

GVPSRFKSGSGTQFTLTISGVQCDDAATYYC (SEQ ID NO: 14); and (h) FR-L4 comprising the amino acid sequence of FGGGTEVVVR (SEQ ID NO: 15). In some embodiments, the antibody comprises a VH sequence of SEQ ID NO: 16 and a VL sequence of SEQ ID NO: 17.

In another aspect, the invention features an isolated antibody that competes for binding to PD-L1 with any one of the preceding antibodies.

In another aspect, the invention features an isolated antibody that binds to the same epitope as any one of the preceding antibodies.

In some embodiments, any one of the preceding antibodies can be a monoclonal antibody. In some embodiments, the monoclonal antibody can be a rabbit monoclonal antibody.

In some embodiments, any one of the preceding antibodies can be an IgG antibody (e.g., an IgG1 antibody).

In some embodiments, any one of the preceding antibodies can be an antibody fragment that specifically binds PD-L1. In some embodiments, 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.

In another aspect, the invention features an immunoconjugate comprising any one of the preceding antibodies.

In another aspect, the invention features an isolated nucleic acid that encodes any of the antibodies described herein. The disclosure features a vector (e.g., an expression vector) comprising the nucleic acid for expressing the antibody. The disclosure also features host cells comprising the preceding nucleic acids and/or vectors. In one aspect, the invention features a vector comprising the preceding nucleic acid. In another aspect, the invention features a host cell comprising the preceding vector.

In some aspects, any one of the preceding antibodies can be for use in detecting the presence or expression level of PD-L1 in a biological sample. In some embodiments, the detecting is by immunohistochemistry (IHC), immunofluorescence (IF), flow cytometry, ELISA, or immunoblot. In some embodiments, the detecting is by IHC. In some embodiments, the sample comprises a fixed tissue. In some embodiments, the fixed tissue is a formalin-fixed paraffin-embedded (FFPE) tissue. In some embodiments, the sample is from a subject having, or at risk of, a cancer or an immune dysfunction. In some embodiments, the immune dysfunction is a T-cell dysfunctional disorder. In some embodiments, the T-cell dysfunctional disorder is an unresolved acute infection, chronic infection, or tumor immunity.

A further aspect of the invention is a method of detecting the presence or expression level of PD-L1 in a biological sample comprising contacting the biological sample with any one of the preceding antibodies and detecting the presence of the bound antibody. In some embodiments, the detecting is by IHC, IF, flow cytometry, ELISA, or immunoblot. In some embodiments, the detecting is by IHC. In some embodiments, the sample comprises a fixed tissue. In some embodiments, the fixed tissue is a FFPE tissue. In some embodiments, the sample is from a subject having, or at risk of, a cancer or an immune dysfunction. In some embodiments, the immune dysfunction is a T-cell dysfunctional disorder. In some embodiments, the T-cell dysfunctional disorder is an unresolved acute infection, chronic infection, or tumor immunity. In some embodiments, the sample is from a subject having a cancer. In some embodiments, the presence or expression level of PD-L1 in the sample indicates that the subject is likely to respond to treatment with an anti-cancer therapy. In some embodiments, the presence or expression

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 embodiments, 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 embodiments, 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 embodiments, the method further comprises administering a therapeutically effective amount of an anti-cancer therapy to the subject.

In one aspect, the invention features use of a therapeutically effective amount of an anti-cancer therapy 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 embodiments, 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 embodiments, the cancer is non-small cell lung cancer (NSCLC). In some embodiments, the NSCLC is adenocarcinoma of the lung or squamous carcinoma of the lung. In some embodiments, the sample is a tumor sample. In some embodiments, the tumor sample comprises tumor-infiltrating immune cells, tumor cells, stromal cells, or any combination thereof. In some embodiments, 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 embodiments, 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 embodiments, 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 embodiments, 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 embodiments, 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 embodiments, 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 embodiments, the anti-cancer therapy comprises a PD-1 axis binding antagonist. In some embodiments, 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 embodiments, the PD-1 axis binding antagonist is a PD-L1 binding antagonist. In some embodiments, the PD-L1 binding antagonist inhibits the binding of PD-L1 to one or more of its ligand binding partners. In some embodiments, the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1. In some embodiments, the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1. In some embodiments, the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1. In some embodiments, the PD-L1 binding antagonist is an antibody. In some embodiments, the antibody is selected from the group consisting of: YW243.55.S70, MPDL3280A (atezolizumab), MDX-1105, MEDI4736 (durvalumab), and MSB0010718C (avelumab). In some embodiments, the PD-1 axis binding antagonist is a PD-1 binding antagonist. In some embodiments, the PD-1 binding antagonist inhibits the binding of PD-1 to one or more of its ligand binding partners. In some embodiments, the PD-1 binding antagonist inhibits the binding of PD-1 to PD L1. In some embodiments, the PD-1 binding antagonist inhibits the binding of PD-1 to PD L2. In some

43. The method of any one of claims 33-41, wherein the presence or expression level of PD-L1 in the sample indicates that the subject is more likely to respond to treatment with an anti-cancer therapy.

44. The method of any one of claims 33-41, wherein 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.

45. The method of any one of claims 41-44, wherein 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.

46. Use of a therapeutically effective amount of an anti-cancer therapy 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 the method of any one of claims 41-45.

47. The method or use of any one of claims 38 and 41-46, wherein 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.

48. The method or use of claim 47, wherein the cancer is non-small cell lung cancer (NSCLC).

49. The method or use of claim 48, wherein the NSCLC is adenocarcinoma of the lung or squamous carcinoma of the lung.

50. The method or use of any one of claims 38 and 41-49, wherein the sample is a tumor sample.

51. The method or use of claim 50, wherein the tumor sample comprises tumor-infiltrating immune cells, tumor cells, stromal cells, or any combination thereof.

52. The method or use of claim 51, wherein 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.

53. The method or use of claim 52, wherein 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.

54. The method of or use claim 53, wherein 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.

55. The method or use of any one of claims 50-54, wherein the tumor sample has a detectable expression level of PD-L1 in about 1% or more of the tumor cells in the tumor sample.

56. The method or use of claim 55, wherein the tumor sample has a detectable expression level of PD-L1 in about 5% or more of the tumor cells in the tumor sample.

57. The method or use of claim 56, wherein the tumor sample has a detectable expression level of PD-L1 in about 10% or more of the tumor cells in the tumor sample.

58. The use of any one of claims 46-57, wherein the anti-cancer therapy comprises a PD-1 axis binding antagonist.

59. The use of claim 58, wherein 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.

60. The use of claim 59, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.

61. The use of claim 60, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to one or more of its ligand binding partners.

62. The use of claim 61, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

63. The use of claim 61, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

64. The use of any one of claims 61-63, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

65. The use of any one of claims 60-64, wherein the PD-L1 binding antagonist is an antibody.

66. The use of claim 65, wherein the antibody is selected from the group consisting of: YW243.55.S70, MPDL3280A (atezolizumab), MDX-1105, and MEDI4736 (durvalumab), and MSB0010718C (avelumab).

67. The use of claim 59, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.

68. The use of claim 67, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to one or more of its ligand binding partners.

69. The use of claim 68, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

70. The use of claim 68, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

71. The use of any one of claims 68-70, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

72. The use of any one of claims 67-71, wherein the PD-1 binding antagonist is an antibody.

73. The use of claim 72, wherein the antibody is selected from the group consisting of: MDX 1106 (nivolumab), MK-3475 (pembrolizumab), CT-011 (pidilizumab), MEDI-0680 (AMP-514), PDR001, REGN2810, and BGB-108.

74. The use of any one of claims 67-71, wherein the PD-1 binding antagonist is an Fc-fusion protein.

75. The use of claim 74, wherein the Fc-fusion protein is AMP-224.

76. The use of any one of claims 46-75, wherein the medicament is to be administered to the patient with an effective amount of a second therapeutic agent.

77. The use of claim 76, wherein the second therapeutic agent is selected from the group consisting of a cytotoxic agent, a growth-inhibitory agent, a radiation therapy agent, an anti-angiogenic agent, and combinations thereof.

78. The method or use of any one of claims 33-77, wherein the subject is a human.