CLAIMS

What is claimed is:

1. A chimeric antigen receptor (CAR) comprising an antigen-binding domain capable of binding Fibroblast Activation Protein (FAP), a transmembrane domain, and an intracellular domain, wherein the antigen-binding domain comprises:

a heavy chain variable region that comprises three heavy chain complementarity determining regions (HCDRs), wherein HCDR1 comprises the amino acid sequence YTITSYSLH (SEQ ID NO: 1), HCDR2 comprises the amino acid sequence EINPANGDHNFSEKFEIK (SEQ ID NO: 2), and HCDR3 comprises the amino acid sequence LDDSRFHWYFDV (SEQ ID NO: 3); and

a light chain variable region that comprises three light chain complementarity determining regions (LCDRs), wherein LCDR1 comprises the amino acid sequence TASSSVSYMY (SEQ ID NO: 4), a LCDR2 comprises the amino acid sequence LTSNLA (SEQ ID NO: 5), and LCDR3 comprises the amino acid sequence QQWSGYPPIT (SEQ ID NO: 6).

2. The CAR of claim 1, wherein the antigen-binding domain comprises:

(a) a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and/or

(b) a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9; and/or

(c) a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9; and/or

(d) an antigen-binding domain selected from the group consisting of a full-length antibody or antigen-binding fragment thereof, a Fab, a single-chain variable fragment (scFv), or a single-domain antibody; and/or

(e) a single-chain variable fragment (scFv) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 11 or 13 .

3. The CAR of any one of claims 1-2, wherein the CAR:

(a) is capable of binding to fibroblast activation protein (FAP); and/or

(b) is capable of binding human FAP; and/or

(c) is capable of binding canine FAP; and/or

(d) is capable of binding murine FAP; and/or

(e) is capable of binding human, canine, and murine FAP; and/or

(f) further comprises a hinge domain, wherein the hinge domain comprises a hinge domain of CD8 alpha.

4. The CAR of any one of claims 1-3, wherein the transmembrane domain:

(a) is selected from the group consisting of an artificial hydrophobic sequence, and a transmembrane domain of a type I transmembrane protein, an alpha, beta, or zeta chain of a T cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, OX40 (CD134), 4-1BB (CD137), ICOS (CD278), and CD154, or a transmembrane domain derived from a killer immunoglobulin-like receptor (KIR); and/or

(b) comprises a transmembrane domain of CD8; and/or

(c) comprises a transmembrane domain of CD8 alpha; and/or

(d) comprises a transmembrane domain derived from a killer immunoglobulin-like receptor (KIR).

5. The CAR of any one of claims 1-4, wherein the intracellular domain:

(a) comprises a costimulatory signaling domain and an intracellular signaling domain; and/or

(b) comprises one or more of a costimulatory domain of a protein selected from the group consisting of proteins in the TNFR superfamily, CD28, 4-1BB (CD137), OX40 (CD134), PD-1, CD7, LIGHT, CD83L, DAP10, DAP12, CD27, CD2, CD5, ICAM-1, LFA-1, Lck, TNFR-I, TNFR-II, Fas, CD30, CD40, ICOS (CD278), NKG2C, and B7-H3 (CD276), or a variant thereof, or an intracellular domain derived from a killer immunoglobulin-like receptor (KIR); and/or

(c) comprises a costimulatory domain of 4-1BB; and/or

(d) comprises a costimulatory domain of DAP12; and/or

(e) comprises a costimulatory domain of CD28; and/or

(f) comprises a costimulatory domain of 4-1BB and a costimulatory domain of CD28; and/or

(g) comprises a costimulatory domain of DAP12 and a costimulatory domain of CD28; and/or

(h) comprises an intracellular domain selected from the group consisting of cytoplasmic signaling domains of a human CD3 zeta chain (CD3ζ), FcγRIII, FcsRI, a cytoplasmic tail of an Fc receptor, an immunoreceptor tyrosine-based activation motif (ITAM) bearing cytoplasmic receptor, TCR zeta, FcR gamma, CD3 gamma, CD3 delta, CD3 epsilon, CD5, CD22, CD79a, CD79b, and CD66d, or a variant thereof; and/or

(i) the intracellular signaling domain comprises an intracellular domain of CD3ζ.

6. A chimeric antigen receptor (CAR) capable of binding Fibroblast Activation Protein (FAP), comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 23 or 25 .

7. A nucleic acid comprising a polynucleotide sequence encoding a CAR of any one of claims 1-6.

8. A nucleic acid comprising a polynucleotide sequence encoding a chimeric antigen receptor (CAR) capable of binding FAP, comprising an antigen-binding domain, a transmembrane domain, and an intracellular domain, wherein the antigen-binding domain comprises:

a heavy chain variable region that comprises three heavy chain complementarity determining regions (HCDRs), wherein HCDR1 comprises the amino acid sequence YTITSYSLH (SEQ ID NO: 1), HCDR2 comprises the amino acid sequence EINPANGDHNFSEKFEIK (SEQ ID NO: 2), and HCDR3 comprises the amino acid sequence LDDSRFHWYFDV (SEQ ID NO: 3); and

a light chain variable region that comprises three light chain complementarity determining regions (LCDRs), wherein LCDR1 comprises the amino acid sequence

TASSSVSYMY (SEQ ID NO: 4), LCDR2 comprises the amino acid sequence LTSNLA (SEQ ID NO: 5), and LCDR3 comprises the amino acid sequence QQWSGYPPIT (SEQ ID NO: 6).

9. The nucleic acid of claim 8, wherein the antigen-binding domain:

(a) comprises a heavy chain variable region encoded by a polynucleotide sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 8; and/or

(b) comprises a light chain variable region encoded by a polynucleotide sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 10; and/or

(c) comprises a heavy chain variable region encoded by a polynucleotide sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 8; and a light chain variable region encoded by a polynucleotide sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 10; and/or

(d) comprises a single-chain variable fragment (scFv) encoded by a polynucleotide sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 12 or 14.

10. The nucleic acid of any one of claims 8-9, wherein:

(a) the transmembrane domain comprises a transmembrane domain of CD8 alpha; and/or

(b) the intracellular domain comprises a costimulatory signaling domain and an intracellular signaling domain; and/or

(c) the intracellular domain comprises a costimulatory signaling domain comprising a costimulatory domain of 4-1BB; and/or

(d) the intracellular domain comprises a costimulatory domain of DAP12; and/or

(e) the intracellular domain comprises a costimulatory domain of CD28; and/or

(f) the intracellular domain comprises a costimulatory domain of 4-1BB and a costimulatory domain of CD28; and/or

(g) the intracellular domain comprises a costimulatory domain of DAP12 and a costimulatory domain of CD28; and/or

(h) the intracellular signaling domain comprises an intracellular domain of CD3ζ.

11. A nucleic acid comprising a polynucleotide sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 22 or 24.

12. A vector comprising the nucleic acid of any one of claims 8-11.

13. The vector of claim 12, wherein the vector is an expression vector and/or the vector is selected from the group consisting of a DNA vector, an RNA vector, a plasmid, a lentiviral vector, an adenoviral vector, an adeno-associated viral vector, and a retroviral vector.

14. A modified immune cell or precursor cell thereof, comprising the CAR of any one of claims 1-7, the nucleic acid of any one of claims 8-11, or the vector of any one of claims 12-13.

15. A modified immune cell or precursor cell thereof, comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP), wherein the CAR comprises:

a heavy chain variable region that comprises three heavy chain complementarity determining regions (HCDRs), wherein HCDR1 comprises the amino acid sequence YTITSYSLH (SEQ ID NO: 1), HCDR2 comprises the amino acid sequence EINPANGDHNFSEKFEIK (SEQ ID NO: 2), and HCDR3 comprises the amino acid sequence LDDSRFHWYFDV (SEQ ID NO: 3); and

a light chain variable region that comprises three light chain complementarity determining regions (LCDRs), wherein LCDR1 comprises the amino acid sequence TASSSVSYMY (SEQ ID NO: 4), a LCDR2 comprises the amino acid sequence LTSNLA (SEQ ID NO: 5), and LCDR3 comprises the amino acid sequence QQWSGYPPIT (SEQ ID NO: 6).

16. The modified immune cell of claim 15, wherein the CAR comprises:

(a) a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9; and/or

(b) a single-chain variable fragment (scFv) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 11 or 13; and/or

(c) an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 23 or 25.

17. The modified cell of any one of claims 14-16, wherein the CAR:

(a) is capable of binding FAP; and/or

(b) is capable of binding human FAP; and/or

(c) is capable of binding canine FAP; and/or

(d) is capable of binding mouse FAP; and/or

(e) is capable of binding human, canine, and mouse FAP.

18. The modified cell of any one of claims 14-17, wherein the modified cell:

(a) is a modified T cell; and/or

(b) is a modified NK cell; and/or

(c) is an autologous cell; and/or

(d) is an autologous cell obtained from a human subject; and/or

(e) is an autologous cell obtained from a canine subject; and/or

(f) is an allogeneic cell.

19. A pharmaceutical composition comprising a therapeutically effective amount of the modified cell of any one of claims 14-18, and a pharmaceutically acceptable excipient.

20. ~~A method of treating a disease in a subject in need thereof, comprising administering to the subject an effective amount of the~~The modified cell of any one of claims 14-18, or the pharmaceutical composition of claim 19 for use in a method of treating a

disease in a subject in need thereof, wherein an effective amount of the modified cell or the pharmaceutical composition is to be administered to the subject.~~.~~

21. Use of the modified cell of any one of claims 14-18, or the pharmaceutical composition of claim 19 in the manufacture of a medicament for the treatment of a disease in a subject in need thereof,~~The method of claim 20,~~ wherein

(a) the disease is selected from the group consisting of an immunological disease, a hematological disease, an autoimmune disease, fibrosis, and cancer; and/or

(b) the disease is cancer; and/or

(c) the disease is cardiac fibrosis; and/or

(d) the disease is cancer, and the cancer comprises a fibroblast activation protein (FAP)-expressing cancer-associated cell, and wherein an effective amount of the modified cell or the pharmaceutical composition is to be administered to the subject.~~.~~

22. The ~~method~~ use of claim 21, wherein

(a) the FAP-expressing cancer-associated cell is a cancer-associated fibroblast (CAF); and/or

(b) the FAP-expressing cancer-associated cell is a FAP-expressing adipocyte; and/or

(c) the FAP-expressing cancer-associated cell is a tumor-associated macrophage (TAM); and/or

(d) the FAP-expressing cancer-associated cell is a tumor-associated neutrophil (TAN) ; and/or

(e) the FAP-expressing cancer-associated cell is a myeloid-derived suppressor cell (MDSC) ; and/or

(f) the FAP-expressing cancer-associated cell is a cancer-initiating cell.

23. Use of ~~A method of treating a cancer in a subject in need thereof, comprising administering to the subject an effective amount of~~ a modified immune cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9;

wherein the cancer comprises FAP-expressing cancer-associated cells, and wherein an effective amount of the modified immune cell is to be administered to the subject.~~.~~

24. Use of a modified immune cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region that comprises three heavy chain complementarity determining regions (HCDRs), wherein HCDR1 comprises the amino acid sequence YTITSYSLH (SEQ ID NO: 1), HCDR2 comprises the amino acid sequence EINPANGDHNFSEKFEIK (SEQ ID NO: 2), and HCDR3 comprises the amino acid sequence LDDSRFHWYFDV (SEQ ID NO: 3); and

a light chain variable region that comprises three light chain complementarity determining regions (LCDRs), wherein LCDR1 comprises the amino acid sequence TASSSVSYMY (SEQ ID NO: 4), a LCDR2 comprises the amino acid sequence LTSNLA (SEQ ID NO: 5), and LCDR3 comprises the amino acid sequence QQWSGYPPIT (SEQ ID NO: 6), and wherein an effective amount of the modified immune cell is to be administered to the subject.

~~24.~~25. The ~~method~~ use of claim 23 or claim 24, wherein the CAR binds to FAP-expressing cancer-associated cells and does not bind to cells that do not express FAP.

~~25. A method of treating a cancer in a subject in need thereof, wherein the cancer is associated with fibroblast activation protein (FAP) expressing cancer-associated fibroblasts, comprising administering to the subject an effective amount~~ The use~~Use~~ of claim 23 or claim 24, wherein the modified immune cell is ~~of~~ a modified T cell ~~comprising a chimeric antigen receptor (CAR) capable of binding~~ fibroblast activation protein (FAP) ~~in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises:~~

a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9, and .wherein the cancer is associated with FAP-expressing cancer-associated fibroblasts, macrophages or neutrophils and wherein an effective amount of the modified T cell is to be administered to the subject.

26. A method of treating a cancer in a subject in need thereof, wherein the cancer is associated with fibroblast activation protein (FAP)-expressing cancer-associated macrophages, comprising administering to the subject an effective amount of Use of a modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9., wherein the cancer is associated with FAP-expressing cancer-associated macrophages, and wherein an effective amount of the modified T cell is to be administered to the subject.

27. A method of treating a cancer in a subject in need thereof, wherein the cancer is associated with fibroblast activation protein (FAP)-expressing cancer-associated neutrophils, comprising administering to the subject an effective amount of Use of a modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

~~a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9.~~, ~~wherein the cancer is associated with FAP-expressing cancer-associated neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.~~

~~28.~~26. ~~A method of treating a cancer in a subject in need thereof, wherein the cancer is associated with fibroblast activation protein (FAP)-expressing cancer-associated fibroblasts, comprising administering to the subject an effective amount of~~ Use of a modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 23 or 25~~.~~, wherein the cancer is associated with FAP-expressing cancer-associated fibroblasts, and wherein an effective amount of the modified T cell is to be administered to the subject.

~~29.~~27. ~~A method of treating a cancer in a subject in need thereof, wherein the cancer is associated with fibroblast activation protein (FAP)-expressing cancer-associated macrophages, comprising administering to the subject an effective amount of~~ Use of a modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 23 or 25, ~~.~~wherein the cancer is associated with FAP-expressing cancer-associated macrophages, and wherein an effective amount of the modified T cell is to be administered to the subject.

~~30.~~28. ~~A method of treating a cancer in a subject in need thereof, wherein the cancer is associated with fibroblast activation protein (FAP)-expressing cancer-associated neutrophils, comprising administering to the subject an effective amount of~~ Use of a

modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the CAR comprises an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 23 or 25~~.~~,
wherein the cancer is associated with FAP-expressing cancer-associated neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.

~~31. A method of treating a solid tumor in a subject in need thereof, wherein the tumor is associated with fibroblast activation protein (FAP)-expressing cancer-associated fibroblasts, comprising administering to the subject an effective amount of a~~ The use of claim 26, wherein the cancer comprises ~~Use of a modified T cell comprising a chimeric antigen receptor (CAR) capable of binding~~ fibroblast activation protein ~~(~~FAP~~)~~ ~~in the manufacture of a medicament for the treatment of~~ a solid tumor~~. in a subject in need thereof, wherein the CAR comprises:~~

~~a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and~~

~~a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9.~~,
~~wherein the tumor is associated with FAP-expressing cancer-associated fibroblasts, and wherein an effective amount of the modified T cell is to be administered to the subject.~~

~~32. A method of treating a solid tumor in a subject in need thereof, wherein the tumor is associated with fibroblast activation protein (FAP)-expressing cancer-associated macrophages, comprising administering to the subject an effective amount of~~ Use of ~~a modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a solid tumor in a subject in need thereof, wherein the CAR comprises:~~

~~a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and~~

~~a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9.~~, ~~wherein the tumor is associated with FAP-expressing cancer-associated macrophages, and wherein an effective amount of the modified T cell is to be administered to the subject.~~

~~33. A method of treating a solid tumor in a subject in need thereof, wherein the tumor is associated with fibroblast activation protein (FAP)-expressing cancer-associated neutrophils, comprising administering to the subject an effective amount of~~ Use of a ~~modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) in the manufacture of a medicament for the treatment of a solid tumor in a subject in need thereof, wherein the CAR comprises:~~

~~a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and~~

~~a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9.~~, ~~wherein the tumor is associated with FAP-expressing cancer-associated neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.~~

29. A modified immune cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) for use in a method of treating a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9,

wherein the cancer comprises FAP-expressing cancer-associated cells, and wherein an effective amount of the modified immune cell is to be administered to the subject.

30. A modified immune cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) for use in a method of treating a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region that comprises three heavy chain complementarity determining regions (HCDRs), wherein HCDR1 comprises the amino acid sequence YTITSYSLH (SEQ ID NO: 1), HCDR2 comprises the amino acid sequence EINPANGDHNFSEKFEIK (SEQ ID NO: 2), and HCDR3 comprises the amino acid sequence LDDSRFHWYFDV (SEQ ID NO: 3); and

a light chain variable region that comprises three light chain complementarity determining regions (LCDRs), wherein LCDR1 comprises the amino acid sequence TASSSVSYMY (SEQ ID NO: 4), a LCDR2 comprises the amino acid sequence LTSNLA (SEQ ID NO: 5), and LCDR3 comprises the amino acid sequence QQWSGYPPIT (SEQ ID NO: 6),

wherein the cancer comprises FAP-expressing cancer-associated cells, and wherein an effective amount of the modified immune cell is to be administered to the subject.

31. A modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) for use in a method of treating a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9, wherein the cancer is associated with FAP-expressing cancer-associated fibroblasts, macrophages or neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.

32. A modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) for use in a method of treating a cancer in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region that comprises three heavy chain complementarity determining regions (HCDRs), wherein HCDR1 comprises the

amino acid sequence YTITSYSLH (SEQ ID NO: 1), HCDR2 comprises the amino acid sequence EINPANGDHNFSEKFEIK (SEQ ID NO: 2), and HCDR3 comprises the amino acid sequence LDDSRFHWYFDV (SEQ ID NO: 3); and

a light chain variable region that comprises three light chain complementarity determining regions (LCDRs), wherein LCDR1 comprises the amino acid sequence TASSSVSYMY (SEQ ID NO: 4), a LCDR2 comprises the amino acid sequence LTSNLA (SEQ ID NO: 5), and LCDR3 comprises the amino acid sequence QQWSGYPPIT (SEQ ID NO: 6),

wherein the cancer is associated with FAP-expressing cancer-associated fibroblasts, macrophages or neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.

33. A modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) for use in a method of treating a cancer in a subject in need thereof, wherein the CAR comprises an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 23 or 25, wherein the cancer is associated with FAP-expressing cancer-associated fibroblasts, macrophages or neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.

34. A modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) for use in a method of treating a solid tumor in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7; and

a light chain variable region comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9,

wherein the tumor is associated with FAP-expressing cancer-associated fibroblasts, macrophages or neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.

35. A modified T cell comprising a chimeric antigen receptor (CAR) capable of binding fibroblast activation protein (FAP) for use in a method of treating a solid tumor in a subject in need thereof, wherein the CAR comprises:

a heavy chain variable region that comprises three heavy chain complementarity determining regions (HCDRs), wherein HCDR1 comprises the amino acid sequence YTITSYSLH (SEQ ID NO: 1), HCDR2 comprises the amino acid sequence EINPANGDHNFSEKFEIK (SEQ ID NO: 2), and HCDR3 comprises the amino acid sequence LDDSRFHWYFDV (SEQ ID NO: 3); and

a light chain variable region that comprises three light chain complementarity determining regions (LCDRs), wherein LCDR1 comprises the amino acid sequence TASSSVSYMY (SEQ ID NO: 4), a LCDR2 comprises the amino acid sequence LTSNLA (SEQ ID NO: 5), and LCDR3 comprises the amino acid sequence QQWSGYPPIT (SEQ ID NO: 6),

wherein the tumor is associated with FAP-expressing cancer-associated fibroblasts, macrophages or neutrophils, and wherein an effective amount of the modified T cell is to be administered to the subject.

~~34.~~36. The ~~method~~ use of any one of claims 2~~1~~0-~~33~~30, the modified cell or the pharmaceutical composition for use of claim 20, the modified immune cell for use of claim 31- or claim 32, and the modified T cell for use of any one of claims ~~35-37~~33-37, further comprising an immune checkpoint inhibitor, tumor antigen vaccine, or neoplastic cell targeted therapies to be administered.

~~35.~~37. The ~~method~~ use of any one of claims ~~20~~21-30 and claim ~~384~~38, the modified cell or the pharmaceutical composition for use of claim 20 or claim ~~38~~38, the modified immune cell for use of any one of claim ~~34~~ 31, 32 and ~~or claim 38~~38, and the modified T cell for use of any one of claims ~~35-37~~33-37 and claim ~~38~~38, wherein the subject is human.

~~36.~~38. The ~~method~~ use of any one of claims 2~~1~~0-30 and claim 38, the modified cell or the pharmaceutical composition for use of claim 20 or claim 38, the modified immune cell for use of any one of claim 31, 32 and 38, and the modified T cell for use of any one of claims 33-37 and claim 38~~33 and claims 38-395, the modified cell or the pharmaceutical composition for use of any one of claim 20 and claim 38-39, the~~

~~modified immune cell for use of any one of claim 34 and claims 38-39 and the modified T cell for use of any one of claims 35-37 and claims 38-39~~, wherein the subject is a non-human animal.