecific antibody of any one of claims 1-9, comprising a first chain comprising the amino acid sequence set forth in SEQ ID NO: 126, and a second chain comprising the amino acid sequence set forth in SEQ ID NO: 127.

11. The multispecific antibody of any one of claims 1-9, comprising a first chain comprising the amino acid sequence set forth in SEQ ID NO: 128, and a second chain comprising the amino acid sequence set forth in SEQ ID NO: 129.

12. An immunoconjugate comprising the multispecific antibody of any one of claims 1-11, linked to a therapeutic agent.

13. The immunoconjugate of claim 12, wherein the therapeutic agent is a cytotoxin.

14. The immunoconjugate of claim 12, wherein the therapeutic agent is a radioactive isotope.

15. An antigen-recognizing receptor comprising an extracellular antigen-binding domain that comprises a multispecific antibody of any one of claims 1-11.

16. The antigen-recognizing receptor of claim 15, which is a chimeric antigen receptor (CAR) or a recombinant T cell receptor.

17. The antigen-recognizing receptor of claim 15 or 16, which is a CAR.

18. The antigen-recognizing receptor of any one of claims 15-17, wherein the multispecific antibody comprised in the extracellular antigen-binding domain comprises a VHH, a scFv, a Fab, a Fab', a di-scFv or any combination thereof.

19. The antigen-recognizing receptor of any one of claims 15-18, wherein the multispecific antibody comprised in the extracellular antigen-binding domain comprises an anti-PDL1 VHH and an anti-VEGF scFv.

20. An immunoresponsive cell comprising an antigen-recognizing receptor of any one of claims 15-19.

21. The immunoresponsive cell of claim 20, wherein the immunoresponsive cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), a regulatory T cell, a Natural Killer T (NKT) cell and a myeloid cell.

22. The immunoresponsive cell of claim 21, wherein the immunoresponsive cell is a T cell.

23. A pharmaceutical composition comprising a) the multispecific antibody of any one of claims 1-11, the immunoconjugate of any one of claims 12-14, the immunoresponsive cell of any one of claims 20-22, and b) a pharmaceutically acceptable carrier.

24. One or more nucleic acid encoding the multispecific antibody of any one of claims 1-1-11.

25. One or more vector comprising the nucleic acid of claim 24.

26. A host cell comprising the nucleic acid of claim 24 or the vector of claim 25.

27. A method for preparing a multispecific antibody of any one of claims 1-11 comprising expressing the multispecific antibody in the host cell of claim 26 and isolating the multispecific antibody from the host cell.

28. A multispecific antibody of any one of claims 1-11 for use as a medicament.

29. A multispecific antibody of any one of claims 1-11 for use in treating cancer.

30. A pharmaceutical composition of claim 23 for use as a medicament.

31. A pharmaceutical composition of claim 23 for use in treating cancer.

32. The multispecific antibody of claim 29 or the pharmaceutical composition of claim 31, wherein the cancer exhibits high microsatellite instability (MSI).

33. The multispecific antibody of claim 29 or the pharmaceutical composition of claim 31, wherein the cancer is selected from the group consisting of mesothelioma, lung cancer, pancreatic cancer, ovarian cancer, breast cancer, colon cancer, pleural tumor, glioblastoma, esophageal cancer, gastric cancer, synovial sarcoma, thymic carcinoma, endometrial carcinoma, stomach cancer, cholangiocarcinoma, head and neck cancer, blood cancer and a combination thereof.

34. A kit comprising an antibody of any one of claims 1-11, an immunoconjugate of any one of claims 12-14, a pharmaceutical composition of claim 23, one or more nucleic acid of claim 24, one or more vector of claim 25 or an immunoresponsive cell of any one of claims 20-22.

35. The kit of claim 34, further comprising a written instruction for treating and/or preventing a neoplasm.