

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: 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: 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: 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: 111, 114, 110, 112, 113, and 115-121, respectively, or wherein SEQ ID NO: 111 is optionally replaced with 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: 125, 128, 124, 126, 127, and 129-135, respectively; and
 - iii. a light chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 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:
 - (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
 - (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: 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

- (4) 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
 - (5) 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
 - (6) 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
 - (7) 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
 - (8) 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
 - (9) 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
 - (10) 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. The isolated antibody or antigen-binding fragment thereof claim 1 or claim 2, 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, 1-15, 17, 18, 20, 22-24, 26, 28-30, 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: 65, 68, 45-64, 66, 67, and 69-70, respectively.
4. The isolated antibody or antigen-binding fragment thereof of claim 1, 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
 - (2) the VH comprises the amino acid sequence of SEQ ID NO:16 or 19, and the VL comprises the amino acid sequence of SEQ ID NO:65.
5. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-4, 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) or an immunoglobulin.
 6. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-5, 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.
 7. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-6, being rodent, chimeric, human, partially humanized, or fully humanized.
 8. The isolated antibody of claim 7, further comprising a constant domain of a human IgG1.
 9. The isolated antibody of claim 8, comprising a heavy chain amino acid sequence of any one of SEQ ID NOs: 278-321 and 348-391, and a light chain amino acid sequence of any one of SEQ ID NOs:322-347.
 10. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-9, further comprising a second antibody moiety, wherein the second antibody moiety is capable of specifically binding to a second antigen, and wherein the second antibody moiety is a Fab, a Fab', a (Fab')₂, an Fv, a single chain Fv (scFv), an ScFv-scFv, a minibody, a diabody, a sdAb, or an antibody mimetic.
 11. The isolated antibody or antigen-binding fragment thereof of claim 10, wherein the second antibody moiety is capable of specifically binding to CTLA-4, TIGIT, TIM-3, or LAG-3, and wherein the second antibody moiety is a sdAb.
 12. The isolated antibody or antigen-binding fragment thereof of claim 11, 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 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.
 13. The isolated antibody or antigen-binding fragment thereof of claim 12, wherein the full-length IgG capable of specifically recognizing PD-L1 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. 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, and a pharmaceutical acceptable carrier.
16. 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 14 or the pharmaceutical composition of claim 15, for use in treating cancer or pathogenic infection in a subject in need thereof.
17. 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 14 or the pharmaceutical composition of claim 15, in the manufacture of a medicament for the treatment of cancer or pathogenic infection in a subject in need thereof.
18. The isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of claim 16, or the use of claim 17, wherein the cancer is a solid tumor or colon cancer.
19. The isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of claim 16 or 18, or the use of any one of claim 17 or 18, in combination with an additional cancer therapy, wherein the additional cancer therapy is a surgery, radiation, chemotherapy, immunotherapy, hormone therapy, or a combination thereof.
20. The isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of claims 16 or 18-19, or the use of any one of claims 17-19, wherein the isolated antibody or antigen-binding fragment or pharmaceutical composition is to be administered systemically or locally, by intravenous administration or intratumoral administration.
21. The isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of claims 16 or 18-20, or the use of any one of claims 17-20, wherein the subject is a human.