CLAIMS

What is claimed:

1. An isolated antibody or antibody fragment thereof comprising an antigen binding region that binds to a variable light chain and variable heavy chain polypeptides, which said antibody or antibody fragment specifically binds to V-domain Ig Suppressor of T cell Activation (VISTA), wherein binding of

   1. (i) the antibody or antibody fragment to VISTA modulates or enhances an immune response.heavy chain of said antibody or antibody fragment comprises a variable heavy chain (V_H) polypeptide comprising a V_H CDR1 consisting of the amino acid sequence of SEQ ID NO:25, a V_H CDR2 consisting of the amino acid sequence of SEQ ID NO:26 and a V_H CDR3 consisting of the amino acid sequence of SEQ ID NO:27, and

   The(ii) the light chain of said antibody or antibody fragment comprises a variable light chain (V_L) polypeptide consisting of a V_L CDR1 consisting of the amino acid sequence of SEQ ID NO:28, a V_L CDR2 consisting of the amino acid sequence of SEQ ID NO:29 and a V_L CDR3 having the amino acid sequence of SEQ ID NO:30.

2. The antibody or antibody fragment of claim 1, wherein thesaid antibody fragment is a Fab, $F(ab')_2$, or scFv antibody fragment.comprising said CDRs.

3. The antibody or antibody fragment of claim 1, which comprises an antibodya human constant region.

4. The antibody or antibody fragment of any one of claims 1-3, wherein said antibody or antibody fragment comprises a variable heavy chain polypeptide of SEQ ID NO: 37 and a variable light chain polypeptide of SEQ ID NO: 44.

5. The antibody or antibody fragment of any one of claims 1 or 3-4, wherein said antibody or antibody fragment comprises a human heavy chain constant region.

~~4.~~6. The antibody or antibody fragment of claim ~~1, wherein VISTA is expressed on a hematopoietic cell~~5, wherein said human heavy chain constant region comprises a human IgG1 heavy chain constant region.

~~5.~~7. The antibody or antibody fragment of claim ~~1, wherein the hematopoietic cell is a myeloid lineage cell and/or a lymphocyte~~6, wherein said human heavy chain constant region comprises the human IgG1 heavy chain constant region contained in SEQ ID NO: 61 or SEQ ID NO: 60.

8. The antibody or antibody fragment of any one of claims 1 or 3-7, wherein said antibody or antibody fragment comprises a human light chain constant region.

~~6.~~9. The antibody or antibody fragment of claim ~~1, wherein the hematopoietic cell is a monocyte or a neutrophil~~8, wherein said human light chain constant region comprises a human IgG1 light chain constant region.

~~7. The antibody or antibody fragment of claim 1, wherein the hematopoietic cell is a T cell.~~

~~8. The antibody or antibody fragment of claim 1, wherein the hematopoietic cell is a B cell, a natural killer (NK) cell or a natural killer T (NKT) cell.~~

~~9. The antibody or antibody fragment of claim 1, wherein VISTA is expressed on a tumor cell.~~

10. ~~The antibody or antibody fragment of claim 1~~ 9, wherein ~~VISTA is expressed in a tumor microenvironment (TME).~~said human IgG1 light chain constant region comprises the amino acid sequence of the light chain constant region in SEQ ID NO: 56.

11. The antibody or antibody fragment of any one of claims 1-~~10, further comprising one or more~~5, wherein said heavy chain ~~complementary determining regions (CDRs) and one or more light chain CDRs; wherein the one~~polypeptide consisting of SEQ ID NO: 55, 59, 60 or 61.

12. The antibody or antibody fragment of any one of claims 1 or more3-4, wherein:

(i) said heavy chain CDRspolypeptide comprises anthe amino acid sequence selected fromof SEQ ID NOs:1-3, 7-9, 13-15, 19-21, 25-27, 31-33NO: 55 and the one or moresaid light chain CDRspolypeptide comprises anthe amino acid sequence selected fromof SEQ ID NOs:4-6, 10-NO: 56;

(ii) said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 59 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56;

(iii) said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 60 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56; or

(iv) said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 61 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56.

11.13. The antibody according to claim 12, 16-18, 22-24, 28-30, 34-36wherein said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 61 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56.

12. The antibody or antibody fragment of any one of claims 1-10, further comprising at least one heavy chain and at least one light chain.

13. An antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises SEQ ID NO:1-3.

14. An antibody or antibody fragment according to claim 12, wherein at least one light chain comprises SEQ ID NO:4-6.

15. An antibody or antibody fragment according to claim 1213, wherein at least one heavy chain comprises SEQ ID NO:1-3 and wherein at least one light chain comprises SEQ ID NO:4-6.

16. An antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises the heavy chain variable region sequence as shown in SEQ ID NO:37-40.

17.14. Ansaid antibody or antibody fragment according to claim 12, wherein at least one light chain comprises the light chain variable region sequence as shown in SEQ ID NO:41-45is expressed in a recombinant cell.

18. An antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises the heavy chain variable region sequence as shown in SEQ ID NO:37-40, and wherein at least one light chain comprises the light chain variable region sequence as shown in SEQ ID NO: 41-45.

19. The antibody or antibody fragment of any one of claims 1-10, wherein the antibody is a monoclonal antibody.

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

21. The antibody or antibody fragment of any one of claims 1-10, wherein the antibody comprises a human constant region.

22. An antibody or antibody fragment according to any one of claims 1-10, wherein the antibody molecule is specific for an epitope within the amino acid sequence SEQ ID NO: 46.

23. The antibody or antibody fragment of any one of claims 1-10, wherein the antibody binds to an epitope of VISTA with an affinity of at least $1x10^{-9}$ liter/mole.

24. The antibody or antibody fragment of any one of claims 1-10, wherein the antibody binds to an epitope of VISTA with an affinity of at least $1x10^{-8}$ liter/mole.

25. The antibody or antibody fragment of any one of claims 1-10, wherein the antibody binds to an epitope of VISTA with an affinity of at least $1x10^{-7}$ liter/mole.

26. The antibody or antibody fragment of any one of claims 1-10, wherein the modulation of the immune response comprises an increase in CD45+ leukocytes, CD4+ T cells, or CD8+ T cells, or a combination thereof, or a decrease in VISTA-expressing immune cells.

27.15. The antibody or antibody fragment of any one of claims 1-10, wherein the modulation of the immune response comprises enhanced production of cytokines, enhanced T-claim 14 wherein said cell response, and/or modulates Foxp3 expressionis deficient in fucosylation enzymes.

28. The antibody or fragment thereof of claim 12, wherein the variable light chain VL domain comprises a human framework region.

29. The antibody or fragment thereof of claim 1, which comprises a whole antibody.

30. The antibody or antibody fragment of any one of claims 1-10, further comprising one or more heavy chain complementary determining regions (CDRs) and one or more light chain CDRs of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).

31. The antibody or antibody fragment of any one of claims 1-10, further comprising at least one heavy chain and at least one light chain of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).

32. An antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises all three heavy chain CDRs of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).

33. The antibody or antibody fragment according to claim 12, wherein at least one light chain comprises all three light chain CDRs of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).

~~34. The antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises all three heavy chain CDRs of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47), and wherein at least one light chain comprises all three light chain CDRs of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).~~

~~35. The antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises the heavy chain variable region sequence of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).~~

~~36. The antibody or antibody fragment according to claim 12, wherein at least one light chain comprises the light chain variable region sequence of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).~~

~~37. The antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises the heavy chain variable region sequence of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47), and wherein at least one light chain comprises the light chain variable region sequence of an antibody selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).~~

~~38. The antibody or antibody fragment of claim 22, wherein the epitope is a conformational epitope.~~

~~39. The antibody or antibody fragment of claim 38, wherein the conformational epitope comprises or is present within residues 103-111 (NLTLLDSGL (SEQ ID NO:62)) and 136-146 (VQTGKDAPSNC (SEQ ID NO:63)) of human VISTA (SEQ ID NO:46).~~

~~40. The antibody or antibody fragment of claim 38, wherein the conformational epitope comprises or is present within residues 24-36 (LLGPVDKGHDVTF (SEQ ID NO:64)), and 54-65 (RRPIRNLTFQDL (SEQ ID NO:65) of human VISTA (SEQ ID NO:46).~~

~~41. The antibody or antibody fragment of claim 38, wherein the conformational epitope comprises amino acid residues in the FG loop of human VISTA (SEQ ID NO:46).~~

~~42.~~16. A composition comprising the antibody or antibody fragment of any one of claims 1-~~27~~14 and a pharmaceutically acceptable carrier, ~~diluent, or~~ excipient~~.~~ or diluent.

~~43.~~17. A composition comprising~~:~~ the antibody or antibody fragment of claim 13 and a pharmaceutically acceptable carrier, excipient or diluent.

~~a VISTA antagonist comprising an~~A nucleic acid which encodes for the expression of the antibody or antibody fragment ~~thereof comprising an antigen binding region that binds~~according to ~~a V-domain Ig Suppressor of T cell Activation (VISTA); and~~

~~a vaccine.~~

18. ~~The composition~~any one of ~~claim 43, wherein the vaccine is a viral~~claims 1-14.

19. A nucleic acid which encodes for the expression of the antibody or antibody fragment according to claim 13.

20. An expression vector ~~vaccine,~~comprising the nucleic acid according to claim 18.

21. An expression vector comprising the nucleic acid according to claim 19.

22. A recombinant cell which expresses an antibody or antibody fragment encoded by the nucleic acid according to claim 18.

23. A recombinant cell which expresses an antibody or antibody fragment encoded by the nucleic acid according to claim 19.

24. The recombinant cell of claim 22 which is a CHO cell.

25. The recombinant cell of claim 23 which is a CHO cell.

26. The recombinant cell of claim 22 which is a CHO cell that is deficient in fucosylation enzymes.

27. The recombinant cell of claim 23 which is a CHO cell that is deficient in fucosylation enzymes.

28. A method of expressing the antibody or antibody fragment according to any one of claims 1-12, comprising culturing a cell which comprises nucleic acids encoding said antibody or antibody fragment under conditions that promote expression of said antibody or antibody fragment.

29. A method of expressing the antibody or antibody fragment according to claim 13, comprising culturing a cell which comprises nucleic acids encoding said antibody or antibody fragment under conditions that promote expression of said antibody or antibody fragment.

30. The method of claim 28 or 29, further comprising isolating said antibody or antibody fragment.

31. A medicament composition or compositions comprising: (i) the antibody or antibody fragment according to any one of claims 1-15; and (ii) a vaccine.

32. A medicament composition or compositions comprising: (i) the antibody or antibody fragment according to claim 13; and (ii) a vaccine.

~~44.~~33. The composition or compositions of claim 31, wherein the vaccine is a bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine~~,~~ or a protein vaccine.

~~45. A pharmaceutical~~ The composition ~~comprising:~~

~~an antibody~~ or ~~antibody fragment thereof comprising an antigen binding region that binds to a V-domain Ig Suppressor of T cell Activation (VISTA); and~~

~~a vaccine,~~

~~wherein binding of the antibody or antibody fragment to VISTA modulates or enhances an immune response.~~

~~46.~~34. ~~The pharmaceutical composition~~compositions of claim ~~45~~32, wherein the vaccine is a ~~viral vector vaccine,~~ bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine~~,~~ or a protein vaccine.

~~47.~~35. ~~The use~~Use of the antibody or antibody fragment ~~of~~according to any one of claims 1-~~27 inthe manufacture~~15, in the preparation of a medicament for ~~treating cancer in an individual in need thereof~~enhancing monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

~~48. The use of the composition of any one of claims 42, 43 and 45 inthe manufacture of a medicament for treating or preventing cancer in an individual in need thereof.~~

~~49. The use of any one of Claims 47-48, wherein the individual is a mammal.~~

~~50. The use of any one of Claims 47-48, wherein the individual is a human.~~

~~51. The use of claim 50, wherein a vaccine is to be used in combination with the medicament.~~

~~52. The use of claim 51, wherein the vaccine is a viral vector vaccine, bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine, or protein vaccine.~~

36. ~~The use of a V-domain Ig Suppressor of T cell Activation (VISTA) antagonist inthe manufacture of a medicament for treating a cancer in an individual in need thereof; wherein~~ Use of the ~~VISTA antagonist comprises an~~ antibody or antibody fragment ~~thereof comprising an antigen binding region that binds~~according to ~~VISTA; and wherein~~claim 13, in the preparation of a medicament for enhancing monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

~~53.~~37. Use of the antibody or antibody fragment ~~binds~~according to any one of claims 1-15, in the preparation of a medicament for treatment of cancer involving VISTA-mediated

immunosuppression or VISTA~~, thereby modulating or enhancing an immune response to the~~ expressing cancer cells.

38. ~~The use of claim 53, wherein the~~Use of the antibody or antibody fragment according to claim 13, in the preparation of a medicament for treatment of cancer involving VISTA-mediated immunosuppression or VISTA expressing cancer cells.

39. The use of claim 37, which promotes monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

40. The use of claim 38, which promotes monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

~~54.~~41. The use of claim 39, wherein said cancer ~~is~~comprises a leukemia, lymphoma, ~~myelodisplastic~~myelodysplastic syndrome or myeloma~~, or a combination thereof.~~.

42. The use of claim ~~54~~40, wherein ~~the~~said cancer comprises a leukemia ~~is a~~ , lymphoma, myelodysplastic syndrome or myeloma.

43. The use of claim 41, wherein said cancer comprises a solid tumor.

44. The use of claim 42, wherein said cancer comprises a solid tumor.

~~55.~~45. The use of claim 41, wherein said cancer comprises lymphocytic leukemia ~~or a~~, myelogenous leukemia~~.~~, acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid (myelogenous) leukemia (AML), chronic myelogenous leukemia (CML); hairy cell leukemia, T-cell prolymphocytic leukemia, large granular lymphocytic leukemia, or adult T-cell leukemia.

~~56.~~46. The use of claim ~~54~~42, wherein ~~the~~said cancer comprises lymphocytic leukemia ~~is~~, myelogenous leukemia, acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid (myelogenous) leukemia (AML), chronic myelogenous leukemia

(CML); hairy cell leukemia, T-cell prolymphocytic leukemia, large granular lymphocytic leukemia, or adult T-cell leukemia.

~~57.~~47. The use of claim ~~53~~39, wherein ~~the~~said cancer ~~is an acute myeloid (myelogenous) leukemia (AML).~~comprises lung, breast or bladder cancer.

~~58.~~48. The use of claim ~~53~~40, wherein ~~the~~said cancer ~~is a chronic myelogenous leukemia (CML).~~comprises lung, breast or bladder cancer.

~~59. The use of claim 53~~47, wherein ~~the cancer is a solid tumor.~~

~~60. The use of claim 53, wherein the solid tumor is surrounded by a tumor stroma comprising myeloid cells, T-cells, or a combination of myeloid cells and T-cells.~~

~~61. The use of claim 59 or 60, wherein the solid tumor is infiltrated with myeloid cells, T cells or a combination of myeloid cells and T-cells.~~

~~62. The use of claim 53, wherein the cancer is a~~said lung cancer~~.~~

~~63.~~49. ~~The use of claim 62, wherein the lung cancer is a~~ comprises non-small cell lung ~~carcinoma~~cancer (NSCLC).

50. The use of claim 48, wherein said lung cancer comprises non-small cell lung cancer (NSCLC).

51. The use of claim 39, further comprising a vaccine.

52. The use of claim 40, further comprising a vaccine.

53. The use of claim 51, wherein the vaccine is a viral vector vaccine, bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine, or protein vaccine.~~The use of the~~

54. The use of claim 52, wherein the vaccine is a viral vector vaccine, bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine, or protein vaccine.

55. The use of claim 39, which further comprises the use of one or more other cancer treatments.

56. The use of claim 40, which further comprises the use of one or more other cancer treatments.

57. The use of claim 55, wherein the one or more other cancer treatments is surgery, chemotherapy, radiation therapy, biologic therapy, targeted therapy, immunomodulatory therapy, or a combination thereof.

58. The use of claim 56, wherein the one or more other cancer treatments is surgery, chemotherapy, radiation therapy, biologic therapy, targeted therapy, immunomodulatory therapy, or a combination thereof.

~~64.~~59. The antibody or antibody fragment of any one of claims 1-~~27~~15, in the ~~manufacture~~preparation of a medicament for ~~suppressing tumor growth~~use in eliciting an ~~individual in need thereof.~~antitumor immune response.

60. ~~The use of any one of claims 47-51, 53-61 and 64~~The antibody or antibody fragment of claim 13, in the preparation of a medicament for use in enhancing an antitumor immune response.

61. The use of claim 59, wherein the medicament is for use in a human subject.

62. The use of claim 60, wherein the medicament is for use in a human subject.

63. The use of claim 61, wherein the medicament is suitable for parenteral or ~~nonparenteral~~non-parenteral administration~~, for example,~~.

64. The use of claim 62, wherein the medicament is suitable for parenteral or non-parenteral administration.

65. The use of claim 61, wherein the medicament is suitable for intravenous, subcutaneous or oral administration.

66. ~~The use of any one of claims 47-51, 53-61 and 64~~The use of claim 62, wherein the medicament is suitable for intravenous, subcutaneous or oral administration.

~~66.~~67. The use of claim 39, wherein the dosage of the ~~composition,~~ antibody or antibody fragment is 0.1-15 mg/kg per administration.

68. ~~The use of any one of claims 47-51, 53-61 and 64~~The use of claim 40, wherein the dosage of the antibody or antibody fragment is 0.1-15 mg/kg per administration.

~~67.~~69. The use of claim 39, wherein the medicament is suitable for administering weekly, once every two weeks, once every three weeks, once every month, once every 2 months, or once every 3 months.

~~68. An antibody or fragment thereof that binds VISTA and which comprises an antibody VH domain comprising a VH CDR1 having an amino acid sequence that is substantially similar to SEQ ID NO:1, a VH CDR2 having an amino acid sequence that is substantially similar to SEQ ID NO:2 and a VH CDR3 having an amino acid sequence that is substantially similar to SEQ ID NO:3, and which further comprises an antibody VL domain comprising a VL CDR1 having an amino acid sequence that is substantially similar to SEQ ID NO:4, a VL CDR2 having an amino acid sequence that is substantially similar to SEQ ID NO:5 and a VL CDR3 having an amino acid sequence that is identical to SEQ ID NO:6.~~

~~69. An isolated nucleic acid which comprises a nucleotide sequence encoding the antibody of~~ The use of claim ~~1.~~

~~70. An expression vector comprising the nucleic acid of claim 69 operably linked to a promoter.~~

~~71. A host cell transformed with the expression vector of claim 70.~~

~~72. A method of producing antibody or fragment thereof of claim 1, the method comprising culturing host cells according to claim 71 under conditions for production of said antibody or fragment.~~

~~73. The method according to claim 72 further comprising isolating said antibody.~~

~~74. An article of manufacture comprising the composition of claim 45 and a container, and further comprising a package insert or label indicating that the composition can be used to treat cancer.~~

~~75. An antibody or antibody fragment thereof~~40, wherein the ~~antibody is selected from the group consisting of: VSTB112 (S2), VSTB116 (S5), VSTB95 (S16), VSTB50 (S41), VSTB53 (S43) and VSTB60 (S47).~~

~~76.~~70. ~~The use of a V-domain Ig Suppressor of T cell Activation (VISTA) antagonist in the manufacture of a~~ medicament ~~for treating a cancer in an individual in need thereof;~~is suitable for administering weekly, once every two weeks, once every three weeks, once every month, once every 2 months, or once every 3 months.

~~wherein the VISTA antagonist comprises an antibody or antibody fragment thereof comprising an antigen binding region that binds to VISTA; wherein the antibody or antibody fragment binds to VISTA, thereby modulating or enhancing an immune response to the cancer; and~~

~~wherein the medicament is used in combination with a second cancer treatment.~~

~~77. The use of claim 76, wherein the second cancer treatment is surgery, chemotherapy, radiation therapy, biologic therapy, targeted therapy, or immunomodulatory therapy, or a combination thereof.~~

~~78. An isolated antibody or antibody fragment thereof comprising an antigen binding region that binds to a V-domain Ig Suppressor of T cell Activation (VISTA), wherein the antibody comprises an antibody VH domain comprising a VH CDR1 having the amino acid sequence of SEQ ID NO:25, a VH CDR2 having the amino acid sequence of SEQ ID NO:26 and a VH CDR3 having the amino acid sequence of SEQ ID NO:27, and which further comprises an antibody VL domain comprising a VL CDR1 having the amino acid sequence of SEQ ID NO:28, a VL CDR2 having the amino acid sequence of SEQ ID NO:29 and a VL CDR3 having the amino acid sequence of SEQ ID NO:30.~~

~~79. The antibody or antibody fragment of claim 78, comprising one or more humanized or human framework regions.~~

~~80. The antibody or antibody fragment of claim 79, wherein the antibody VH domain comprises SEQ ID NO:37.~~

81. The antibody of claim 79 or 80, wherein the antibody VL domain comprises SEQ ID NO:44.

82. The antibody or antibody fragment of any one of claims 78-80, wherein the antibody comprises a heavy chain constant region.

83. The antibody or antibody fragment of claim 82, wherein the heavy chain constant region is a human heavy chain constant region.

84. The antibody or antibody fragment of claim 82, wherein the heavy chain constant region is an IgG1 heavy chain constant region.

85. The antibody or antibody fragment of claim 84, wherein the IgG1 heavy chain constant region comprises the amino acid sequence of the IgG1 heavy chain constant region present in SEQ ID NO:61.

86. The antibody or antibody fragment of claim 84, wherein the IgG1 heavy chain constant region has been modified to enhance protease resistance of the antibody.

87. The antibody or antibody fragment of claim 86, wherein the IgG1 heavy chain constant region that has been modified to enhance protease resistance of the antibody comprises the amino acid sequence of the IgG1 heavy chain constant region present in SEQ ID NO:60.

88. The antibody or antibody fragment of claim 82, wherein the antibody comprises a light chain constant region.

89. The antibody or antibody fragment of claim 88, wherein the light chain constant region is a human light chain constant region.

90. The antibody or antibody fragment of claim 89, wherein the human light chain constant region comprises the amino acid sequence of the light chain constant region present in SEQ ID NO:56.

91. The antibody or antibody fragment of any one of claims 78-80, wherein the antibody comprises a heavy chain comprising SEQ ID NO:60 and a light chain comprising SEQ ID NO:56.

92. The antibody or antibody fragment of any one of claims 78-80, wherein the antibody comprises a heavy chain comprising SEQ ID NO:61 and a light chain comprising SEQ ID NO:56.

93. The antibody or antibody fragment of any one of claims 78-80, wherein the antibody or antibody fragment is expressed in a cell that is deficient in fucosylation enzymes.

94. The antibody or antibody fragment of claim 93, wherein the cell is a Chinese hamster ovary (CHO) cell.

95. A composition comprising the antibody or antibody fragment of any one of claims 78-94 and a pharmaceutically acceptable carrier, diluent, or excipient.

96. The use of the antibody or antibody fragment of any one of claims 78-94 in the manufacture of a medicament for treating cancer in an individual in need thereof.

97. The use of the composition of claim 95 in the manufacture of a medicament for treating cancer in an individual in need thereof.

98. The use of claim 96 or 97, wherein the cancer is a lung cancer.

99. The use of claim 96 or 97, wherein the medicament is used in combination with a second cancer treatment.

100. The use of claim 99, wherein the second cancer treatment is surgery, chemotherapy, radiation therapy, biologic therapy, targeted therapy, or immunomodulatory therapy, or a combination thereof.

101. The use of claim 96 or 97, wherein the cancer is a bladder cancer.

102. The use of claim 96 or 97, wherein the cancer is a breast cancer.

~~103. The use of the antibody or antibody fragment of any one of claims 78-94 in the manufacture of a medicament for treating a non-small cell lung carcinoma (NSCLC) in an individual in need thereof.~~

~~104. The use of the composition of claim 95 in the manufacture of a medicament for treating a non-small cell lung carcinoma (NSCLC) in an individual in need thereof.~~

~~105. The use of an antibody or an antibody fragment thereof in the manufacture of a medicament of enhancing an immune response in an individual in need thereof, wherein the antibody binds V-domain Ig Suppressor of T cell Activation (VISTA), and the antibody fragment comprises an antigen binding region that binds to VISTA, thereby enhancing an immune response to the cancer.~~

~~106. The use of Claim 105, wherein the immune response is an antitumor immune response.~~

~~107. The use of an antibody or an antibody fragment thereof in the manufacture of a medicament of eliciting a biological response in an individual in need thereof, wherein the antibody binds V-domain Ig Suppressor of T cell Activation (VISTA), and the antibody fragment comprises an antigen binding region that binds to VISTA, thereby enhancing an immune response to the cancer, wherein the biological response is selected from the group consisting of:~~

~~a. activation of monocytes;~~

~~b. induction of T-cell proliferation and cytokine secretion;~~

~~c. increased survival of monocytes;~~

~~d. induction of antibody-dependent cell-mediated cytotoxicity (ADCC) in cells expressing VISTA; and~~

~~e. induction of antibody-dependent cellular phagocytosis (ADCP) in cells expressing VISTA.~~

~~108. An isolated antibody or antibody fragment thereof that competitively inhibits binding of the antibody or antibody fragment of Claim 1 to human VISTA (SEQ ID NO:46).~~