

What is claimed is:

1. A Melanoma-Associated Antigen A4 (MAGE-A4)-specific chimeric antigen receptor (CAR), wherein said MAGE-A4-specific chimeric antigen receptor interacts with amino acids 286-294, or a portion thereof, of SEQ ID NO: 32, and wherein said MAGE-A4-specific CAR specifically binds to an HLA bound MAGE-A4 polypeptide.

2. A Melanoma-Associated Antigen A4 (MAGE-A4)-specific chimeric antigen receptor (CAR), wherein said MAGE-A4-specific chimeric antigen receptor interacts with amino acids 230-239, or a portion thereof, of SEQ ID NO: 32, and wherein said MAGE-A4-specific CAR specifically binds to an HLA bound MAGE-A4 polypeptide.

3. The MAGE-A4-specific CAR of claim 1 or 2, wherein said MAGE-A4-specific CAR comprises, from N-terminus to C-terminus: (a) an extracellular ligand-binding domain comprising an anti-MAGE-A4 antigen-binding domain; (b) a hinge; (c) a transmembrane domain; and (d) a cytoplasmic domain comprising a costimulatory domain and a signaling domain.

4. The MAGE-A4-specific CAR of claim 3, wherein the extracellular ligand-binding domain comprises an anti-MAGE-A4 single chain variable fragment (scFv) domain comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), optionally wherein the anti-MAGE-A4 scFv domain comprises a first linker between the LCVR and the HCVR, and optionally wherein the MAGE-A4-specific CAR comprises a second linker between the extracellular ligand-binding domain and the hinge;

~~5. The MAGE-A4-specific CAR of claim 4, wherein the anti-MAGE-A4 scFv domain comprises a first linker between the LCVR and the HCVR.~~

~~6. The MAGE-A4-specific CAR of any one of claims 1-5, further comprising a second linker between the extracellular ligand-binding domain and the hinge.~~

~~7. The MAGE-A4-specific CAR of claim 6, optionally wherein the first linker and the second linker comprise amino acid sequences selected from the group consisting of SEQ ID NOs: 23-26.~~

8. ~~The MAGE A4 specific CAR of claim 7, optionally~~ wherein the first linker comprises the amino acid sequence of SEQ ID NO: 25 and the second linker comprises the amino acid sequence of SEQ ID NO: 23.

95. The MAGE-A4-specific CAR of any one of claims 1-84, wherein:
- (a) the hinge, the transmembrane domain, or both, are from a CD8 α polypeptide;
10. ~~The MAGE A4 specific CAR of any one of claims 1-9, wherein (b)~~ the costimulatory domain comprises a 4-1BB costimulatory domain;
11. ~~The MAGE A4 specific CAR of any one of claims 1-9, wherein (c)~~ the hinge, the transmembrane domain, or both, are from a CD28 polypeptide;
12. ~~The MAGE A4 specific CAR of claim 11, wherein (d)~~ the costimulatory domain comprises a CD28 costimulatory domain; or
13. ~~The MAGE A4 specific CAR of any one of claims 1-12, wherein (e)~~ the signaling domain comprises a CD3zeta signaling domain.

146. The MAGE-A4-specific CAR of any one of claims 1 or 3-135, wherein:
- (a) the LCVR comprises the complementarity determining regions (CDRs) of a LCVR comprising an amino acid sequence of SEQ ID NO: 10;
- (b) ~~15. The MAGE A4 specific CAR of any one of claims 1 or 3-13, wherein~~ the LCVR comprises the complementarity determining regions (CDRs) of a LCVR comprising an amino acid sequence of SEQ ID NO: 37;
16. ~~The MAGE A4 specific CAR of claim 14 or 15, wherein (c)~~ the LCVR comprises LCDR1-LCDR2-LCDR3 comprising the amino acid sequences, respectively, of SEQ ID NOs: 12-14-16;
17. ~~The MAGE A4 specific CAR of any one of claims 1 or 3-16, wherein (d)~~ the HCVR comprises the CDRs of a HCVR comprising an amino acid sequence of SEQ ID NO: 2;
- (e) ~~18. The MAGE A4 specific CAR of claim 17, wherein~~ the HCVR comprises HCDR1-HCDR2-HCDR3 comprising the amino acid sequences, respectively, of SEQ ID NOs: 4-6-8;
19. ~~The MAGE A4 specific CAR of any one of claims 1 or 3-18, wherein (f)~~ the LCVR comprises an amino acid sequence of SEQ ID NO: 10, or an amino

acid sequence having 95%-99% sequence identity to an amino acid sequence of SEQ ID NO: 10; and the HCVR comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 2, or an amino acid sequence having 95%-99% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 2;

(g) ~~20.~~ The MAGE A4 specific CAR of any one of claims 1 or 3-18, wherein the LCVR comprises an amino acid sequence of SEQ ID NO: 37, or an amino acid sequence having 95%-99% sequence identity to an amino acid sequence of SEQ ID NO: 37; and the HCVR comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 2, or an amino acid sequence having 95%-99% sequence identity to an amino acid sequence of SEQ ID NO: 2;

~~21.~~ The MAGE A4 specific CAR of claim 19 or 20, wherein (h) the LCVR comprises an amino acid sequence of SEQ ID NO: 10, and the HCVR comprises an amino acid sequence of SEQ ID NO: 2; or

~~22.~~ The MAGE A4 specific CAR of claim 19 or 20, wherein (i) the LCVR comprises an amino acid sequence of SEQ ID NO: 37, and the HCVR comprises an amino acid sequence of SEQ ID NO: 2.

~~23.~~ The MAGE-A4-specific CAR of any one of claims 2-13, wherein:

(a) the LCVR comprises the complementarity determining regions (CDRs) of a LCVR comprising an amino acid sequence of SEQ ID NO: 59;

~~24.~~ The MAGE A4 specific CAR of claim 23, wherein (b) the LCVR comprises LCDR1-LCDR2-LCDR3 comprising the amino acid sequences, respectively, of SEQ ID NOs: 61-63-65;

~~25.~~ The MAGE A4 specific CAR of any one of claims 2-13 or 23-24, wherein (c) the HCVR comprises the CDRs of a HCVR comprising an amino acid sequence of SEQ ID NO: 51;

~~26.~~ The MAGE A4 specific CAR of claim 25, wherein (d) the HCVR comprises HCDR1-HCDR2-HCDR3 comprising the amino acid sequences, respectively, of SEQ ID NOs: 53-55-57;

~~27.~~ The MAGE A4 specific CAR of any one of claims 2-13 or 23-26, wherein (e) the LCVR comprises an amino acid sequence of SEQ ID NO: 59, or an amino acid sequence having 95%-99% sequence identity to an amino acid sequence of SEQ ID NO: 59;

and the HCVR comprises an of SEQ ID NO: 51, or an amino acid sequence having 95%-99% sequence identity to an amino acid sequence of SEQ ID NO: 51; or

~~28. The MAGE-A4 specific CAR of claim 27, wherein (f) the LCVR comprises an amino acid sequence of SEQ ID NO: 59, and the HCVR comprises an amino acid sequence of SEQ ID NO: 51.~~

~~29. The MAGE-A4-specific CAR of any one of claims 1-10 and 13-28, wherein~~
~~:~~

~~(a) the hinge comprises the amino acid sequence of SEQ ID NO: 27;~~

~~30. The MAGE-A4 specific CAR of any one of claims 1-10 and 13-29, wherein~~
~~(b) the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 28;~~

~~31. The MAGE-A4 specific CAR of any one of claims 1-10 and 13-30, wherein~~
~~the (c) the 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO: 29;~~

~~32. The MAGE-A4 specific CAR of any one of claims 1-8 and 11-28, wherein (d)~~
~~the hinge comprises the amino acid sequence of SEQ ID NO: 41;~~

~~33. The MAGE-A4 specific CAR of any one of claims 1-8, 11-28, and 32,~~
~~wherein (e) the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 43;~~

~~34. The MAGE-A4 specific CAR of any one of claims 1-8, and 11-28, and 32-33,~~
~~wherein (f) the CD28 costimulatory domain comprises the amino acid sequence of SEQ ID NO: 45; or~~

~~35. The MAGE-A4 specific CAR of any one of claims 1-34, wherein (g) the CD3zeta signaling domain comprises the amino acid sequence of SEQ ID NO: 30.~~

~~36. The MAGE-A4-specific CAR of claim 1, comprising the amino acid sequence of SEQ ID NO: 22.~~

~~37. The MAGE-A4 specific CAR of claim 1, comprising the amino acid sequence of SEQ ID NO: 39.~~

~~38. The MAGE-A4 specific CAR of claim 1, comprising, or the amino acid sequence of SEQ ID NO: 47.~~

~~39~~10. The MAGE-A4-specific CAR of claim 2, comprising the amino acid sequence of SEQ ID NO: 71.

~~40. The MAGE-A4 specific CAR of claim 2, comprising, or the amino acid sequence of SEQ ID NO: 73.~~

~~41~~11. The MAGE-A4-specific CAR of any one of claims 1 and 3-22, wherein said chimeric antigen receptor specifically binds to one or more amino acids at positions 286-294 of SEQ ID NO: 32.

~~42. The MAGE-A4 specific CAR of any one of claims and 2-13 and 23-28, wherein said chimeric antigen receptor specifically binds to one or more amino acids at positions 230-239 of SEQ ID NO: 32.~~

~~43. The MAGE-A4 specific CAR of any one of claims 1-26~~10, wherein said HLA is HLA-A2.

~~44~~12. An isolated nucleic acid molecule encoding the MAGE-A4-specific CAR of any one of claims 1-43.

~~45. The isolated~~11, optionally wherein the nucleic acid molecule ~~of claim 44, comprising~~comprises a nucleotide sequence of SEQ ID NO: 21.

~~46. The isolated nucleic acid molecule of claim 44, comprising,~~ a nucleotide sequence of SEQ ID NO: 38.

~~47. The isolated nucleic acid molecule of claim 44, comprising,~~ a nucleotide sequence of SEQ ID NO: 48.

~~48. The isolated nucleic acid molecule of claim 44, comprising,~~ a nucleotide sequence of SEQ ID NO: 70.

49. ~~The isolated nucleic acid molecule of claim 44, comprising, or a nucleotide sequence of SEQ ID NO: 72.~~

50. ~~A; or a vector comprising the nucleic acid molecule of any one of claims 44-49.~~

51. ~~The vector of claim 50, optionally~~ wherein the vector is a DNA vector, an RNA vector, a plasmid, a lentivirus vector, an adenovirus vector, or a retroviral vector.

52. ~~The vector of claim 51, wherein the vector is a lentivirus vector.~~

53. ~~13. A cell comprising the nucleic acid molecule of any one of claims 44-49, or a vector of any one of claims 50-52.~~

54. ~~The cell of claim 53, optionally~~ wherein the cell is a human T cell.

55. ~~14. An engineered cell comprising a chimeric antigen receptor of any one of claims 1-43, optionally wherein:~~

56. ~~The (a) the engineered cell of claim 55 that is an immune cell;~~

(b) ~~the engineered cell~~ is an immune cell.

57. ~~The engineered cell of claim 56, wherein, and~~ the immune cell is an immune effector cell;

58. ~~The (c) the engineered cell of claim 57, wherein is a T lymphocyte;~~

(d) ~~the immune effector~~ engineered cell is a T lymphocyte.

59. ~~The engineered cell of claim 58, wherein and~~ the T lymphocyte is an inflammatory T lymphocyte, a cytotoxic T lymphocyte, a regulatory T lymphocyte, or a helper T lymphocyte, ~~optionally a CD8+ cytotoxic T lymphocyte.~~

15. ~~60. The Use of the engineered cell of claim 59 that is a CD8+ cytotoxic T lymphocyte.~~

61. ~~The engineered cell of any one~~ 14 in the manufacture of claims 55-60a medicament for use in the treatment of treating a MAGE-A4-expressing cancer.

~~62. The engineered cell of claim 61, optionally~~ wherein the MAGE-A4-expressing cancer is multiple myeloma-

~~63. The engineered cell of claim 61, wherein the MAGE-A4-expressing cancer is~~
or melanoma.

~~64~~16. An engineered human T cell comprising a chimeric antigen receptor comprising, from N-terminus to C-terminus: (a) an extracellular ligand-binding domain comprising an anti-MAGE-A4 single chain variable fragment (scFv) domain comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR); (b) a hinge; (c) a transmembrane domain; and (d) a cytoplasmic domain comprising a 4-1BB costimulatory domain or a CD28 costimulatory domain and a CD3zeta signaling domain-optionally wherein:

~~65. The engineered human T cell of claim 64, wherein said (a) the anti-~~
MAGE-A4 scFv specifically binds to one or more amino acid residues of positions 286-294 of SEQ ID NO: 32-;
~~2~~

~~66. The engineered human T cell of claim 64 or 65, wherein (b) the scFv~~
domain comprises a HCVR/LCVR amino acid sequence pair comprising the amino acid sequences of SEQ ID NOs: 2/10-;
~~2~~

~~67. The engineered human T cell of claim 64 or 65, wherein (c) the scFv~~
domain comprises a HCVR/LCVR amino acid sequence pair comprising the amino acid sequences of SEQ ID NOs: 2/37-;
~~2~~

~~68. The engineered human T cell of claim 64, wherein said (d) the anti-~~
MAGE-A4 scFv domain specifically binds to one or more amino acid residues of positions 230-239 of SEQ ID NO: 32-;
~~2~~

~~69. The engineered human T cell of claim 64 or 65, wherein (e) the scFv~~
domain comprises a HCVR/LCVR amino acid sequence pair comprising the amino acid sequences of SEQ ID NOs: 51/59-;
~~2~~

~~70. The engineered human T cell of any one of claims 64-69, wherein (f) the~~
hinge comprises the amino acid sequence of SEQ ID NO: 27-;
~~2~~

~~71. The engineered human T cell of any one of claims 64-70, wherein (g) the~~
transmembrane domain comprises the amino acid sequence of SEQ ID NO: 28-;
~~2~~

~~72. The engineered human T cell of any one of claims 64-71, wherein (h) the 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO: 29;~~

~~73. The engineered human T cell of any one of claims 64-69, wherein (i) the hinge comprises the amino acid sequence of SEQ ID NO: 41;~~

~~74. The engineered human T cell of any one of claims 64-69 and 73, wherein (j) _____ the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 43;~~

~~75. The engineered human T cell of any one of claims 64-69 and 73-74, wherein (k) _____ the CD28 costimulatory domain comprises the amino acid sequence of SEQ ID NO: 45;~~

~~76. The engineered human T cell of any one of claims 64-75, wherein (l) the CD3zeta signaling domain comprises the amino acid sequence of SEQ ID NO: 30;~~

~~77. The engineered human T cell of claim 64, comprising a (m) _____ the chimeric antigen receptor comprising the amino acid sequence of SEQ ID NO: 22;~~

~~78. The engineered human T cell of claim 65, comprising a chimeric antigen receptor comprising the amino acid sequence of SEQ ID NO: 39;~~

~~79. The engineered human T cell of claim 65, comprising a chimeric antigen receptor comprising the amino acid sequence of SEQ ID NO: 47;~~

~~80. The engineered human T cell of claim 65, comprising a chimeric antigen receptor comprising the amino acid sequence of SEQ ID NO: 71;~~

~~81. The engineered human T cell of claim 65, comprising a chimeric antigen receptor comprising or the amino acid sequence of SEQ ID NO: 73.~~

~~82~~17. A pharmaceutical composition comprising:

(a) _____ a genetically-modified human T cell and a pharmaceutically acceptable carrier, wherein the genetically-modified human T cell comprises a chimeric antigen receptor according to any one of claims 1-~~43~~11;

~~83. A pharmaceutical composition comprising (b) _____ the engineered cell of any one of claims 55-63~~claim 14 and a pharmaceutically acceptable carrier; or

~~84. A pharmaceutical composition comprising (c) the engineered human T cell of any one of claims 64-81~~claim 16 and a pharmaceutically acceptable carrier.

~~18. 85. The Use of the pharmaceutical composition of any one of claims 82-84 for use~~claim 17 in the ~~treatment~~manufacture of a medicament for treating a MAGE-A4-expressing cancer.

~~86. The pharmaceutical composition of claim 85, optionally~~ wherein the MAGE-A4-expressing cancer is multiple myeloma.

~~87. The pharmaceutical composition of claim 85, wherein the MAGE-A4-expressing cancer is or~~ melanoma.

~~88~~19. Use of the chimeric antigen receptor of any one of claims 1-~~43~~11, the nucleic acid molecule of ~~any one of claims 44-49, or~~ the vector of ~~any one of claims 50-52~~claim 12, the cell of claim ~~53 or 54~~13, the engineered cell of ~~any one of claims 55-63~~claim 14, or the engineered human T cell of ~~any one of claims 64-81~~claim 16 in the manufacture of a medicament for the treatment of a MAGE-A4-expressing cancer.

~~89. The use of claim 88, optionally~~ wherein the MAGE-A4-expressing cancer is multiple myeloma.

~~90. The use of claim 88, wherein the MAGE-A4-expressing cancer is or~~ melanoma.

~~20. 91. A method of enhancing T lymphocyte activity in a subject comprising, introducing into the subject~~Use of:

(a) ~~a T lymphocyte comprising a chimeric antigen receptor of any one of claims 1-43.~~

~~92. A method for treating a subject suffering from cancer comprising, introducing into the subject~~11 in the manufacture of a therapeutically effective amount of medicament for enhancing T lymphocyte activity in a subject;

(b) ~~a T lymphocyte comprising a chimeric antigen receptor of any one of claims 1-43.~~11 in the manufacture of a medicament for treating a subject suffering from cancer;

~~93. — A method (c) a cell genetically modified to express a chimeric antigen receptor of any one of claims 1-11 in the manufacture of a medicament for stimulating a T cell-mediated immune response to a target cell population or tissue in a subject comprising administering to the subject an effective amount of a cell genetically modified to express a chimeric antigen receptor of any one of claims 1-43; or~~

~~94. — A method of providing anti-tumor immunity in a subject, the method comprising administering to the subject an effective amount of (d) a cell genetically modified to express a chimeric antigen receptor of any one of claims 1-43 in the manufacture of a medicament for providing anti-tumor immunity in a subject.~~

~~95~~²¹. The ~~method~~^{use} of ~~any one of claims 91-94~~^{claim 20}, wherein the subject is a human-

~~96. — The method of any one of claims 91-95; and/or wherein the subject has multiple myeloma, synovial sarcoma, esophageal cancer, head and neck cancer, lung cancer, bladder cancer, ovarian cancer, uterine cancer, stomach cancer, cervical cancer, breast cancer, or melanoma, optionally wherein the subject has multiple myeloma.~~

~~97. — The method of claim 96, wherein the subject has multiple myeloma.~~

~~98~~²². A method of engineering a population of cells to express a chimeric antigen receptor, comprising:

(a) introducing into a population of immune cells nucleic acid molecules encoding a chimeric antigen receptor of any one of claims 1-43¹¹, which have optionally been obtained from a subject;

(b) culturing said population of immune cells under conditions to express said nucleic acid molecules; and

(c) isolating said immune cells expressing said chimeric antigen receptor at the cells' surface.

~~99. — The method~~²³. Use of claim 98, further comprising obtaining said a population of immune cells from a subject prior to introducing said nucleic acid molecule.

~~100.~~—A method engineered according to claim 22 in the manufacture of a medicament for treating a MAGE-A4-expressing cancer in a subject, comprising:

- ~~(a)~~—~~engineering a population of cells according to claim 99; and~~
- ~~(b)~~—by reintroducing said population of cells expressing said chimeric antigen receptor into said subject.

~~101.~~—~~The method of claim 100,~~ optionally wherein ~~said~~ the MAGE-A4-expressing cancer is multiple myeloma.

~~102~~24. An isolated antigen-binding protein that competes for binding with, or that binds to the same epitope as, a MAGE-A4-specific CAR of any one of claims 1-43.

~~103.~~—~~The isolated antigen-binding protein of claim 102,~~11, optionally wherein said isolated antigen-binding protein is a CAR.

~~104.~~—~~An isolated antigen-binding protein that binds to the same epitope as a MAGE-A4 specific CAR of any one of claims 1-43.~~

~~105.~~—~~The isolated antigen-binding protein of claim 104, wherein said isolated antigen-binding protein is a CAR.~~

~~106~~25. An isolated recombinant antibody or antigen-binding fragment thereof that specifically binds to a Melanoma-Associated Antigen A4 (MAGE-A4) polypeptide, wherein the antibody has one or more of the following characteristics:

- (a) binds to the MAGE-A4 polypeptide with an EC₅₀ of less than about 10⁻⁹ M;
- (b) demonstrates an increase in survival in an animal with cancer after administration to said animal, as compared to a comparable animal without said administration; and/or
- (c) comprises (i) three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2, and HCDR3) contained within a heavy chain variable region (HCVR) comprising an amino acid sequence having at least about 90% sequence identity to an HCVR set forth in Table 1; and (ii) three light chain CDRs (LCDR1, LCDR2, and LCDR3) contained within a light chain variable region (LCVR) comprising the amino acid sequence having at least about 90% sequence identity to an LCVR set forth in Table 1.

- ~~107~~26. The antibody or antigen-binding fragment of claim ~~106~~25, wherein:
- (a) the the MAG-E-A4 polypeptide is an HLA-A2 bound MAG-E-A4 polypeptide;
- ~~108. The~~(b) the the isolated antibody or antigen-binding fragment thereof ~~of any one of claims 106 and 107, comprising~~comprises an HCVR having an amino acid sequence of SEQ ID NO: 2;
- ~~109. The~~(c) the the isolated antibody or antigen-binding fragment thereof ~~of any one of claims 107-108, comprising~~comprises an LCVR having an amino acid sequence of SEQ ID NO: 10;
- ~~110. The~~(d) the the isolated antibody or antigen-binding fragment thereof ~~of any one of claims 106-109, comprising~~comprises an HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 2/10;
- ~~111. The~~(e) the the isolated antibody or antigen-binding fragment thereof ~~of any one of claims 107-108, comprising~~comprises an LCVR having an amino acid sequence of SEQ ID NO: 37;
- ~~112. The isolated antibody;~~ or
- (f) the the isolated antibody or antigen-binding fragment thereof ~~of any one of claims 106-108 and 111, comprising~~comprises an HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 2/37.
- ~~113~~27. An isolated antibody or antigen-binding fragment thereof ~~of any one of claims 106-112, comprising~~claim 25 or 26:
- (A) comprising:
- _____ (a) an HCDR1 domain having an amino acid sequence of SEQ ID NO: 4;
- _____ (b) an HCDR2 domain having an amino acid sequence of SEQ ID NO: 6;
- _____ (c) an HCDR3 domain having an amino acid sequence of SEQ ID NO: 8;
- _____ (d) an LCDR1 domain having an amino acid sequence of SEQ ID NO: 12;
- _____ (e) an LCDR2 domain having an amino acid 14; and
- _____ (f) an LCDR3 domain having an amino acid sequence of SEQ ID NO: 16;
- _____ ; or

~~114.~~—The isolated antibody or antigen binding fragment thereof of any one of ~~claims 106 and 107~~, (B) comprising an HCVR having an amino acid sequence of SEQ ID NO: 51;

~~115.~~—The isolated antibody or antigen binding fragment thereof of any one of ~~claims 106, 107, and 114~~, and/or comprising an LCVR having an amino acid sequence of SEQ ID NO: 59; or

~~116.~~—An isolated antibody or antigen binding fragment thereof of any one of ~~claims 106, 107, 114, and 115~~, comprising:

(C) comprising:

_____ (a) an HCDR1 domain having an amino acid sequence of SEQ ID NO: 53;

_____ (b) an HCDR2 domain having an amino acid sequence of SEQ ID NO: 55;

_____ (c) an HCDR3 domain having an amino acid sequence of SEQ ID NO: 57;

_____ (d) an LCDR1 domain having an amino acid sequence of SEQ ID NO: 61;

_____ (e) an LCDR2 domain having an amino acid sequence of SEQ ID NO: 63;

and

_____ (f) an LCDR3 domain having an amino acid sequence of SEQ ID NO: 65; or

~~117.~~—The isolated antibody or antigen binding fragment thereof of any one of ~~claims 106, 107, and 114-116~~, (D) comprising an HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 51/59; or

~~118.~~—The isolated antibody or antigen binding fragment thereof of any one of ~~claims 106-117~~ (E) which is an IgG1 antibody; or

~~119.~~—The isolated antibody or antigen binding fragment thereof of any one of ~~claims 106-117~~ (F) which is an IgG4 antibody; or

~~120.~~—The isolated antibody or antigen binding fragment thereof of any one of ~~claims 106-119~~ (G) which is a bispecific antibody.

~~121-128.~~ A pharmaceutical composition comprising the isolated antibody or antigen-binding fragment thereof of any one of ~~claims 106-120~~ 25-27 and a pharmaceutically acceptable carrier or diluent.

~~122.~~—The ~~pharmaceutical composition of claim 121~~, optionally wherein said pharmaceutical composition further comprises a second therapeutic agent.

~~123.~~—~~The pharmaceutical composition of claim 122, wherein said second therapeutic agent is, which is optionally~~ selected from the group consisting of: an anti-tumor agent, steroids, and targeted therapies.

~~124~~29. A polynucleotide molecule comprising a polynucleotide sequence that encodes an HCVR or an LCVR of an antibody as set forth in any one of claims ~~106-120~~25-27; or a vector comprising the polynucleotide; or a cell comprising the vector.

~~125.~~—~~A vector comprising the polynucleotide of claim 124.~~

~~126.~~—~~A cell comprising the vector of claim 125.~~

~~127.~~—~~A method of treating a MAGE-A4 expressing cancer, the method comprising administering~~30. Use of an antibody or antigen-binding fragment of any one of claims 106-120~~25-27, or the pharmaceutical composition of any one of claims 121-123, to~~claim 28 in the manufacture of a medicament for treating a MAGE-A4 expressing cancer in a subject.

~~128.~~—~~The method of claim 127, optionally~~ wherein said pharmaceutical composition is ~~administered~~for use in combination with a second therapeutic agent.

~~129.~~—~~The method of claim 128, wherein said second therapeutic agent is, which is optionally~~ selected from the group consisting of: an anti-tumor agent, steroids, and targeted therapies.