

WHAT IS CLAIMED IS:

1. Use of genetically engineered anti-tumor human T cells in the manufacture of a medicament for treating cancer in a patient in need thereof,
 - 5 wherein the anti-tumor human T cells comprise a chimeric antigen receptor (CAR) comprising a placental alkaline phosphatase (ALPP) antigen binding domain;
wherein the antigen binding domain comprises an antibody or antibody fragment thereof;
and
wherein the antibody or antibody fragment thereof comprises a heavy chain variable
10 region (VH) comprising an amino acid sequence selected from SEQ ID NO: 1 or SEQ ID NO: 3; and a light chain variable region (VL) comprising an amino acid sequence selected from SEQ ID NO: 2 or SEQ ID NO: 4.
2. The use of claim 1, wherein the antibody or antibody fragment thereof comprises a VH
15 comprising an amino acid sequence set forth in SEQ ID NO: 1, and a VL comprising an amino acid sequence set forth in SEQ ID NO: 2.
3. The use of claim 1, wherein the antibody or antibody fragment thereof comprises a VH
comprising an amino acid sequence set forth in SEQ ID NO: 3, and a VL comprising an
20 amino acid sequence set forth in SEQ ID NO: 4.
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
25 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:
 - 30 (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.

5. The chimeric antigen receptor of claim 4, wherein the VH comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, or 13; and the VL comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, or 14.

6. The chimeric antigen receptor of claim 4 or 5, wherein the antigen-binding domain comprises an scFv comprising the VH and the VL.

7. The chimeric antigen receptor of any one of claims 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.

8. The chimeric antigen receptor of any of claims 4-7, wherein the transmembrane domain comprises a transmembrane region of CD4, CD8, or CD28.

9. The chimeric antigen receptor of any of claims 4-8, wherein the intracellular signaling region comprises an activating cytoplasmic signaling domain, wherein the intracellular signaling region comprises a functional signaling domain of CD3 zeta.

10. The chimeric antigen receptor of any of claims 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.

11. A chimeric antigen receptor comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 18, 20, 22, 24, 26, 28, 30, 91, 92, or 93.
12. A polynucleotide encoding the chimeric antigen receptor of any of claims 4-11.
13. A vector comprising the polynucleotide of claim 12.
14. The vector of claim 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.
15. An engineered cell, comprising the chimeric antigen receptor of any one of claims 4-11.
16. A method for producing the engineered cell, comprising introducing a vector of claim 13 or 14 into a cell *in vitro* or *ex vivo*.
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 12, or a nucleic acid encoding the chimeric antigen receptor of any one of claims 4-11.
18. Use of the engineered cell of claim 15 in the manufacture of a medicament for treating an ALPP-associated disease or disorder in a subject.
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, 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;
 - (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
 - (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. 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% identical to SEQ ID NO: 1, 3, 5, 7, 9, 11, or 13, and a light chain variable region (VL) comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 2, 4, 6, 8, 10, 12, and 14.
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.