

WHAT IS CLAIMED IS:

~~1. A method of treating cancer, comprising:~~

~~administering an effective amount of genetically engineered anti-tumor human T cells to a patient to treat cancer of the patient, wherein the anti-tumor human T cells have been obtained by incorporating a recombinant DNA sequence encoding a CAR into T cells extracted from the patient, wherein the encoded CAR comprises an ALPP antigen binding domain that binds to ALPP expressed in cancer cells.~~

~~2. The method of treating a patient of claim 1, wherein the cancer is lung cancer.~~

~~3. The method of treating a patient of claim 1, wherein the cancer is gastric cancer.~~

~~4. The method of treating a patient of claim 1, wherein the cancer is pancreatic cancer.~~

~~5. The method of treating a patient of claim 1, wherein the cancer is head & neck cancer.~~

~~6. The method of treating a patient of claim 1, wherein the cancer is colorectal cancer.~~

~~7. The method of treating a patient of claim 1, wherein the cancer is urothelial cancer.~~

~~8. The method of treating a patient of claim 1, wherein the cancer is renal cancer.~~

~~9. The method of treating a patient of claim 1, wherein the cancer is cancer of reproductive organs.~~

~~10. The method of treating a patient of claim 8, wherein the cancer of reproductive organs is ovarian cancer.~~

~~11. The method of treating a patient of claim 8, wherein the cancer of reproductive organs is endometrial cancer.~~

~~12. The method of treating a patient of claim 8, wherein the cancer of reproductive organs is cervical cancer.~~

13. The method of treating a patient of claim 8, wherein the cancer of reproductive organs is testicular cancer.

5 ~~14.1. Use of genetically engineered anti-tumor human T cells in the manufacture of a medicament for A method of treating cancer~~ in a patient in need thereof, comprising:
administering an effective amount of genetically engineered anti-tumor human T cells to a
patient to treat cancer of the patient, wherein the anti-tumor human T cells ~~have been~~
obtained by incorporating a recombinant DNA sequence encoding comprise a chimeric
10 antigen receptor (CAR) comprising into T cells extracted from the patient, wherein the
~~encoded CAR comprises a~~ placental alkaline phosphatase (ALPP) antigen binding domain;
wherein the ~~CAR T cell~~ antigen binding domain ~~consists of~~ comprises an antibody or
antibody fragment thereof; and
wherein the ~~said~~ antibody or antibody fragment thereof comprises a heavy chain variable
15 region (VH) comprising an amino acid sequence ~~has a variable heavy chain region~~ selected
from SEQ ID NO: 1 or SEQ ID NO: 3; and a light chain variable region (VL) comprising an
amino acid sequence ~~variable light chain region~~ selected from SEQ ID NO: 2 or SEQ ID NO:
4.

20 ~~15.2. A method of treating cancer~~ The use of claim ~~141~~, wherein the antibody ~~is murine~~
~~antibody against ALPP having a variable heavy chain region or antibody fragment thereof~~
comprises a VH comprising an amino acid sequence set forth in SEQ ID NO: 1, and a VL
comprising an amino acid sequence set forth in ~~—and variable light chain region—~~ SEQ ID NO:
2.

25 ~~16.3. A method of treating cancer~~ The use of claim ~~141~~, wherein the antibody or antibody
fragment thereof comprises a VH comprising an amino acid sequence set forth in ~~is~~
~~humanized antibody against ALPP having a variable heavy chain region~~ SEQ ID NO: 3, and
a VL comprising an amino acid sequence set forth in ~~variable light chain region~~ SEQ ID NO:
30 4.

17.4. A chimeric antigen receptor comprising: (a) an extracellular antigen-binding domain
that specifically recognizes alkaline phosphatase, placental (ALPP); (b) a transmembrane

domain; and (c) an intracellular signaling region, wherein the antigen-binding domain comprises a heavy chain variable region (VH) and a light chain variable region (VL), and the VH comprises heavy chain complementarity determining regions (CDRs) 1, 2, and 3 and the VL comprises VL CDRs 1, 2, and 3,

wherein the VH CDRs 1, 2, and 3 amino acid sequences and the VL CDRs, 1, 2, and 3 amino acid sequences are one of the following:

(1) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 45, 46, and 47, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 48, 49, and 50, respectively;

(2) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 51, 52, and 53, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 54, 55, and 56, respectively;

(3) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 57, 58, and 59, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 60, 61, and 62, respectively;

(4) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 63, 64, and 65, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 66, 67, and 68, respectively; and

(5) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 81, 82, and 83, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 84, 85, and 86, respectively.

~~18. The chimeric antigen receptor of claim 17, wherein the antigen-binding domain comprises a heavy chain variable domain (VH) and a light chain variable domain (VL).~~

~~19. The chimeric antigen receptor of claim 18, wherein the VH comprises heavy chain complementarity determining regions (CDRs) 1, 2, and 3 and the VL comprises VL CDRs 1, 2, and 3,~~

~~wherein the VH CDRs 1, 2, and 3 amino acid sequences and the VL CDRs, 1, 2, and 3 amino acid sequences are one of the following:~~

~~(1) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 45, 46, and 47, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 48, 49, and 50, respectively;~~

(2) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID Nos: 51, 52, and 53, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 54, 55, and 56, respectively;

(3) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 57, 58, and 59, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 60, 61, and 62, respectively;

(4) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 63, 64, and 65, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 66, 67, and 68, respectively; and

(5) the VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 81, 82, and 83, respectively, and the VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 84, 85, and 86, respectively.

20.5. The chimeric antigen receptor of claim ~~18 or 194~~, wherein the VH ~~consist of or~~ comprises an amino acid sequence having at least 90%, ~~91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100%~~ sequence identity to SEQ ID NOs: 1, 3, 5, 7, 9, 11, or 13; and the VL ~~consists of or~~ comprises an amino acid sequence having at least 90%, ~~91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100%~~ sequence identity to SEQ ID NOs: 2, 4, 6, 8, 10, 12, or 14.

~~21. The chimeric antigen receptor of claim 20, wherein the VH comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 1 and the VL comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 2.~~

~~22. The chimeric antigen receptor of claim 20, wherein the VH comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 3 and the VL comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 4.~~

~~23. The chimeric antigen receptor of claim 20, wherein the VH comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 5 and the VL comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 6.~~

~~24. The chimeric antigen receptor of claim 20, wherein the VH comprises an amino acid~~

~~sequence having at least 90% identity to SEQ ID NO: 7 and the VL comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 8.~~

~~25. The chimeric antigen receptor of claim 20, wherein the VH comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 9 and the VL comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 10.~~

~~26. The chimeric antigen receptor of claim 20, wherein the VH comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 11 and the VL comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 12.~~

~~27. The chimeric antigen receptor of claim 20, wherein the VH comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 13 and the VL comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 14.~~

~~28.~~6. The chimeric antigen receptor of ~~any one of claims 17-27~~claim 4 or 5, wherein the antigen-binding domain comprises an scFv comprising the VH and the VL.

~~29. The chimeric antigen receptor of any one of claims 17-28, wherein the VH region and the VL region are joined by a flexible linker.~~

~~30. The chimeric antigen receptor of claim 29, wherein the flexible linker comprises the amino acid sequence of EKGRSGGGGSGGGGSGGGGS (SEQ ID NO: 37).~~

~~31. The chimeric antigen receptor of claim 29, wherein the flexible linker comprises the amino acid sequence of GGGGSGGGGSGGGGS (SEQ ID NO: 87).~~

~~32.~~7. The chimeric antigen receptor of any one of claims ~~17-31~~4-6, wherein the chimeric antigen receptor further comprises a hinge region, wherein the hinge region comprises a membrane-proximal region from IgG, CD8, or CD28.

~~33. The chimeric antigen receptor of claim 32, wherein the hinge region comprises a membrane proximal region from IgG, CD8, or CD28.~~

34. ~~The chimeric antigen receptor of claim 33, wherein the hinge region comprises a CD8 membrane proximal region.~~
- 5 ~~35.8.~~ The chimeric antigen receptor of any of claims ~~17-344-7~~, wherein the transmembrane domain comprises a transmembrane region of CD4, CD8, or CD28.
- ~~36. The chimeric antigen receptor of claim 35, wherein the transmembrane domain comprises a CD8 transmembrane region.~~
- 10 ~~37. The chimeric antigen receptor of claim 34 or 36, wherein the hinge region and/or the transmembrane region are from human CD8.~~
- ~~38. The chimeric antigen receptor of any one of claims 17-37, wherein the chimeric antigen receptor comprises an amino acid sequence set forth in SEQ ID NO: 38, or an amino acid sequence that is at least 90% identical to SEQ ID NO: 38.~~
- 15 ~~39.9.~~ The chimeric antigen receptor of any of claims ~~17-384-8~~, wherein the intracellular signaling region comprises an activating cytoplasmic signaling domain, wherein the intracellular signaling region comprises a functional signaling domain of CD3 zeta.
- 20 ~~40. The chimeric antigen receptor of claim 39, wherein the activating cytoplasmic signaling domain is capable of inducing a primary activation signal in a T cell, is a T cell receptor (TCR) component, and/or comprises an immunoreceptor tyrosine-based activation motif (ITAM).~~
- 25 ~~41. The chimeric antigen receptor of claims 17-40, wherein the intracellular signaling region is or comprises a functional signaling domain of CD3 zeta.~~
- 30 ~~42. The chimeric antigen receptor of claim 41, wherein the CD3 zeta is human CD3 zeta.~~
- ~~43. The chimeric antigen receptor of claim 42, wherein the intracellular signaling region is or comprises the amino acid sequence set forth in SEQ ID NO: 40 or an amino acid sequence~~

that is at least 90% sequence identical to SEQ ID NO: 40.

44.10. The chimeric antigen receptor of any of claims ~~17-43~~4-9, wherein the intracellular signaling region further comprises a costimulatory signaling region, wherein the costimulatory signaling region comprises a functional signaling domain from a protein selected from the group consisting of OX40, CD28, 4-1BB, ICOS, or a signaling portion thereof.

~~45. The chimeric antigen receptor of claims 44, wherein the costimulatory signaling region is between the transmembrane domain and the intracellular signaling region.~~

~~46. The chimeric antigen receptor of claim 44 or 45, wherein the costimulatory signaling region comprises a functional signaling domain from a protein selected from the group consisting of a MHC class I molecule, a TNF receptor protein, an Immunoglobulin-like protein, a cytokine receptor, an integrin, a signaling lymphocytic activation molecule (SLAM protein), an activating NK cell receptor, BTLA, a Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1, CD11a/CD18, 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRP1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R-beta, IL2R-gamma, IL7R-alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, and CD19a.~~

~~47. The chimeric antigen receptor of claim 46, wherein the costimulatory signaling region is or comprises a functional signaling domain from OX40, CD28, 4-1BB, ICOS, or a signaling portion thereof.~~

~~48. The chimeric antigen receptor of claim 47, wherein the costimulatory signaling region comprises an intracellular signaling domain of 4-1BB.~~

49. The chimeric antigen receptor of claim 48, wherein the ~~4-1BB~~ is human ~~4-1BB~~.

50. The chimeric antigen receptor of claim 49, wherein the costimulatory signaling region is
or comprises an amino acid sequence set forth in SEQ ID NO: 39 or an amino acid sequence
that is at least 90% identical to SEQ ID NO: 39.

51. The chimeric antigen receptor of claim 47, wherein the costimulatory signaling region
comprises intracellular signaling domains of CD28 and ~~4-1BB~~.

52. The chimeric antigen receptor of claim 50, wherein the CD28 is human CD28 and the ~~4-1BB~~
is human ~~4-1BB~~.

53. The chimeric antigen receptor of claim 52, wherein the costimulatory signaling region is
or comprises an amino acid sequence set forth in SEQ ID NO: 90 or an amino acid sequence
that is at least 90% identical to SEQ ID NO: 90.

54.11. A chimeric antigen receptor comprising an amino acid sequence having at least 90%;
~~91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100%~~ identity to SEQ ID NO: 18, 20,
22, 24, 26, 28, 30, 91, 92, or 93.

55. The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least
90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO:
~~18.~~

56. The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least
90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO:
~~20.~~

57. The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least
90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO:
~~22.~~

58. ~~The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 24.~~
- 5 59. ~~The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 26.~~
60. ~~The chimeric antigen receptor of claim 51, wherein the amino acid sequence is at least~~
10 ~~90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 28.~~
61. ~~The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least~~
15 ~~90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 30.~~
62. ~~The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least~~
20 ~~90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 91.~~
63. ~~The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least~~
25 ~~90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 92.~~
64. ~~The chimeric antigen receptor of claim 54, wherein the amino acid sequence is at least~~
90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 93.
- 30 65.12. A polynucleotide encoding the chimeric antigen receptor of any of claims ~~17-64~~11.
- 66.13. A vector comprising the polynucleotide of claim ~~65~~12.
- 67.14. The vector of claim ~~66~~13, wherein the vector further comprises a nucleic acid

encoding an anti-PD-1 antibody, an anti-PD-L1 antibody, or antigen binding fragment thereof.

~~68. The vector of claim 66, wherein the vector further comprises a nucleic acid encoding an anti PD-L1 antibody or antigen binding fragment thereof.~~

~~69. The vector of any one of claims 66-68, wherein the vector is a viral vector.~~

~~70. The vector of claim 69, wherein the viral vector is a retroviral vector or a lentiviral vector.~~

~~71.~~15. An engineered cell, comprising the chimeric antigen receptor of any one of claims ~~17-644~~11.

~~72. An engineered cell, comprising the polynucleotide of claim 65 or the vector of any one of claims 66-70.~~

~~73. The engineered cell of claim 71 or 72, wherein the engineered cell is a primary cell obtained from a subject (e.g., a human subject).~~

~~74. The engineered cell of claim 71 or 72, wherein the engineered cell is a cell line.~~

~~75. The engineered cell of any one of claims 71-74, wherein the engineered cell is an immune cell.~~

~~76. The engineered cell of claim 75, wherein the immune cell is an NK cell or a T cell.~~

~~77. The engineered cell of any one of claims 71-76, wherein the engineered cell is a T cell.~~

~~78. The engineered cell of claim 77, wherein the T cell is CD8+.~~

~~79. The engineered cell of claim 77, wherein the T cell is CD4+.~~

~~80. The engineered cell of any one of claims 76-79, wherein the T cell is isolated from a~~

human subject.

~~81. The engineered cell of any one of claims 71-80, wherein the engineered cell expresses the chimeric antigen receptor.~~

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~~82. The engineered cell of any one of claims 71-81, wherein the engineered cell expresses a cytokine and/or a co-stimulatory ligand.~~

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~~83. The engineered cell of claim 82, wherein the cytokine and/or the co-stimulatory ligand is membrane tethered.~~

~~84. The engineered cell of claim 82, wherein the cytokine and/or the co-stimulatory ligand is secreted.~~

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~~85. The engineered cell of any one of claims 82-84, wherein the cytokine is IL-2, IL-5, or IL-12.~~

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~~86. The engineered cell of any one of claims 82-84, wherein the co-stimulatory ligand is CD40L (CD154) or 41-BBL (CD137L).~~

~~87. The engineered cell of any one of claims 71-86, wherein the engineered cell expresses an antibody or antigen-binding fragment thereof (e.g., an scFv).~~

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~~88. The engineered cell of any one of claims 87, wherein the antibody or antigen-binding fragment thereof is an immune checkpoint inhibitor.~~

~~89. The engineered cell of claim 88, wherein the antibody or antigen-binding fragment thereof specifically binds to PD-1, PD-L1, or CTLA-4.~~

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~~90.~~ 16. A method for producing the engineered cell, comprising introducing a vector of ~~claims 66-70~~ claim 13 or 14 into a cell *in vitro* or *ex vivo*.

~~91. The method of claim 90, wherein the vector is a viral vector and the introducing is carried~~

~~out by transduction.~~

92.17. A method of generating a population of cells, comprising introducing a nucleic acid into a cell, where the nucleic acid comprises the polynucleotide of claim ~~65~~12, or a nucleic acid encoding the chimeric antigen receptor of any one of claims ~~17-644~~11.

93.18. ~~Use of the engineered cell of claim 15 in the manufacture of a medicament~~ A method ~~offor~~ treating an ALPP-associated disease or disorder in a subject, ~~comprising administering the engineered cell of any of claims 71-89 to the subject.~~

~~94. The method of claim 93, wherein the ALPP-associated disease or disorder is a cancer.~~

~~95. The method of claim 94, wherein the cancer is testicular cancer, endometrial cancer, ovarian cancer, cervical cancer, urothelial cancer, pancreatic cancer, liver cancer, or stomach cancer.~~

~~96. The method of any one of claims 93-95, wherein the method further comprises administering a checkpoint inhibitor to the subject.~~

~~97. The method of claim 96, wherein the checkpoint inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof, an anti-PD-L1 antibody or antigen-binding fragment thereof, or an anti-CTLA-4 antibody or antigen-binding fragment thereof.~~

98.19. An anti-ALPP antibody or antigen-binding fragment thereof comprising:

a heavy chain variable region (VH) comprising complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDR1 region comprises an amino acid sequence that is at least 80% identical to a selected VH CDR1 amino acid sequence, the VH CDR2 region comprises an amino acid sequence that is at least 80% identical to a selected VH CDR2 amino acid sequence, and the VH CDR3 region comprises an amino acid sequence that is at least 80% identical to a selected VH CDR3 amino acid sequence; and
a light chain variable region (VL) comprising CDRs 1, 2, and 3, wherein the VL CDR1 region comprises an amino acid sequence that is at least 80% identical to a selected VL CDR1 amino acid sequence, the VL CDR2 region comprises an amino acid sequence that

is at least 80% identical to a selected VL CDR2 amino acid sequence, and the VL CDR3 region comprises an amino acid sequence that is at least 80% identical to a selected VL CDR3 amino acid sequence,

wherein the selected VH CDRs 1, 2, and 3 amino acid sequences and the selected VL CDRs,

5 1, 2, and 3 amino acid sequences are one of the following:

(1) the selected VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 51, 52, and 53, respectively, and the selected VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 54, 55, and 56, respectively;

10 (2) the selected VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 57, 58, and 59, respectively, and the selected VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 60, 61, and 62, respectively;

(3) the selected VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 63, 64, and 65, respectively, and the selected VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 66, 67, and 68, respectively; and

15 (4) the selected VH CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 81, 82, and 83, respectively, and the selected VL CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 84, 85, and 86, respectively.

20 99.20. An antibody or antigen-binding fragment thereof that binds to ALPP comprising a heavy chain variable region (VH) comprising an amino acid sequence that is at least 90%, ~~91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%~~ identical to SEQ ID NO: 1, 3, 5, 7, 9, 11, or 13a-selected VH sequence, and a light chain variable region (VL) comprising an amino acid sequence that is at least 90%, ~~91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%~~ identical to SEQ ID NO: 2, 4, 6, 8, 10, 12, and 14a-selected VL sequence, wherein ~~the selected VH sequence is selected from SEQ ID NOs: 1, 3, 5, 7, 9, 11, and 13, and the selected VL sequence is selected from SEQ ID NOs: 2, 4, 6, 8, 10, 12, and 14.~~

30 100.21. The ~~use of any one of claims 1-3, wherein the cancer is lung cancer, gastric cancer, pancreatic cancer, head and neck cancer, colorectal cancer, urothelial cancer, renal cancer, ovarian cancer, endometrial cancer, cervical cancer, or testicular cancer~~ antibody or antigen-binding fragment thereof of claim 98 or 99, wherein the antibody or antigen-binding fragment specifically binds to human ALPP.

~~101. The antibody or antigen binding fragment thereof of any one of claims 98-100, wherein the antibody or antigen binding fragment is a humanized antibody or antigen binding fragment thereof.~~

5 ~~102. The antibody or antigen binding fragment thereof of any one of claims 98-101, wherein the antibody or antigen binding fragment is a single chain variable fragment (scFv).~~

~~103. An antibody or antigen binding fragment thereof comprising the VH CDRs 1, 2, and 3, and the VL CDRs 1, 2, and 3 of the antibody or antigen binding fragment thereof of any one~~
10 ~~of claims 98-102.~~

~~104. A chimeric antigen receptor comprising the VH CDRs 1, 2, and 3, and the VL CDRs 1, 2, and 3 of the antibody or antigen binding fragment thereof of any one of claims 98-103.~~

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