

We claim:

1. An isolated monoclonal antibody, or antigen-binding portion thereof, which binds to human glucocorticoid-inducible TNF receptor (GITR)), comprising heavy chain CDR1, CDR2, and exhibits the following properties:
 - (a) ~~binds to soluble human GITR;~~
 - (b) ~~binds to membrane bound human GITR;~~
 - (c) ~~binds to membrane bound cynomolgus GITR;~~
 - (d) ~~induces or enhances T cell activation;~~
 - (e) ~~inhibits the binding of GITR ligand to GITR on 3A9 hGITR cells;~~
 - (f) ~~at most partially inhibiting the binding of GITR ligand to GITR on activated T cells;~~
 - (g) ~~binds to a conformational epitope on mature human GITR (SEQ ID NO: 4);~~
 - (h) ~~binds to both O-linked CDR3 sequences comprising SEQ ID NOs: 20, 21, and N-glycosylated 22, respectively, and unglycosylated human GITR;~~
 - (i) ~~has agonist activity in the absence of binding to an Fc receptor, but wherein binding to an Fc receptor further enhances the agonist activity;~~ light chain CDR1, CDR2, and
 - (j) ~~competes in either direction or both directions for binding to human GITR with one or more of antibodies 28F3, 3C3 1, 3C3 2, 2G6, 8A6, 9G7 1, 9G7 2, 14E3, 19H8 1, 19H8 2, 19D3, 18E10 CDR3 sequences comprising SEQ ID NOs: 23, 24, and 6G1025, respectively.~~
2. The antibody, ~~or antigen-binding portion thereof~~, of claim 1, wherein the antibody ~~stimulates an anti-tumor immune response~~ comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 13 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 14.
3. The antibody, ~~or antigen-binding portion thereof~~, of claim 1 or claim 2, wherein the antibody stimulates an antigen-specific T cell response.
4. The antibody, ~~or antigen-binding portion thereof~~, of any one of the preceding claims, ~~wherein the antibody increases IL-2 and/or IFN- γ production in GITR-expressing T cells.~~

5. — The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody increases T cell proliferation.

6. — The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody does not bind to Fc receptors.

7. — The antibody, or antigen binding portion thereof, of any one of claims 1-5, wherein the antibody binds to one or more activating FcγRs.

8. — The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody binds to soluble human GITR with a K_D of 10 nM or less as measured by Biacore.

9. — The antibody, or antigen binding portion thereof, of any one of the preceding claims 1-3, wherein the antibody binds to membrane bound human GITR with a K_D of 1 nM or less as measured by Scatchard analysis.

105. The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody binds to membrane bound human GITR with an EC_{50} of 1 nM or less as measured by FACS.

11. — The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody binds to membrane bound cynomolgus GITR with an EC_{50} of 10 nM or less as measured by FACS.

12. — The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody induces or enhances T cell activation without requiring multivalent cross-linking.

13. — ~~The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody inhibits the binding of GITR ligand to GITR with an EC₅₀ of 1 µg/mL or less as measured by FACS.~~

14. — ~~The antibody, or antigen binding portion thereof, of any one of the preceding claims 4, wherein the antibody binds to PTGGPGCGPGRLLLGTGT (SEQ ID NO: 217) and CRDYPGEE (SEQ ID NO: 218) of mature human GITR (SEQ ID NO: 4), as determined by HDX-MS.~~

15. — ~~An isolated monoclonal antibody, or antigen binding portion thereof, which specifically binds to glucocorticoid inducible TNF receptor (GITR) and comprise the three variable heavy chain CDRs and the three variable light chain CDRs that are in the variable heavy chain and variable light chain pairs selected from the group consisting of:~~

- ~~— (a) SEQ ID NOs: 13 and 14;~~
- ~~— (b) SEQ ID NOs: 26 and 27;~~
- ~~— (c) SEQ ID NOs: 39 and 40;~~
- ~~— (d) SEQ ID NOs: 52 and 53;~~
- ~~— (e) SEQ ID NOs: 52 and 54;~~
- ~~— (f) SEQ ID NOs: 71 and 72;~~
- ~~— (g) SEQ ID NOs: 84 and 85;~~
- ~~— (h) SEQ ID NOs: 97 and 98;~~
- ~~— (i) SEQ ID NOs: 97 and 99;~~
- ~~— (j) SEQ ID NOs: 115 and 116;~~
- ~~— (k) SEQ ID NOs: 128 and 129;~~
- ~~— (l) SEQ ID NOs: 128 and 130; and~~
- ~~— (m) SEQ ID NOs: 335 and 336.~~

16. — ~~An isolated monoclonal antibody, or antigen binding portion thereof, which binds to glucocorticoid inducible TNF receptor (GITR), comprising:~~

- ~~— (a) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 20, 21, and 22, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 23, 24, and 25, respectively;~~

——(b) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 33, 34, and 35, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 36, 37, and 38, respectively;

(c) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 46, 47, and 48, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 49, 50, and 51, respectively;

(d) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 62, 63, and 64, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 65, 66, and 67, respectively;

(e) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 62, 63, and 64, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 68, 69, and 70, respectively;

(f) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 78, 79, and 80, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 81, 82, and 83, respectively;

(g) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 91, 92, and 93, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 94, 95, and 96, respectively;

(h) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 106, 107, and 108, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 109, 110, and 111, respectively;

(i) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 106, 107, and 108, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 112, 113, and 114, respectively;

(j) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 122, 123, and 124, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 125, 126, and 127, respectively;

(k) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 138, 139, and 140, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 141, 142, and 143, respectively;

~~(l) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 138, 139, and 140, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 144, 145, and 146, respectively; or~~

~~(m) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 342-344, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 345-347, respectively.~~

~~17. The antibody, or antigen binding portion thereof, of claim 16, wherein the antibody comprises heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 20, 21, and 22, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 23, 24, and 25, respectively.~~

~~18. The antibody, or antigen binding portion thereof, of claim 16, wherein the antibody comprises heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 33, 34, and 35, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 36, 37, and 38, respectively.~~

~~19. The antibody, or antigen binding portion thereof, of claim 16, wherein the antibody comprises heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 46, 47, and 48, respectively, and/or light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 49, 50, and 51, respectively.~~

~~20. An isolated monoclonal antibody, or antigen binding portion thereof, which binds to glucocorticoid-inducible TNF receptor (GITR) and comprises heavy and light chain variable regions, wherein the heavy chain variable region comprises an amino acid sequence which is at least 90% identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 13, 26, 39, 52, 71, 84, 97, 115, 128, and 335.~~

~~21. An isolated monoclonal antibody, or antigen binding portion thereof, which binds to glucocorticoid-inducible TNF receptor (GITR) and comprises heavy and light chain variable regions, wherein the light chain variable region comprises an amino acid sequence which is at~~

least 90% identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 27, 40, 53, 54, 72, 85, 98, 99, 116, 129, 130, and 336.

~~22. — An isolated monoclonal antibody, or antigen binding portion thereof, which binds to glucocorticoid-inducible TNF receptor (GITR) and comprises heavy and light chain variable region sequences at least 85% identical to the amino acid sequences selected from the group consisting of:~~

- ~~—— (a) SEQ ID NOs: 13 and 14, respectively;~~
- ~~—— (b) SEQ ID NOs: 26 and 27, respectively;~~
- ~~(c) SEQ ID NOs: 39 and 40, respectively;~~
- ~~(d) SEQ ID NOs: 52 and 53, respectively;~~
- ~~(e) SEQ ID NOs: 52 and 54, respectively;~~
- ~~(f) SEQ ID NOs: 71 and 72, respectively;~~
- ~~(g) SEQ ID NOs: 84 and 85, respectively;~~
- ~~(h) SEQ ID NOs: 97 and 98, respectively;~~
- ~~(i) SEQ ID NOs: 97 and 99, respectively;~~
- ~~(j) SEQ ID NOs: 115 and 116, respectively;~~
- ~~(k) SEQ ID NOs: 128 and 129, respectively;~~
- ~~(l) SEQ ID NOs: 128 and 130, respectively; and~~
- ~~(m) SEQ ID NOs: 335 and 336, respectively.~~

~~23. — The antibody, or antigen binding portion thereof, of claim 22, wherein the heavy and light chain variable regions comprise an amino acid sequence at least 90% identical to the heavy and light chain variable regions selected from the group consisting of (a)–(m).~~

~~24. — The antibody, or antigen binding portion thereof, of claim 23, wherein the heavy and light chain variable region comprises an amino acid sequence at least 95% identical to the heavy and light chain variable regions selected from the group consisting of (a)–(m).~~

~~25. — The antibody, or antigen binding portion thereof, of claim 24, wherein the heavy and light chain variable region comprises the heavy and light chain variable regions selected from the group consisting of (a)–(m).~~

~~26. — The antibody, or antigen binding portion thereof, of claim 25, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 13 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 14.~~

~~27. — The antibody, or antigen binding portion thereof, of claim 25, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 26 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 27.~~

~~28. — The antibody, or antigen binding portion thereof, of claim 25, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 39 and/or a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 40.~~

~~29. — An isolated monoclonal antibody, or antigen binding portion thereof, which binds to glucocorticoid-inducible TNF receptor (GITR) and comprises heavy chain and light chain sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to the amino acid sequences selected from the group consisting of:~~

- ~~—— (a) SEQ ID NOs: 15 and 16, respectively;~~
- ~~—— (b) SEQ ID NOs: 17 and 19, respectively;~~
- ~~—— (c) SEQ ID NOs: 18 and 19, respectively;~~
- ~~—— (d) SEQ ID NOs: 28 and 29, respectively;~~
- ~~—— (e) SEQ ID NOs: 30 and 32, respectively;~~
- ~~—— (f) SEQ ID NOs: 31 and 32, respectively;~~
- ~~—— (g) SEQ ID NOs: 41 and 42, respectively;~~
- ~~—— (h) SEQ ID NOs: 43 and 45, respectively;~~

(i) SEQ ID NOs: 44 and 45, respectively;
(j) SEQ ID NOs: 55 and 56, respectively;
(k) SEQ ID NOs: 55 and 57, respectively;
(l) SEQ ID NOs: 58 and 60, respectively;
(m) SEQ ID NOs: 59 and 60, respectively;
(n) SEQ ID NOs: 58 and 61, respectively;
(o) SEQ ID NOs: 59 and 61, respectively;
(p) SEQ ID NOs: 73 and 74, respectively;
(q) SEQ ID NOs: 75 and 77, respectively;
(r) SEQ ID NOs: 76 and 77, respectively;
(s) SEQ ID NOs: 86 and 87, respectively;
(t) SEQ ID NOs: 88 and 90, respectively;
(u) SEQ ID NOs: 89 and 90, respectively;
(v) SEQ ID NOs: 102 and 104, respectively;
(w) SEQ ID NOs: 103 and 104, respectively;
(x) SEQ ID NOs: 100 and 101, respectively;
(y) SEQ ID NOs: 100 and 371, respectively;
(z) SEQ ID NOs: 102 and 105, respectively;
(za) SEQ ID NOs: 103 and 105, respectively;
(zb) SEQ ID NOs: 117 and 118, respectively;
(zc) SEQ ID NOs: 119 and 121, respectively;
(zd) SEQ ID NOs: 120 and 121, respectively;
(ze) SEQ ID NOs: 131 and 132, respectively;
(zf) SEQ ID NOs: 134 and 136, respectively;
(zg) SEQ ID NOs: 135 and 136, respectively;
(zh) SEQ ID NOs: 131 and 133, respectively;
(zi) SEQ ID NOs: 134 and 137, respectively;
(zj) SEQ ID NOs: 135 and 137, respectively;
(zk) SEQ ID NOs: 337 and 338, respectively;
(zl) SEQ ID NOs: 339 and 341, respectively; and
(zm) SEQ ID NOs: 340 and 341, respectively.

30. — ~~The antibody, or antigen binding portion thereof, of claim 29, wherein the heavy and light chains comprises the heavy and light chains selected from the group consisting of (a) (zm).~~

31. — ~~The antibody, or antigen binding portion thereof, of claim 30, wherein the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 17 and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 19.~~

32. — ~~The antibody, or antigen binding portion thereof, of claim 30, wherein the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 18 and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 19.~~

33. — ~~An isolated monoclonal antibody, or antigen binding portion thereof, which (a) binds to the same epitope on GITR as the antibody of claim 25, and (b) inhibits binding of the antibody of claim 25 to GITR on activated T cells by at least 90% as measured by FACS.~~

34. — ~~The antibody, or antigen binding portion thereof, of any one of claims 15-33, wherein the antibody binds to PTGGPGCGPGRLLLGTGT (SEQ ID NO: 217) and CRDYPGEE (SEQ ID NO: 218) of mature human GITR (SEQ ID NO: 4).~~

35. — ~~The antibody, or antigen binding portion thereof, of any one of claims 15-34, wherein the antibody binds to both human and cynomolgus GITR.~~

36. — ~~The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein the antibody is selected from the group consisting of an IgG1, an IgG2, an IgG3, an IgG4 or a variant thereof.~~

37. — ~~The antibody, or antigen binding portion thereof, of claim 36, wherein the antibody is an IgG1 antibody.~~

38. — The antibody, or antigen binding portion thereof, of claim 36, wherein the antibody comprises an effectorless IgG1 Fc.

39. — The antibody, or antigen binding portion thereof, of claim 38, wherein the antibody, or antigen binding portion thereof, comprises an effectorless IgG1 Fc that comprises the following mutations: L234A, L235E, G237A, A330S and P331S.

40. — The antibody of claim 36, wherein the antibody, or antigen binding portion thereof, comprises an Fc having enhanced binding to an activating FcγR.

41. — The antibody, or antigen binding portion thereof, of any one of the preceding claims, wherein methionine residues in the CDR regions are substituted for amino acid residues that do not undergo oxidation.

42. — The antibody, or antigen binding portion thereof, of any one of claims 15-41, wherein the antibody, or antigen binding portion thereof, is a human or humanized antibody.

43. — A bispecific molecule comprising the antibody of any one of the preceding claims linked to a molecule having a second binding specificity.

44. — A nucleic acid encoding the heavy and/or light chain variable region of the antibody, or antigen binding portion thereof, of any one of claims 1-42.

45. — An expression vector comprising the nucleic acid molecule of claim 44.

46. — A cell transformed with an expression vector of claim 45.

47. — An immunoconjugate comprising the antibody according to any one of claims 1-42, linked to an agent.

48. — A composition comprising the antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47, and a carrier.

49. — A kit comprising the antibody, or antigen binding portion thereof, or bispecific molecule, or immunoconjugate of any one of claims 1-43 and 47 and instructions for use.

50. — A method of preparing an anti-GITR antibody, or antigen binding portion thereof, comprising expressing the antibody, or antigen binding portion thereof, in the cell of claim 46 and isolating the antibody, or antigen binding portion thereof, from the cell.

51. — A method of stimulating an antigen-specific T cell response comprising contacting the T cell with the antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47 such that an antigen-specific T cell response is stimulated.

52. — A method of activating or co-stimulating an effector T cell, comprising contacting an effector T cell with an anti-GITR antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47 and CD3, wherein the effector T cell is activated or co-stimulated.

53. — A method of increasing IL-2 and/or IFN- γ production in a T cell comprising contacting the T cell with an effective amount of the antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47.

54. — A method of increasing T cell proliferation comprising contacting the cell with an effective amount of the antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47.

55. — A method of increasing IL-2 and/or IFN- γ production in T cells in a subject comprising administering an effective amount of the antibody, or antigen binding portion thereof, bispecific

molecule or immunoconjugate, of any one of claims 1-43 and 47, to increase IL-2 and/or IFN- γ production from the T cells.

56. — A method of reducing or depleting the number of T regulatory cells in a tumor of a subject in need thereof comprising administering an effective amount of an antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47, wherein the antibody, or antigen binding portion thereof, has effector or enhanced effector function, to reduce the number of T regulatory cells in the tumor.

57. — A method of stimulating an immune response in a subject comprising administering the antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47 to the subject such that an immune response in the subject is stimulated.

58. — The method of claim 57, wherein the subject has a tumor and an immune response against the tumor is stimulated.

59. — A method for inhibiting the growth of tumor cells in a subject comprising administering to the subject the antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47, such that growth of the tumor is inhibited in the subject.

60. — A method of treating cancer comprising administering to a subject in need thereof a therapeutically effective amount of the antibody, or antigen binding portion thereof, bispecific molecule or immunoconjugate, of any one of claims 1-43 and 47, to treat the cancer.

61. — The method of claim 60, wherein the cancer is selected from the group consisting of: bladder cancer, breast cancer, uterine/cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, pancreatic cancer, colorectal 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, and virus-related cancer.

62. — The method of claim 60 or 61, wherein the cancer is a metastatic cancer, refractory cancer, or recurrent cancer.

63. — The method of any one of claims 56–62, further comprising administering one or more additional therapeutics.

64. — The method of claim 63, wherein the additional therapy is an anti-PD1 antibody, a LAG-3 antibody, a CTLA-4 antibody, or a PD-L1 antibody.

~~18.~~ 65. — A method of detecting the presence of glucocorticoid-inducible TNF-receptor (GITR) in a sample comprising contacting the sample with the antibody, or antigen-binding portion thereof, of any one of claims 1–42, under conditions that allow for formation of a complex between the antibody, or antigen-binding portion thereof, and GITR, and detecting the formation of a complex.

66. — An isolated anti-GITR antibody comprising a modified heavy chain constant region that comprises an IgG2 hinge and at least one of CH1, CH2 and CH3 that is not of an IgG2 isotype, wherein the anti-GITR antibody has enhanced agonist activity relative to the same anti-GITR antibody but with a non-IgG2 hinge.

67. — The isolated anti-GITR antibody of claim 66, wherein the modified heavy chain constant region comprises a heavy chain constant region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 223–226 and 283–290 or a heavy chain constant region that differs therefrom in at most 5 amino acids or is at least 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence of SEQ ID NOs: 223–226 and 283–290.

~~68. The isolated anti-GITR antibody of claim 67, wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 15, 17, 18, 28, 30, 31, 41, 43, 44, 55, 58, 59, 73, 75, 76, 86, 88, 89, 100, 102, 103, 117, 119, 120, 131, 134, 135, 227-275, 337, 339, 340, 348-352, 361, and 362, or a heavy chain chain that differs therefrom in at most 10 amino acids or is at least 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence of SEQ ID NOs: 15, 17, 18, 28, 30, 31, 41, 43, 44, 55, 58, 59, 73, 75, 76, 86, 88, 89, 100, 102, 103, 117, 119, 120, 131, 134, 135, 227-275, 337, 339, 340, 348-352, 361, and 362.~~

6. The antibody of claim 1, wherein the antibody comprises heavy and light chain sequences comprising the amino acid sequences set forth in SEQ ID NOs: 15 and 16, respectively.

7. The antibody of claim 1, wherein the antibody comprises heavy and light chain sequences comprising the amino acid sequences set forth in SEQ ID NOs: 17 and 19, respectively.

8. The antibody of claim 1, wherein the antibody comprises heavy and light chain sequences comprising the amino acid sequences set forth in SEQ ID NOs: 18 and 19, respectively.

9. The antibody of any one of the claims 1-5, wherein the antibody is an IgG1, an IgG2, or an IgG4 antibody.

10. The antibody of any one of claims 1-9, wherein the antibody is a human or humanized antibody.

11. A nucleic acid encoding the heavy and light chain, or variable regions thereof, of the antibody of any one of claims 1-10.

12. An expression vector comprising the nucleic acid molecule of claim 11.

13. An isolated host cell transformed with (i) an expression vector of claim 12 or (ii) an expression vector comprising a nucleic acid encoding the heavy chain of the antibody of any one

of claims 1-10 and a separate expression vector comprising a nucleic acid encoding the light chain of the antibody of any one of claims 1-10.

14. A composition comprising the antibody of any one of claims 1-10, and a carrier.

15. The composition of claim 14, further comprising one or more additional therapeutics.

16. The composition of claim 15, wherein the one or more additional therapeutics are selected from the group consisting of: an anti-PD1 antibody, an anti-LAG-3 antibody, an anti-CTLA-4 antibody, an anti-PD-L1 antibody, and combinations thereof.

17. The antibody of any one of claims 1-10 for use in treating cancer.

18. The antibody for the use in claim 17, wherein one or more additional therapeutics are to be administered.

19. The antibody for the use in claim 18, wherein the additional therapeutic is an anti-PD1 antibody, an anti-LAG-3 antibody, an anti-CTLA-4 antibody, or an anti-PD-L1 antibody.

20. The antibody of any one of claims 1-10 for use in therapy.

21. Use of the antibody of any one of claims 1-10 in the manufacture of a medicament for treating cancer.

22. The use of claim 21, wherein one or more additional therapeutics are to be administered.

23. The use of claim 22, wherein the additional therapeutic is an anti-PD1 antibody, an anti-LAG-3 antibody, an anti-CTLA-4 antibody, or an anti-PD-L1 antibody.