

[0007] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety.

SUMMARY

[0008] Provided are isolated antibodies that bind to human OX40.

[0009] Provided are anti-human OX40 agonist antibodies wherein the antibody is a depleting antibody. In one embodiment, provided are anti-human OX40 agonist antibodies wherein the antibody depletes cells that express human OX40 *in vitro* and binds human OX40 with an affinity of less than or equal to about 1 nM. In some embodiments, the antibodies deplete CD4⁺ effector T cells. In some embodiments the antibodies deplete regulatory T cells (Treg). In some embodiments, the depleting is by ADCC and/or phagocytosis. In some embodiments, the depleting is by ADCC. In one aspect, the present invention refers to an antibody that binds human OX40, wherein the antibody comprises: (1) a heavy chain variable domain (VH) comprising (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:2; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:3; and (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:4; and (2) a light chain variable domain (VL) comprising (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:7. In another aspect, the present invention refers to an antibody that binds human OX40, wherein the antibody comprises: (1) a heavy chain variable domain (VH) comprising the sequence of SEQ ID NO:56; and (2) a light chain variable domain (VL) comprising the sequence of SEQ ID NO: 57. In still another aspect, the present invention refers to an antibody that binds human OX40, wherein the antibody comprises: (1) a heavy chain variable domain (VH) comprising the sequence of SEQ ID NO:56; (2) a light chain variable domain (VL) comprising the sequence of SEQ ID NO: 57; and (3) a human IgG1 Fc region. In another aspect, the present invention refers to an isolated nucleic acid encoding the antibody of the present invention. In one other aspect, the present invention refers to a host cell comprising the nucleic acid of the present invention. In one other aspect, the present invention refers to a method of producing an antibody comprising culturing the host cell of the present invention so that the antibody is produced. In one other aspect, the present invention refers to an immunoconjugate comprising the antibody of the present invention conjugated to a cytotoxic agent or label. In one other aspect, the present invention refers to a composition comprising the antibody of the present invention and a pharmaceutically acceptable carrier. In one other aspect, the present invention refers to the use of the antibody of the present invention in the manufacture of a medicament for treatment of cancer. In one other aspect, the present invention refers to the use of the antibody of the present invention in the manufacture of a medicament for enhancing immune function in an individual.

[0010] Provided are anti-human OX40 agonist antibodies that bind human OX40 with an affinity of less than or equal to about 0.45 nM. In some embodiments, the antibody binds human OX40 with an affinity of less than or equal to about 0.4 nM. In some embodiments, antibody binding affinity is determined using radioimmunoassay. In some embodiments, the antibody binds human OX40 and cynomolgus OX40. In some embodiments, binding to human and cynomolgus OX40 is determined using a FACS assay. In some embodiments, binding to human OX40 has an EC50 of less than or equal to 0.2 ug/ml. In some embodiments, binding to human OX40 has an EC50 of less than or equal to 0.3 ug/ml or lower. In some embodiments, binding to cynomolgus OX40 has an EC50 of less than or equal to 1.5 ug/ml. In some embodiments, binding to cynomolgus OX40 has an EC50 of less than or equal to 1.4 ug/ml.

[0011] In another embodiment, the disclosure provides anti-human OX40 agonist antibodies that increase (are capable of increasing) CD4+ effector T cell proliferation and/or increasing cytokine production by the CD4+ effector T cell as compared to proliferation and/or cytokine production prior to treatment with anti-human OX40 agonist antibody. In some embodiments, the cytokine is gamma interferon.

[0012] In another embodiment, the disclosure provides anti-human OX40 agonist antibodies that increase (are capable of increasing) memory T cell proliferation and/or increasing cytokine production by the memory cell. In some embodiments, the cytokine is gamma interferon.

[0013] In another embodiment, the disclosure provides anti-human OX40 agonist that inhibit (are capable of inhibiting) Treg function. In some embodiments, the antibodies inhibit Treg suppression of effector T cell function. In some embodiments, effector T cell function is effector T cell proliferation and/or cytokine production. In some embodiments, the effector T cell is a CD4+ effector T cell.

[0014] In another embodiment, the disclosure provides anti-human OX40 agonist antibodies that increase (are capable of increasing) OX40 signal transduction in a target cell that expresses OX40. In some

embodiments, OX40 signal transduction is detected by monitoring NFkB downstream signaling (e.g., in the OX40 expressing cell, e.g., CD4+ effector T cell, CD8+ effector T cell, CD4+ memory T cell).

[0015] In another embodiment, provided are anti-human OX40 agonist antibodies that are stable after treatment at 40C for two weeks.

[0016] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibodies comprise a variant IgG1 Fc polypeptide comprising a mutation that eliminates binding to human effector cells, wherein the antibodies have diminished activity relative to anti-human OX40 agonist antibodies comprising native sequence IgG1 Fc portion. In some embodiments, the antibodies comprise a variant Fc portion comprising a mutation that eliminates binding to FcR (e.g., a DANA or N297G mutation). In some embodiments, the activity is one or more of: increasing CD4+ effector T cell proliferation and/or cytokine production, increasing CD4+ memory T cell proliferation and/or cytokine production, and/or depleting cells by ADCC and/or phagocytosis.

[0017] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein antibody cross-linking is required for anti-human OX40 agonist antibody function. In some embodiments, anti-human OX40 agonist antibody function is one or more of: increasing CD4+ effector T cell proliferation and/or cytokine production, increasing CD4+ memory T cell proliferation and/or cytokine production, and/or depleting cells by ADCC and/or phagocytosis.

[0018] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises (a) a VH domain comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 2, 8 or 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 3, 10, 11, 12, 13 or 14, and (iii) HVR-H3 comprising an amino acid sequence selected from SEQ ID NO: 4, 15, or 19; and (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 7, 22, 23, 24, 25, 26, 27, or 28.

[0019] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:2; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:3; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:4; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising an amino acid sequence selected from SEQ ID NO:7.

[0020] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:2; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:3; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:4; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e)

HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising an amino acid sequence selected from SEQ ID NO:26.

[0021] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:2; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:3; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:4; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising an amino acid sequence selected from SEQ ID NO:27.

[0022] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 108, 114, 116, 183, or 184.

[0023] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises, wherein the antibody comprises a light chain variable domain (VL) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 109, 115 or 117.

[0024] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises a heavy chain variable domain (VH) sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:56. In some embodiments, the VH sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-human OX40 agonist antibody comprising that sequence retains the ability to bind to human OX40. In some embodiments, total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:56. In some embodiments, the VH comprises one, two or three HVRs selected from: (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:2, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:3, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:4.

[0025] In another embodiment, provided are anti-human OX40 agonist antibodies, wherein the antibody comprises a light chain variable domain (VL) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:57. In some embodiments, the VL sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity contains substitutions (e.g., conservative substitutions), insertions, or deletions relative to the reference sequence, but an anti-human OX40 agonist antibody comprising that sequence retains

the ability to bind to human OX40. In some embodiments, a total of 1 to 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO: 57. In some embodiments, the VL comprises one, two or three HVRs selected from (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

[0026] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO: 56.

[0027] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VL sequence of SEQ ID NO: 57.

[0028] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO:56 and a VL sequence of SEQ ID NO: 57.

[0029] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO: 94.

[0030] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VL sequence of SEQ ID NO: 95.

[0031] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO:94 and a VL sequence of SEQ ID NO: 95.

[0032] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO: 96.

[0033] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VL sequence of SEQ ID NO: 97.

[0034] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO:96 and a VL sequence of SEQ ID NO: 97.

[0035] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO: 180.

[0036] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VL sequence of SEQ ID NO: 179.

[0037] In another embodiment, provided are agonist anti-human OX40 antibodies comprising a VH sequence of SEQ ID NO:180 and a VL sequence of SEQ ID NO: 179.

[0038] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VH sequence of SEQ ID NO: 182.

[0039] In another embodiment, provided are anti-human OX40 agonist antibodies comprising a VL sequence of SEQ ID NO: 181.

[0040] In another embodiment, provided are agonist anti-human OX40 antibodies comprising a VH sequence of SEQ ID NO:182 and a VL sequence of SEQ ID NO: 181.

[0041] In some embodiments of any of the antibodies of the disclosure, the antibody is a full length human IgG1 antibody.

[0042] In some embodiments of any of the antibodies of the disclosure, the antibody is a human antibody. In some embodiments of any of the antibodies of the disclosure, the antibody is a humanized antibody. In some embodiments of any of the antibodies of the disclosure, the antibody is a chimeric antibody.

[0043] In some embodiments of any of the antibodies of the disclosure, the antibody is a naked antibody.

[0044] In another embodiment, provided are isolated nucleic acids encoding any of the anti-human OX40 antibodies (e.g., agonist antibodies) provided herein.

[0045] In another embodiment, provided are host cells comprising the nucleic acid encoding any of the anti-human OX40 antibodies (e.g., agonist antibodies) provided herein.

[0046] In another embodiment, provided are methods of producing an antibody comprising culturing the host cell provided herein so that the antibody is produced. In some embodiments, the methods further comprise recovering the antibody from the host cell.

[0047] In another embodiment, provided are immunoconjugates comprising any of the anti-human OX40 antibodies (e.g., agonist antibodies) provided herein and a cytotoxic agent.

[0048] In another embodiment, provided are pharmaceutical formulations comprising any of the anti-human OX40 antibodies (e.g., agonist antibodies) provided herein and a pharmaceutically acceptable carrier. In yet another embodiment, provided are pharmaceutical formulations comprising (a) any of the anti-human OX40 agonist antibodies described herein at a concentration between about 10 mg/mL and about 100 mg/mL, (b) a polysorbate, wherein the polysorbate concentration is about 0.02% to about 0.06%; (c) a histidine buffer at about pH 5.0 to about pH 6.0; and (d) a saccharide, wherein the saccharide concentration is about 120mM to about 320 mM. In some embodiments, the histidine buffer is at pH 5.0 to 6.0. In some embodiments, the saccharide is sucrose. In some embodiments, the pharmaceutical formulation comprises (a) any of the anti-human OX40 agonist antibodies described herein, (b) polysorbate 20, wherein the polysorbate concentration is about 0.02%; (c) a histidine acetate buffer at pH 6.0; and (d) sucrose, wherein the sucrose concentration is about 320 mM. In some embodiments, the pharmaceutical formulation comprises (a) any of the anti-human OX40 agonist antibodies described herein, (b) polysorbate 20, wherein the polysorbate concentration is about 0.02%; (c) a histidine acetate buffer at pH 5.5; and (d) sucrose, wherein the sucrose concentration is about 240 mM. In some embodiments, the pharmaceutical formulation comprises (a) any of the anti-human OX40 agonist antibodies described herein, (b) polysorbate 20, wherein the polysorbate concentration is about 0.04%; (c) a histidine acetate buffer at pH 6.0; and (d) sucrose, wherein the sucrose concentration is about 120 mM. In some embodiments, the pharmaceutical

[0049] In another embodiment, an anti-human OX0 agonist antibody provided herein is for use as a medicament.

[0050] In another embodiment, an anti-human OX0 agonist antibody provided herein is for use in treating cancer.

[0051] In another embodiment, an anti-human OX0 agonist antibody provided herein is for use in one or more of: inhibiting Treg function (e.g., inhibiting the suppressive function of Tregs), killing OX40 expressing cells (e.g., cells that express high levels of OX40), increasing effector T cell function and/or increasing memory T cell function, decrease tumor immunity, enhance T cell function and/or depleting OX-40 expressing cells.

[0052] In another embodiment, provided is use of an anti-human OX0 agonist antibody provided herein in the manufacture of a medicament for treatment of cancer.

[0053] In another embodiment, provided is use of an anti-human OX0 agonist antibody provided herein in the manufacture of a medicament for one or more of: inhibiting Treg function (e.g., inhibiting the suppressive function of Tregs), killing OX40 expressing cells (e.g., cells that express high levels of OX40), increasing effector T cell function and/or increasing memory T cell function, decrease tumor immunity, enhance T cell function and/or depleting OX-40 expressing cells.

[0054] In another embodiment, provided are methods of treating an individual having cancer comprising administering to the individual an effective amount of any of the anti-human OX40 agonist antibodies provided herein. In some embodiments, the methods further comprise administering an additional therapeutic agent. In some embodiments, the additional therapeutic agent comprises a chemotherapeutic agent. In some embodiments, the additional therapeutic agent comprises a PD-1 axis binding antagonist.

[0055] In another embodiment, provided are methods of diagnosis or detection using any of the anti-human OX40 antibodies disclosed herein.

[0056] In another embodiment, provided are kits or articles of manufacture comprising any of the anti-human OX40 antibodies disclosed herein. In some embodiments, the kits or articles of manufacture comprise a medicament comprising an anti-human OX40 agonist antibody described herein and an optional pharmaceutically acceptable carrier. In some embodiments, the kits or articles of manufacture further comprise instructions for administration of the medicament for treatment of cancer.

[0057] It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present disclosure. These and other aspects of the invention will become apparent to one of skill in the art. These and other embodiments of the disclosure are further described by the detailed description that follows.

CLAIMS

WHAT IS CLAIMED IS:

1. An antibody that binds human OX40, wherein the antibody comprises:

(1) a heavy chain variable domain (VH) comprising (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:2; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:3; and (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:4; and

(2) a light chain variable domain (VL) comprising (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.
2. The antibody of claim 1, wherein the antibody binds human OX40 with an affinity of less than or equal to about 0.4 nM.
3. The antibody of claim 1 or claim 2, wherein the antibody binds human OX40 and cynomolgus OX40.
4. The antibody of any one of claims 1-3, wherein the antibody is stable after treatment at 40°C for two weeks.
5. The antibody of any one of claims 1-4, wherein the VH sequence has at least 90% sequence identity to the amino acid sequence of SEQ ID NO:56.
6. The antibody of claim 5, wherein the VH sequence has at least 95% identity to the amino acid sequence of SEQ ID NO:56.
7. The antibody of any one of claims 1-6, wherein the VL has at least 90% sequence identity to the amino acid sequence of SEQ ID NO:57.
8. The antibody of claim 7, wherein the VL sequence has at least 95% identity to the amino acid sequence of SEQ ID NO:57.
9. The antibody of any one of claims 1-8, comprising a VH sequence of SEQ ID NO: 56.
10. The antibody of any one of claims 1-9, comprising a VL sequence of SEQ ID NO: 57.
11. The antibody of any one of claims 1-10, further comprising a human IgG1 Fc region.

12. The antibody of any one of claims 1-11, wherein the antibody is a monoclonal antibody.
13. The antibody of any one of claims 1-12, wherein the antibody is a humanized antibody.
14. An antibody that binds human OX40, wherein the antibody comprises:
 - (1) a heavy chain variable domain (VH) comprising the sequence of SEQ ID NO:56;and
 - (2) a light chain variable domain (VL) comprising the sequence of SEQ ID NO: 57.
15. The antibody of claim 14, wherein the antibody is a monoclonal antibody.
16. An antibody that binds human OX40, wherein the antibody comprises:
 - (1) a heavy chain variable domain (VH) comprising the sequence of SEQ ID NO:56;
 - (2) a light chain variable domain (VL) comprising the sequence of SEQ ID NO: 57;and
 - (3) a human IgG1 Fc region.
17. The antibody of claim 16, wherein the antibody is a monoclonal antibody.
18. An isolated nucleic acid encoding the antibody of any one of the preceding claims.
19. A host cell comprising the nucleic acid of claim 18.
20. A method of producing an antibody comprising culturing the host cell of claim 19 so that the antibody is produced.
21. The method of claim 20, further comprising recovering the antibody from the host cell.
22. An immunoconjugate comprising the antibody of any one of the preceding claims conjugated to a cytotoxic agent or label.
23. The immunoconjugate of claim 22, wherein the label is selected from the group consisting of a fluorescent label, a chromophoric label, an electron-dense label, a chemiluminescent label, a radioactive label, an enzyme, and a ligand.

24. The immunoconjugate of claim 22, wherein the cytotoxic agent is selected from the group consisting of a radioactive isotope, a chemotherapeutic agent, and an antibiotic.
25. A composition comprising the antibody of any one of claims 1-17 and a pharmaceutically acceptable carrier.
26. The composition of claim 25, wherein the composition comprises a buffer, a surfactant, and a saccharide.
27. The composition of claim 25, wherein the composition comprises 10 mg/mL - 100 mg/mL antibody, 0.01% - 0.1% (w/v) surfactant, 100 mM - 320 mM saccharide, 1 mM - 50 mM histidine buffer, and has a pH of 5.0 - 6.0.
28. The composition of claim 25, wherein the composition comprises 10 mg/mL - 100 mg/mL antibody, 0.01% - 0.1% (w/v) surfactant, 100 mM - 150 mM saccharide, 1 mM - 25 mM histidine buffer, and has a pH of 5.0 - 6.0.
29. The composition of claim 25, wherein the composition comprises 50 mg/mL - 75 mg/mL antibody, 0.01% - 0.1% (w/v) surfactant, 110 mM - 130 mM saccharide, 20 mM - 30 mM histidine buffer, and has a pH of 5.0 - 6.0.
30. The composition of claim 25, wherein the composition comprises 10 mg/mL - 100 mg/mL antibody, 0.02% - 0.06% (w/v) polysorbate, 100 mM - 320 mM sucrose, 1 mM - 50 mM histidine buffer, and has a pH of 5.0 - 6.0.
31. The composition of claim 25, wherein the composition comprises 60 mg/mL antibody, 0.03% (w/v) polysorbate, 120 mM sucrose, 20 mM histidine acetate buffer, and has a pH of 5.5.
32. The antibody of any one of claims 1-17 or the composition of any one of claims 25-31 for use as a medicament.
33. The antibody of any one of claims 1-17 or the composition of any one of claims 25-31 for use in treating cancer.
34. The antibody of any one of claims 1-17 or the composition of any one of claims 25-31 for use in enhancing immune function in an individual.
35. Use of the antibody of any one of claims 1-17 in the manufacture of a medicament for treatment of cancer.

36. Use of the antibody of any one of claims 1-17 in the manufacture of a medicament for enhancing immune function in an individual.
37. The antibody or composition for use of claim 33 or claim 34 or the use of claim 35 or claim 36, wherein the medicament, antibody, or composition is to be administered with an additional therapeutic agent.
38. The antibody for use, composition for use, or use of claim 37, wherein the additional therapeutic agent comprises a chemotherapeutic agent.
39. The antibody for use, composition for use, or use of claim 37, wherein the additional therapeutic agent comprises a PD-1 axis binding antagonist.
40. The antibody for use, composition for use, or use of claim 39, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.
41. The antibody for use, composition for use, or use of claim 40, wherein the PD-L1 binding antagonist is an anti-PD-L1 antibody.
42. The antibody for use, composition for use, or use of claim 41, wherein the anti-PD-L1 antibody is MPDL3280A.
43. The antibody for use, composition for use, or use of claim 39, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.
44. The antibody for use, composition for use, or use of claim 43, wherein the PD-1 binding antagonist is an anti-PD-1 antibody.
45. The antibody for use, composition for use, or use of claim 44, wherein the anti-PD-1 antibody is nivolumab or pembrolizumab.
46. The antibody or composition for use of claim 33 or the use of claim 35, wherein the cancer is selected from the group consisting of breast cancer, lung cancer, melanoma, renal cell cancer, bladder cancer, colorectal cancer, and ovarian cancer.
47. The antibody or composition for use of claim 33 or the use of claim 35, wherein the cancer is triple-negative breast cancer.
48. The antibody or composition for use of claim 33 or the use of claim 35, wherein the cancer is non-small cell lung cancer.

49. The antibody or composition for use of claim 33 or the use of claim 35, wherein the cancer is a cancer of the urinary tract.