

We claim:

1. An isolated monoclonal antibody that binds to human Inducible COStimulator molecule (ICOS), wherein the antibody comprises a heavy chain variable domain comprising CDR1, CDR2, and CDR3 regions comprising the amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively, and a light chain variable domain comprising CDR1, CDR2, and CDR3 regions comprising the amino acid sequences of SEQ ID NOs: 12, 14 and 15, respectively.

10 2. An isolated monoclonal antibody that binds to human ICOS, wherein the antibody comprises a heavy and light chain variable domain comprising the amino acid sequence of SEQ ID NOs: 5 and 6, respectively.

3. The antibody of claim 2, wherein the antibody comprises heavy and light chains comprising the amino acid sequences of SEQ ID NOs: 7 and 8, respectively.

4. The antibody of claim 1, wherein the antibody is a humanized antibody.

5. The antibody of claim 2, wherein the antibody is a humanized antibody.

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6. The antibody of claim 1, wherein the antibody is an IgG1 or IgG2a antibody.

7. The antibody of claim 2, wherein the antibody is an IgG1 or IgG2a antibody.

8. The antibody of claim 6, wherein the antibody comprises one amino acid substitution in the Fc region compared to human IgG1 amino acid sequence set forth in SEQ ID NO: 206.

30 9. The antibody of claim 7, wherein the antibody comprises one amino acid substitution in the Fc region compared to the human IgG1 amino acid sequence set forth in SEQ ID NO: 206.

10. The antibody of claim 8, wherein the substitution enhances affinity of the antibody to Fc $\gamma$  type IIb receptor (Fc $\gamma$ RIIb) and/or reduces antibody-dependent cell-mediated cytotoxicity (ADCC) activity compared to an IgG1 control antibody.

11. The antibody of claim 9, wherein the substitution enhances affinity of the antibody to Fc $\gamma$ RIIb and/or reduces antibody-dependent cell-mediated cytotoxicity (ADCC) activity compared to an IgG1 control antibody.

10 12. The antibody of claim 1, wherein the antibody blocks the binding and/or the interaction of ICOS Ligand (ICOS-L) to human ICOS.

13. The antibody of claim 2, wherein the antibody blocks the binding and/or the interaction of ICOS-L to human ICOS.

14. The antibody of claim 1, wherein the antibody binds to human, cynomolgus, mouse, and rat ICOS.

15. The antibody of claim 2, wherein the antibody binds to human, cynomolgus, mouse, and rat ICOS.

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16. An isolated nucleic acid encoding a heavy chain variable domain and/or light chain variable domain of an antibody that binds to human ICOS, wherein the heavy and light chain variable domains comprise the amino acid sequences of SEQ ID NOs: 5 and 6, respectively.

17. The nucleic acid of claim 16, wherein the nucleic acid encodes a heavy chain and/or light chain comprising the amino acid sequences of SEQ ID NOs: 7 and 8, respectively.

30 18. A method of producing an antibody that binds to human ICOS, comprising expressing one or more nucleic acids encoding the heavy and light chain variable domain amino acid sequences of SEQ ID NOs: 5 and 6, respectively, in a host cell, thereby producing the antibody.

19. The method of claim 18, wherein the one or more nucleic acids encode the heavy and light chain amino acid sequences of SEQ ID NOs: 7 and 8.

20. A composition comprising the antibody of claim 1 and a pharmaceutically acceptable carrier.

21. The composition of claim 20, further comprising an additional therapeutic agent, wherein the additional therapeutic agent is an anti-cancer therapeutic agent, an immunostimulatory therapeutic agent, a chemotherapeutic agent, a radiotherapeutic agent, an immunotherapeutic agent, and/or an immunogenic therapeutic agent.

22. The composition of claim 21, wherein the additional therapeutic agent is an anti-programmed death protein 1 (PD-1) antibody, an anti-programmed death ligand 1 (PD-L1) antibody, and/or an anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) antibody.

23. A composition comprising the antibody of claim 2 and a pharmaceutically acceptable carrier.

24. The composition of claim 23, further comprising an additional therapeutic agent, wherein the additional therapeutic agent is an anti-cancer therapeutic agent, an immunostimulatory therapeutic agent, a chemotherapeutic agent, a radiotherapeutic agent, an immunotherapeutic agent, and/or an immunogenic therapeutic agent.

25. The composition of claim 24, wherein the additional therapeutic agent is an anti-PD-1 antibody, anti-PD-L1 antibody, and/or an anti-CTLA-4 antibody.

26. A composition comprising the antibody of claim 3 and a pharmaceutically acceptable carrier.

27. The composition of claim 26, further comprising an additional therapeutic agent, wherein the additional therapeutic agent is an anti-cancer therapeutic agent, an immunostimulatory therapeutic agent, a chemotherapeutic agent, a radiotherapeutic agent, an immunotherapeutic agent, and/or an immunogenic therapeutic agent.

28. The composition of claim 27, wherein the additional therapeutic agent is an anti-PD-1 antibody, anti-PD-L1 antibody, and/or an anti-CTLA-4 antibody.

29. The antibody of any one of claims 1, 4, 6, 8, 10, 12 and 14 for use as a medicament.

30. The antibody of any one of claims 2, 3, 5, 7, 9, 11, 13 and 15 for use as a medicament.

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31. The antibody of any one of claims 1, 4, 6, 8, 10, 12 and 14 for use in the treatment of cancer.

32. The antibody for use of claim 31, wherein the cancer is bladder cancer, breast cancer, uterine/cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, pancreatic cancer, colon cancer, kidney cancer, head and neck cancer, lung cancer, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid cancer, skin cancer, neoplasm of the central nervous system, lymphoma, leukemia, myeloma, sarcoma, or virus-related cancer.

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33. The antibody for use of claim 31, wherein the cancer is colorectal cancer (CRC), head and neck squamous cell carcinoma (HNSCC), melanoma, NSCLC-adenocarcinoma type (NSCLC-AD), NSCLC-squamous cell type (NSCLC-SQC), adenocarcinoma of the prostate (PRC), renal cell carcinoma (RCC), or urothelial carcinoma (UCC).

34. The antibody of any one of claims 2, 3, 5, 7, 9, 11, 13 and 15 for use in the treatment of cancer.

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35. The antibody for use of claim 34, wherein the cancer is bladder cancer, breast cancer, uterine/cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, pancreatic cancer, colon cancer, kidney cancer, head and neck cancer, lung cancer, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid

cancer, skin cancer, neoplasm of the central nervous system, lymphoma, leukemia, myeloma, sarcoma, or virus-related cancer.

36. The antibody for use of claim 34, wherein the cancer is colorectal cancer (CRC), head and neck squamous cell carcinoma (HNSCC), melanoma, NSCLC-adenocarcinoma type (NSCLC-AD), NSCLC-squamous cell type (NSCLC-SQC), adenocarcinoma of the prostate (PRC), renal cell carcinoma (RCC), or urothelial carcinoma (UCC).

10 37. The antibody of any one of claims 1, 4, 6, 8, 10, 12 and 14 for use in enhancing an immune response.

38. The antibody of any one of claims 2, 3, 5, 7, 9, 11, 13 and 15 for use in enhancing an immune response.

39. Use of the antibody of any one of claims 1, 4, 6, 8, 10, 12 and 14 in the manufacture of a medicament for treatment of cancer.

20 40. Use of the antibody of any one of claims 2, 3, 5, 7, 9, 11, 13 and 15 in the manufacture of a medicament for treatment of cancer.

41. The antibody of any one of claims 1, 4, 6, 8, 10, 12 and 14 for use in for treating or delaying progression of cancer in a human subject, wherein an effective amount of the antibody is to be administered to the human subject.

42. The antibody for use of claim 41, where in the antibody is to be administered with one or more additional therapeutic agent to the human subject.

30 43. The antibody for use of claim 42, wherein the additional therapeutic agent is a chemotherapeutic agent.

44. The antibody for use of claim 42, wherein the additional therapeutic agent is an anti-PD-1 antibody, an anti-PD-L1 antibody, and/or an anti-CTLA-4 antibody.

45. The antibody for use of any one of claims 41-44, wherein the antibody is to be administered in at least one administration cycle, wherein for each of the at least one cycles, at least one dose of the antibody is to be administered at a dose of about 375 mg.

46. The antibody of any one of claims 2, 3, 5, 7, 9, 11, 13 and 15 for use in for treating or delaying progression of cancer in a human subject, wherein an effective amount of the antibody is to be administered to the human subject.

10 47. The antibody for use of claim 46, where in the antibody is to be administered with one or more additional therapeutic agent to the human subject.

48. The antibody for use of claim 47, wherein the additional therapeutic agent is a chemotherapeutic agent.

49. The antibody for use of claim 47, wherein the additional therapeutic agent is an anti-PD-1 antibody, an anti-PD-L1 antibody, and/or an anti-CTLA-4 antibody.

20 50. The antibody for use of any one of claims 46-49, wherein the antibody is to be administered in at least one administration cycle, wherein for each of the at least one cycles, at least one dose of the antibody is to be administered at a dose of about 375 mg.

51. The antibody of any one of claims 1, 4, 6, 8, 10, 12 and 14 for use in stimulating an immune response in a human subject, wherein an effective amount of the antibody is to be administered to the human subject.

52. The antibody for use of claim 51, wherein the subject has a tumor and an immune response against the tumor is stimulated.

30 53. The antibody for use of claim 51, wherein the subject has a chronic viral infection and an immune response against the viral infection is stimulated.

54. The antibody for use of claim 51, wherein the antibody is to be administered in an amount or frequency sufficient to achieve and/or maintain a receptor occupancy of less than about 80%.

55. The antibody of any one of claims 2, 3, 5, 7, 9, 11, 13 and 15 for use in stimulating an immune response in a human subject, wherein an effective amount of the antibody is to be administered to the human subject.

56. The antibody for use of claim 55, wherein the subject has a tumor and an immune response against the tumor is stimulated.

10 57. The antibody for use of claim 55, wherein the subject has a chronic viral infection and an immune response against the viral infection is stimulated.

58. The antibody for use of claim 55, wherein the antibody is to be administered in an amount or frequency sufficient to achieve and/or maintain a receptor occupancy of less than about 80%.