

CLAIMS**What is claimed is:**

1. A bispecific antibody, comprising IgG domains having heavy chains and light chains, and two scFv components being connected to either C terminal of the heavy chains or N terminal of the light chains, wherein the IgG domains have a first binding specificity to a first antigen, wherein the scFv components have a second binding specificity to a second antigen, and wherein the first antigen and the second antigen are different and are independently selected from α -CTLA4, α -PD-1, and α -PD-L1.
2. The bispecific antibody of Claim 1, wherein the two scFv components are connected to the C terminal of the heavy chain.
3. The bispecific antibody of Claim 2, wherein the first antigen comprises α -CTLA4 and the second antigen comprises α -PD-1 or α -PD-L1.
4. The bispecific antibody of Claim 2, wherein the first antigen comprises α -PD-1 or α -PD-L1 and the second antigen comprises α -CTLA4.
5. The bispecific antibody of Claim 1, wherein the two scFv components are connected to the N terminal of the light chain.
6. The bispecific antibody of Claim 5, wherein the first antigen comprises α -PD-1 or α -PD-L1 and the second antigen comprises α -CTLA4.
7. The bispecific antibody of Claim 5, wherein the first antigen comprises α -CTLA4 and the second antigen comprises α -PD-1 or α -PD-L1.
8. The bispecific antibody of Claim 1, wherein the bispecific antibody is an isolated monoclonal antibody.
9. The bispecific antibody of Claim 1, comprising an antigen-binding fragment having a sequence having at least 98% similarity with SEQ ID No. 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, or 134.
10. The bispecific antibody of Claim 1, having a first binding specificity to α -CTLA4 and a second binding specificity to α -PD-1 or α -PD-L1, wherein neither the first nor the second has a K_d greater than 70nM.
11. The bispecific antibody of Claim 1, having a first binding specificity to α -CTLA4 and a second specificity to α -PD-1, wherein neither the first nor the second has a K_d greater than 70nM.
12. The bispecific antibody of Claim 1, having a first binding specificity to α -CTLA4 and a second binding specificity to α -PD-L1, wherein neither the first nor the second has a K_d greater than 70nM.
13. The bispecific antibody of Claim 1, comprising a human framework region.

14. The bispecific antibody of Claim 1, wherein the antibody is a humanized antibody, a chimeric antibody, or a recombinant antibody.
15. The bispecific antibody of Claim 1, wherein the IgG domain comprises an IgG1 constant region, wherein the IgG1 constant region comprises an amino acid sequence having at least 98% similarity with SEQ ID No. 136.
16. An IgG1 heavy chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 02, 06, 08, 10, 12, 14, 16, 18, 20, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 72, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, or 132.
17. A kappa light chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 04, 28, 32, 36, 40, 44, 48, 52, 56, 60, and 64.
18. A variable light chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, or 134.
19. A variable heavy chain, comprising an amino acid sequence having at least 98% similarity with SEQ ID No. 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, or 132.
20. An isolated nucleic acid encoding the bispecific antibody of Claim 1, the IgG1 heavy chain of Claim 16, the kappa light chain of Claim 17, the variable light chain of Claim 18, or the variable heavy chain of Claim 19.
21. An expression vector comprising the isolated nucleic acid of Claim 20.
22. The expression vector of Claim 21, wherein the vector is expressible in a cell.
23. A host cell comprising the nucleic acid of Claim 20.
24. A host cell comprising the expression vector of Claim 21.
25. The host cell of Claim 23 or 24, wherein the host cell is a prokaryotic cell or a eukaryotic cell.
26. A method of producing a bispecific antibody, comprising culturing the host cell of one of Claims 23-25 so that the bispecific antibody is produced.
27. An immunoconjugate comprising the bispecific antibody of Claim 1 and a cytotoxic agent.
28. The immunoconjugate according to claim 27, wherein the cytotoxic agent comprises a chemotherapeutic agent, a growth inhibitory agent, a toxin, or a radioactive isotope.
29. A pharmaceutical composition, comprising the bispecific antibody of Claim 1 and a pharmaceutically acceptable carrier.
30. The pharmaceutical composition of Claim 29, further comprising radioisotope, radionuclide, a toxin, a therapeutic agent, a chemotherapeutic agent or a combination thereof.

31. A pharmaceutical composition, comprising the immunoconjugate of Claim 30 and a pharmaceutically acceptable carrier.
32. A method of treating a subject with a cancer, comprising administering to the subject an effective amount of the bispecific antibody of Claim 1
33. The method of Claim 32, wherein the cancer comprises cells expressing PD-L1.
34. The method of Claim 32, wherein the cancer comprises breast cancer, colorectal cancer, pancreatic cancer, head and neck cancer, melanoma, ovarian cancer, prostate cancer, non-small lung cell cancer, small cell lung cancer, glioma, esophageal cancer, nasopharyngeal cancer, kidney cancer, gastric cancer, liver cancer, bladder cancer, cervical cancer, brain cancer, lymphoma, leukaemia, myeloma.
35. The method of Claim 32, further comprising co-administering an effective amount of a therapeutic agent.
36. The method of Claim 35, wherein the therapeutic agent comprises an antibody, a chemotherapy agent, an enzyme, or a combination thereof.
37. The method of Claim 36, wherein the therapeutic agent comprises capecitabine, cisplatin, trastuzumab, fulvestrant, tamoxifen, letrozole, exemestane, anastrozole, aminoglutethimide, testolactone, vorozole, formestane, fadrozole, letrozole, erlotinib, lapatinib, dasatinib, gefitinib, imatinib, pazopanib, lapatinib, sunitinib, nilotinib, sorafenib, nab-palitaxel, a derivative or a combination thereof.
38. The method of Claim 32, wherein the subject is a human.
39. A solution comprising an effective concentration of the bispecific antibody of Claim 1, wherein the solution is blood plasma in a subject.
40. A bispecific antibody, having a first binding specificity to a first antigen and a second binding specificity to a second antigen, wherein both the first and the second antigen are check point antigens, and wherein neither the first specificity nor the second specificity has a K_d greater than 70nM.
41. A bispecific antibody, comprising IgG domains having heavy chains and light chains, and two scFv components being connected to either C terminal of the heavy chains or N terminal of the light chains, wherein the IgG domains have a first binding specificity to a first antigen, wherein the scFv components have a second binding specificity to a second antigen, and wherein both the first antigen and the second antigen are checkpoint antigens and wherein the first antigen differs from the second antigen.