

level of PD-L1 in the sample indicates that the subject is more likely to respond to treatment with an anti-cancer therapy. In some examples, the presence or expression level of PD-L1 in the sample indicates the likelihood that the subject will exhibit benefit from treatment with an anti-cancer therapy. In some examples, the method further comprises selecting an anti-cancer therapy for the subject based on the presence or expression level of PD-L1 in the sample. In some examples, the method further comprises administering a therapeutically effective amount of an anti-cancer therapy to the subject.

In one example, the disclosure features use of a therapeutically effective amount of an anti-cancer therapy comprising a PD-1 axis binding antagonist in the manufacture of a medicament for treating a subject having a cancer, wherein the subject is one who has been selected based on the presence or expression of PD-L1 in a biological sample from the subject according to any of the preceding methods.

In some examples, the cancer is selected from the group consisting of non-small cell lung cancer, squamous cell cancer, small-cell lung cancer, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, leukemia, and head and neck cancer. In some examples, the cancer is non-small cell lung cancer (NSCLC). In some examples, the NSCLC is adenocarcinoma of the lung or squamous carcinoma of the lung. In some examples, the sample is a tumor sample. In some examples, the tumor sample comprises tumor-infiltrating immune cells, tumor cells, stromal cells, or any combination thereof. In some examples, the tumor sample has a detectable expression level of PD-L1 in tumor-infiltrating immune cells that comprise about 1% or more of the tumor sample by area. In some examples, the tumor sample has a detectable expression level of PD-L1 in tumor-infiltrating immune cells that comprise about 5% or more of the tumor sample by area. In some examples, the tumor sample has a detectable expression level of PD-L1 in tumor-infiltrating immune cells that comprise about 10% or more of the tumor sample by area. In some examples, the tumor sample has a detectable expression level of PD-L1 in about 1% or more of the tumor cells in the tumor sample. In some examples, the tumor sample has a detectable expression level of PD-L1 in about 5% or more of the tumor cells in the tumor sample. In some examples, the tumor sample has a detectable expression level of PD-L1 in about 10% or more of the tumor cells in the tumor sample. In some examples, the anti-cancer therapy comprises a PD-1 axis binding antagonist. In some examples, the PD-1 axis binding antagonist is selected from the group consisting of a PD-L1 binding antagonist, a PD-1 binding antagonist, and a PD-L2 binding antagonist. In some examples, the PD-1 axis binding antagonist is a PD-L1 binding antagonist. In some examples, the PD-L1 binding antagonist inhibits the binding of PD-L1 to one or more of its ligand binding partners. In some examples, the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1. In some examples, the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1. In some examples, the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1. In some examples, the PD-L1 binding antagonist is an antibody. In some examples, the antibody is selected from the group consisting of: YW243.55.S70, MPDL3280A (atezolizumab), MDX-1105, MEDI4736 (durvalumab), and MSB0010718C (avelumab). In some examples, the PD-1 axis binding antagonist is a PD-1 binding antagonist. In some examples, the PD-1 binding antagonist inhibits the binding of PD-1 to one or more of its ligand binding partners. In some examples, the PD-1 binding antagonist inhibits the binding of PD-1 to PD L1. In some examples, the PD-1 binding antagonist inhibits the binding of PD-1 to PD L2. In some

WHAT IS CLAIMED IS:

1. An isolated antibody that specifically binds PD-L1, wherein the antibody comprises the following hypervariable regions (HVRs):
 - (a) an HVR-H1 comprising the amino acid sequence of SNGLT (SEQ ID NO: 2);
 - (b) an HVR-H2 comprising the amino acid sequence of TINKDASAYYASWAKG (SEQ ID NO: 3);
 - (c) an HVR-H3 comprising the amino acid sequence of IAFKTGTSI (SEQ ID NO: 4);
 - (d) an HVR-L1 comprising the amino acid sequence of QASESVYSNNYLS (SEQ ID NO: 9);
 - (e) an HVR-L2 comprising the amino acid sequence of LASTLAS (SEQ ID NO: 10); and
 - (f) an HVR-L3 comprising the amino acid sequence of IGGKSSSTDGNA (SEQ ID NO: 11).
2. The antibody of claim 1, further comprising the following heavy chain variable domain (VH) framework regions (FRs):
 - (a) FR-H1 comprising the amino acid sequence of QSLEESGGRLVKPDETLTITCTVSGIDLS (SEQ ID NO: 5);
 - (b) FR-H2 comprising the amino acid sequence of WVRQAPGEGLEWIG (SEQ ID NO: 6);
 - (c) FR-H3 comprising the amino acid sequence of RLTISKPSSTKVLDLKITSPPTTEDTATYFCGR (SEQ ID NO: 7); and
 - (d) FR-H4 comprising the amino acid sequence of WGPGLTVTVSS (SEQ ID NO: 8).
3. The antibody of claim 1 or 2, further comprising a VH sequence of SEQ ID NO:16.
4. The antibody of any one of claims 1-3, further comprising the following light chain variable domain (VL) FRs:
 - (a) FR-L1 comprising the amino acid sequence of AIVMTQTPSPVSAVGGTVTINC (SEQ ID NO: 12);
 - (b) FR-L2 comprising the amino acid sequence of WFQQKPGQPPKLLIY (SEQ ID NO: 13);
 - (c) FR-L3 comprising the amino acid sequence of GVPSRFKSGSGTQFTLTISGVQCDDAATYYC (SEQ ID NO: 14); and
 - (d) FR-L4 comprising the amino acid sequence of FGSGTEVVVR (SEQ ID NO: 15)
5. The antibody of claim 4, further comprising a VL sequence of SEQ ID NO:17.
6. The antibody of claim 1, wherein the antibody comprises (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 16 and (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17.
7. The antibody of any one of claims 1-6, wherein the antibody comprises a VH sequence of SEQ ID NO: 16 and a VL sequence of SEQ ID NO: 17.
8. The antibody of any one of claims 1-7, wherein the antibody is a monoclonal antibody.

9. The antibody of claim 8, wherein the monoclonal antibody is a rabbit monoclonal antibody.
10. The antibody of any one of claims 1-7, wherein the antibody is an IgG antibody.
11. The antibody of any one of claims 1-7, wherein the antibody is an antibody fragment that specifically binds PD-L1.
12. The antibody of claim 11, wherein the antibody fragment is selected from the group consisting of Fab, single chain variable fragment (scFv), Fv, Fab', Fab'-SH, F(ab')₂, and diabody.
13. An isolated nucleic acid encoding an isolated antibody of any one of claims 1-12.
14. A vector comprising the nucleic acid of claim 13.
15. A host cell comprising the vector of claim 14.
16. An immunoconjugate comprising the antibody of any one of claims 1-12.
17. The antibody of any one of claims 1-12 for use in detecting the presence or expression level of PD-L1 in a biological sample.
18. The antibody of claim 17, wherein the detecting is by immunohistochemistry (IHC), immunofluorescence (IF), flow cytometry, Enzyme-Linked Immunosorbant Assay (ELISA), or immunoblotting.
19. The antibody of claim 18, wherein the detecting is by IHC.
20. The antibody of any one of claims 17-19, wherein the sample comprises a fixed tissue.
21. The antibody of claim 20, wherein the fixed tissue is a formalin-fixed paraffin-embedded (FFPE) tissue.
22. The antibody of any one of claims 17-21, wherein the sample is from a subject having, or at risk of, a cancer or an immune dysfunction, wherein the immune dysfunction is an unresolved acute infection, chronic infection, or an autoimmune disease.
23. A method of detecting the presence or expression level of PD-L1 in a biological sample comprising contacting the biological sample with the antibody of any one of claims 1-12 and detecting the presence of the bound antibody.

24. The method of claim 23, wherein the detecting is by IHC, IF, flow cytometry, ELISA, or immunoblotting.

25. The method of claim 24, wherein the detecting is by IHC.

26. The method of any one of claims 23-25, wherein the sample comprises a fixed tissue.

27. The method of claim 26, wherein the fixed tissue is a FFPE tissue.

28. The method of any one of claims 23-27, wherein the sample is from a subject having, or at risk of, a cancer or an immune dysfunction, wherein the immune dysfunction is an unresolved acute infection, chronic infection, or an autoimmune disease.

29. The method of claim 28, wherein the sample is from a subject having a cancer.

30. The method of any one of claims 23-29, wherein an expression level of PD-L1 in the sample that is increased relative to a control expression level of PD-L1 indicates that the subject is likely to respond to treatment with an anti-cancer therapy comprising a PD-1 axis binding antagonist.

31. The method of any one of claims 23-29, wherein an expression level of PD-L1 in the sample that is increased relative to a control expression level of PD-L1 indicates that the subject is more likely to respond to treatment with an anti-cancer therapy comprising a PD-1 axis binding antagonist.

32. The method of any one of claims 23-29, wherein an expression level of PD-L1 in the sample that is increased relative to a control expression level of PD-L1 indicates the likelihood that the subject will exhibit benefit from treatment with an anti-cancer therapy comprising a PD-1 axis binding antagonist.

33. The method of any one of claims 29-32, wherein the method further comprises selecting an anti-cancer therapy comprising a PD-1 axis binding antagonist for the subject based on the expression level of PD-L1 in the sample.