~~PROPOSED AMENDED~~ CLAIMS

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What is claimed:

1. ~~(Amended)~~ 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 binding of the antibody or antibody fragment to VISTA modulates or enhances an immune response, and wherein the antibody comprises:

a) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:1,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:2 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:3,

and

b) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:4,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:5 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:6;

or

c) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:13,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:14 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:15,

and

d) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:16,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:17 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:18.

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

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

~~4.~~ (Canceled) ~~The antibody or antibody fragment of claim 1, wherein VISTA is expressed on a hematopoietic cell.~~

~~5.~~ (Canceled) ~~The antibody or antibody fragment of claim 1, wherein the hematopoietic cell is a myeloid lineage cell and/or a lymphocyte.~~

~~6.~~ (Canceled) ~~The antibody or antibody fragment of claim 1, wherein the hematopoietic cell is a monocyte or a neutrophil.~~

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

~~8.~~ (Canceled) ~~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.~~ (Canceled) ~~The antibody or antibody fragment of claim 1, wherein VISTA is expressed on a tumor cell.~~

~~10.~~ (Canceled) ~~The antibody or antibody fragment of claim 1 wherein VISTA is expressed in a tumor microenvironment (TME).~~

11. (Canceled) ~~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; wherein the one or more heavy chain CDRs comprises an amino acid sequence selected from SEQ ID NOs:1-3, 7-9, 13-15, 19-21, 25-27, 31-33 and the one or more light chain CDRs comprises an amino acid sequence selected from SEQ ID NOs:4-6, 10-12, 16-18, 22-24, 28-30, 34-36.~~

4 3
~~12.~~ ~~(Amended).~~ 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.~~ (Canceled) ~~An antibody or antibody fragment according to claim 12, wherein at least one heavy chain comprises SEQ ID NO:1-3.~~

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

5 4
~~15.~~ ~~(Amended)~~ An antibody or antibody fragment according to claim ~~12,~~ 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~~the antibody comprises:

a) an antibody VH domain comprising:

   i) a VH CDR1 having the amino acid sequence of SEQ ID NO:1,

   ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:2 and

   iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:3,

and

b) an antibody VL domain comprising:

   i) a VL CDR1 having the amino acid sequence of SEQ ID NO:4,

   ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:5 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:6.

16. (Canceled) ~~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. (Canceled) ~~An 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:41-45.~~

~~18.~~ ~~(Amended)~~ 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~~38, and wherein at least one light chain comprises the light chain variable region sequence as shown in SEQ ID NO: ~~41-45~~41.

~~19.~~ ~~(Amended).~~ The antibody or antibody fragment of any one of claims 1-~~10~~18, wherein the antibody is a monoclonal antibody.

~~20.~~ ~~(Amended).~~ The antibody or antibody fragment of any one of claims 1-~~10~~19, wherein the antibody is a humanized antibody.

~~21.~~ ~~(Amended)~~ The antibody or antibody fragment of any one of claims 1-~~10~~19, wherein the antibody comprises a human constant region.

~~22.~~ ~~(Amended)~~ An antibody or antibody fragment according to any one of claims 1-~~10~~21, wherein the antibody molecule is specific for an epitope within the amino acid sequence SEQ ID NO: 46.

~~23.~~ (Canceled) ~~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.~~ (Canceled) ~~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.~~ (Canceled) ~~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.~~

11 10

~~26.~~ ~~(Amended).~~ The antibody or antibody fragment of any one of claims 1-~~10~~22, ~~,~~ 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.

12. 10

~~27.~~ ~~(Amended).~~ The antibody or antibody fragment of any one of claims 1-~~10~~22, wherein the modulation of the immune response comprises enhanced production of cytokines, enhanced T-cell response, and/or modulates Foxp3 expression.

13

~~28.~~ ~~(Amended).~~ The antibody or fragment thereof of claim ~~1~~21, wherein the ~~variable light chain~~ antibody VL domain comprises a human framework region.

14.

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

30. (Canceled) ~~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.~~ (Canceled) ~~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.~~ (Canceled) ~~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.~~ (Canceled) ~~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.~~ (Canceled) ~~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. (Canceled) ~~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. (Canceled) ~~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.~~ (Canceled) ~~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.~~ ~~(Amended)~~ 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. (Canceled) ~~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. (Canceled) ~~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.~~ A composition comprising the antibody or antibody fragment of any one of claims 1-~~27~~ and a pharmaceutically acceptable carrier, diluent, or excipient.

~~43. A composition comprising:~~

~~a VISTA antagonist 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.~~

~~44. The composition of claim 43, wherein the vaccine is a viral vector vaccine, bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine, or protein vaccine.~~

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

18

~~47.~~ The use of the antibody or antibody fragment of any one of claims 1 ~~27~~ 12 in the manufacture of a medicament for treating cancer in an individual in need thereof.

19

~~48.~~ The use of the composition of ~~any one of~~ claims ~~42, 43 and 45~~ 17 in the manufacture of a medicament for treating or preventing cancer in an individual in need thereof.

20

~~49.~~ The use of any one of Claims ~~47-48~~ 18-19, wherein the individual is a mammal.

21

~~50.~~ The use of any one of Claims ~~47-48,~~ 18-19 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.~~

22

~~53.~~ ~~(Amended)~~ The use of a V-domain Ig Suppressor of T cell Activation (VISTA) antagonist antibody or antibody fragment thereof comprising an antigen binding region that binds to VISTA in the manufacture of a medicament for treating a cancer in an individual in need thereof, wherein the antibody comprises:

a) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:1,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:2 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:3,

and

b) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:4,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:5 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:6;

or

c) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:13,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:14 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:15,

and

d) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:16,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:17 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:18.

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

23 22
~~54.~~ The use of claim ~~53,~~ wherein the cancer is a leukemia, lymphoma, myelodisplastic syndrome or myeloma, or a combination thereof.

24 23
~~55.~~ The use of claim ~~54;~~ wherein the leukemia is a lymphocytic leukemia or a myelogenous leukemia.

25 23
~~56.~~ The use of claim 54, wherein the leukemia is 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.

26 22
~~57.~~ The use of claim ~~53,~~ wherein the cancer is an acute myeloid (myelogenous) leukemia (AML).

27 22
~~58.~~ The use of claim ~~53,~~ wherein the cancer is a chronic myelogenous leukemia (CML).

28 22
~~59.~~ The use of claim ~~53,~~ wherein the cancer is a solid tumor.

29 28
~~60.~~ ~~(Amended)~~ The use of claim ~~53~~59, wherein the solid tumor is surrounded by a tumor stroma comprising myeloid cells, T-cells, or a combination of myeloid cells and T-cells.

30 ~~28~~ 29
~~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.

31 22
~~62.~~ The use of claim ~~53,~~ wherein the cancer is a lung cancer.

32 31
~~63.~~ The use of claim ~~62,~~ wherein the lung cancer is a non-small cell lung carcinoma (NSCLC).

33

~~64.~~ The use of the antibody or antibody fragment of claims 1~~-27~~ (12) in the manufacture of a medicament for suppressing tumor growth in an individual in need thereof.

34

~~65.~~ ~~(Amended)~~ The use of any one of claims ~~47-51, 53-61 and 64,~~ (18-30 and 33) wherein the medicament is suitable for parenteral or nonparenteral administration~~, for example, intravenous, subcutaneous or oral administration~~.

35

~~66.~~ The use of any one of claims ~~47-51, 53-61 and 64,~~ (18-30 and 33) wherein the dosage of the composition, antibody or fragment is 0.1-15 mg/kg per administration.

36

~~67.~~ The use of any one of claims ~~47-51, 53-61 and 64,~~ (18-30 and 33) 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.~~

37

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

38

~~70.~~ An expression vector comprising the nucleic acid of claim ~~69~~ (37) operably linked to a promoter.

39

~~71.~~ A host cell transformed with the expression vector of claim ~~70.~~ (38)

40

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

41 40

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

~~76. 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;~~

~~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.~~

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105. ~~(Amended)~~ The use of an antibody or an antibody fragment thereof in the manufacture of a medicament ~~of enhancing an immune response~~ for treating a tumor in an individual in need thereof, wherein the antibody binds V-domain Ig Suppressor of T cell Activation (VISTA) and comprises:

a) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:1,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:2 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:3,

and

b) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:4,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:5 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:6;

or

c) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:13,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:14 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:15,

and

d) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:16,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:17 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:18,

and the antibody fragment comprises an antigen binding region that binds to VISTA~~, thereby enhancing an immune response to the cancer~~.

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

43

~~107.~~ ~~(Amended)~~ The use of an antibody or an antibody fragment thereof in the manufacture of a medicament ~~of eliciting a biological response~~ for treating cancer in an individual in need thereof, wherein the antibody binds V-domain Ig Suppressor of T cell Activation (VISTA) and comprises:

a) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:1,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:2 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:3,

and

b) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:4,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:5 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:6;

or

c) an antibody VH domain comprising:

i) a VH CDR1 having the amino acid sequence of SEQ ID NO:13,

ii) a VH CDR2 having the amino acid sequence of SEQ ID NO:14 and

iii) a VH CDR3 having the amino acid sequence of SEQ ID NO:15,

and

d) an antibody VL domain comprising:

i) a VL CDR1 having the amino acid sequence of SEQ ID NO:16,

ii) a VL CDR2 having the amino acid sequence of SEQ ID NO:17 and

iii) a VL CDR3 having the amino acid sequence of SEQ ID NO:18,

and the antibody fragment comprises an antigen binding region that binds to VISTA~~, thereby enhancing an immune response to the cancer~~, wherein the

antibody or antibody fragment elicits a 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.~~ (Canceled) ~~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).~~ 44

~~109.~~ ~~(New)~~ An antibody or antibody fragment according to claim ~~12~~ or ~~18~~, wherein at least one heavy chain comprises the heavy chain sequence as shown in SEQ ID NO:47, and wherein at least one light chain comprises the light chain sequence as shown in SEQ ID NO:48. 45

~~110.~~ ~~(New)~~ An antibody or antibody fragment according to claim ~~12~~, wherein at least one heavy chain comprises the heavy chain sequence as shown in SEQ ID NO:51, and wherein at least one light chain comprises the light chain sequence as shown in SEQ ID NO:52. 46

~~111.~~ ~~(New)~~ The use of any one of claims ~~53-67, 105~~ and ~~107~~, wherein the antibody comprises the heavy chain variable region sequence as shown in SEQ ID NO:38, and the light chain variable region sequence as shown in SEQ ID NO: 41. 47

~~112.~~ ~~(New)~~ The use of any one of claims ~~53-67, 105, 107 and 111~~, wherein the antibody comprises the heavy chain sequence as shown in SEQ ID NO:47, and the light chain sequence as shown in SEQ ID NO:48.

48 22-36, 42 and 43

~~113.~~ ~~(New)~~ The use of any one of claims ~~53-67, 105 and 107~~, wherein the antibody comprises the heavy chain sequence as shown in SEQ ID NO:51, and the light chain sequence as shown in SEQ ID NO:52.

49 4, 6, 44

~~114.~~ ~~(New)~~ An antibody or antibody fragment according to claim 1, 3, ~~12, 18, 109~~ or ~~110~~ 45, wherein the heavy chain constant region is an IgG1 heavy chain constant region.

50 22-36, 42, 43 and 46-48

~~115.~~ ~~(New)~~ The use of any one of claims ~~53-67, 105, 107 and 111-113~~, wherein the antibody comprises an IgG1 heavy chain constant region.