

CLAIMS

1. An isolated antibody or an antigen-binding fragment thereof, comprising:
 - (a) a heavy chain variable domain (VH) comprising,
 - i. a heavy chain CDR1 comprising an amino acid sequence ~~selected from the group consisting of SEQ ID NOs~~NO: 72, 75, 71, 73, 74, and 76-82, respectively;
 - ii. a heavy chain CDR2 comprising an amino acid sequence ~~selected from the group consisting of SEQ ID NOs~~NO: 84, 87, 83, 85, 86, and 88-94, respectively, or wherein SEQ ID NO: 87 is optionally replaced with any one of SEQ ID NOs: 95-97, respectively; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence ~~selected from the group consisting of SEQ ID NOs~~NO: 99, 102, 98, 100, 101, and 103-109, respectively, and
 - (b) a light chain variable domain (VL) comprising, ~~respectively,~~
 - i. a light chain CDR1 comprising an amino acid sequence ~~selected from the group consisting of SEQ ID NOs~~NO: 111, 114, 110, 112, 113, and 115-121, respectively, or wherein SEQ ID NO: 111 is optionally replaced with or SEQ ID NO: 122, and SEQ ID NO: 114 is optionally replaced with SEQ ID NO: 123;
 - ii. a light chain CDR2 comprising an amino acid sequence ~~selected from the group consisting of SEQ ID NOs~~NO: 125, 128, 124, 126, 127, and 129-135, respectively; and; and
 - iii. a light chain CDR3 comprising an amino acid sequence ~~selected from the group consisting of SEQ ID NOs~~NO: 137, 140, 136, 138, 139, and 141-147, respectively,

wherein the antibody or antigen-binding fragment is capable of specifically binding to a PD-L1; ~~preferably a human PD-L1.~~

2. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein: the PD-L1 is human PD-L1.

~~(1) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 87 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively; or~~

3. The isolated antibody or antigen-binding fragment thereof of claim 1 or 2, wherein:

~~(1) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 72, 84 and 99, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 111, 125 and 137, respectively; or~~

~~(3) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 87 and 102, respectively, and the VL comprises the light chain~~

CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively; or

(2) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 72, 84 and 99, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 122, 125 and 137, respectively; or

(1) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 95 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively; or

(2) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 96 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively; or

(3) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 97 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively; or

(4) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 95 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively; or

(5) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 96 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively; or

(6) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 97 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively.

3.4. The isolated antibody or antigen-binding fragment thereof ~~claim of any one of claims 1 or claim 2-3~~, wherein the VH comprises an amino acid sequence that is at least 90% identical to a sequence selected from the group consisting of SEQ ID NOs: 27, 31, 21, 25, 16, 19, 14, 17, 18, 20, 22-24, 26, 28-30, 19, and 32-44, and the VL comprises an amino acid sequence that is at least 90% identical to a

sequence selected from the group consisting of SEQ ID NOs: 46, 57, 59, 60, 61, 65, 68, 45-64, 66, 67, and 69-70, respectively~~67~~.

4.5. The isolated antibody or antigen-binding fragment thereof of ~~claim 1~~ any one of claims 1-4, wherein:

(1) ~~the VH comprises the amino acid sequence of SEQ ID NO:21, 25, 27 or 31, and the VL comprises the amino acid sequence of SEQ ID NO:68; or~~

the VH comprises the amino acid sequence of SEQ ID NO: 16 or 19, or 20, and the VL comprises the amino acid sequence of SEQ ID NO:65.

5.6. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-45, wherein the VH is fused to a heavy chain constant region of an immunoglobulin; and/or the VL is fused to a light chain constant region (CL) of an immunoglobulin.

6.7. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-56, wherein the K_D of the binding between the antibody or antigen-binding fragment thereof and the PD-L1 is 10^{-7} M to about 10^{-12} M, preferably about 10^{-8} M to about 10^{-12} M, or ~~more preferably about 10^{-9} M to about 10^{-12} M.~~ 10^{-12} M.

7.8. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-67, being rodent, chimeric, ~~human~~, partially humanized, or fully humanized.

8.9. The isolated antibody of claim 78, further comprising a constant domain of a human IgG1.

9.10. The isolated antibody of claim 89, comprising a heavy chain amino acid sequence of any one of SEQ ID NOs: 278-321, 279, 293-297, 349, and 348-391, 363-367, and a light chain amino acid sequence of any one of SEQ ID NOs: 322-347, 323, 334, 336-338, and 342-344.

11. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-910, further comprising a second antibody moiety, wherein the second antibody moiety is capable of specifically binding to a second antigen, ~~preferably.~~

10.12. The isolated antibody or antigen-binding fragment thereof of claim 11, wherein the second antibody moiety is a Fab, a Fab', a (Fab')₂, an Fv, a single chain Fv (scFv), an ~~ScFv~~ scFv-scFv, a minibody, a diabody, a sdAb, or an antibody mimetic.

13. The isolated antibody or antigen-binding fragment thereof of claim 1012, wherein the second antibody moiety is a sdAb.

11.14. The isolated antibody or antigen-binding fragment thereof of any one of claims 11-13, wherein the second antibody moiety is capable of specifically binding to CTLA-4, TIGIT, TIM-3, or LAG-3; ~~preferably the second antibody moiety is a sdAb.~~

12.15. The isolated antibody or antigen-binding fragment thereof of claim 1114, wherein the amino-terminus or carboxyl-terminus of the heavy chain or light chain of ~~a full-length IgG capable of~~

~~specifically recognizing PD-L1~~the isolated antibody or antigen-binding fragment thereof is fused, optionally via a peptide linker, to the carboxyl-terminus or amino-terminus of the sdAb capable of specifically binding to CTLA-4, TIGIT, TIM-3 or LAG-3.

16. The isolated antibody or antigen-binding fragment thereof of claim 15, wherein the isolated antibody or antigen-binding fragment thereof is fused via a peptide linker to the carboxyl-terminus or amino terminus of the sdAb capable of specifically binding to CTLA-4, TIGIT, TIM-3 or LAG-3.

~~13-17.~~ The isolated antibody or antigen-binding fragment thereof of claim 15 or 16, wherein the full-length IgG capable of specifically recognizing PD-L1isolated antibody or antigen-binding fragment thereof is fused to the sdAb capable of specifically binding to CTLA-4, TIGIT, TIM-3 or LAG-3 via a peptide linker having the amino acid sequence of one of SEQ ID NOs: 397-399.

~~14.~~ A second isolated antibody or antigen-binding fragment thereof capable of specifically binding to PD-L1 competitively with the isolated antibody or antigen-binding fragment thereof of any one of claims 1-13.

~~15-18.~~ A pharmaceutical composition comprising the isolated antibody or antigen-binding fragment thereof of any one of claims 1-13 or the second isolated antibody or antigen-binding fragment thereof of claim 14,17 and a pharmaceutical acceptable carrier.

~~16-19.~~ The isolated antibody or antigen-binding fragment thereof of any one of claims 1-13, the second isolated antibody or antigen-binding fragment thereof of claim 1417 or the pharmaceutical composition of claim 1518, for use in treating a PD-L1 related disease in a subject in need thereof, preferably the PD-L1 related disease is cancer or a pathogenic infection.

~~17-20.~~ Use of the isolated antibody or antigen-binding fragment thereof of any one of claims 1-13, the second isolated antibody or antigen-binding fragment thereof of claim 1417 or the pharmaceutical composition of claim 1518, in the manufacture of a medicament for the treatment of PD-L1 related disease in a subject in need thereof, preferably the PD-L1 related disease is cancer or a pathogenic infection in a subject in need thereof.

~~18-21.~~ The isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of claim 1619, or the use of claim 1720, wherein the cancer is a solid tumor, preferably the solid tumor is colon cancer.

~~19.~~ An isolated nucleic acid encoding isolated antibody or antigen-binding fragment any one of claims 1-13 or the secondThe isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of claim 14.

22. 19, or the use of claim 20.—, wherein the cancer is a solid tumor and the solid tumor is colon cancer.

23. An isolated nucleic acid encoding the isolated antibody or antigen-binding fragment of any one of claims 1-17.

20-24. A vector comprising the isolated nucleic acid of claim ~~19~~23.