

WHAT IS CLAIMED:

1. An antibody or antigen binding fragment thereof that binds glypican-3 (GPC3), comprising
an HCDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-10, an HCDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 11-20, and an HCDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 21-30, and
a LCDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 31-40, a LCDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 41-50, and a LCDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 51-60.
2. The antibody or antigen binding fragment of claim 1, wherein
 - (i) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 1, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 11, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 21, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 31, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 41, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 51, or
 - (ii) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 2, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 12, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 22, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 32, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 42, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 52, or
 - (iii) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 3, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 13, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 23, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 33, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 43, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 53, or
 - (iv) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 4, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 14, the HCDR3 comprises

- the amino acid sequence of SEQ ID NO: 24, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 34, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 44, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 54, or
- (v) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 5, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 15, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 25, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 35, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 45, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 55, or
- (vi) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 6, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 16, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 26, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 36, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 46, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 56, or
- (vii) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 7, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 17, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 27, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 37, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 47, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 57, or
- (viii) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 8, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 18, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 28, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 38, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 48, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 58, or
- (ix) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 9, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 19, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 29, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 39, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 49, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 59, or

- (x) the HCDR1 comprises the amino acid sequence of SEQ ID NO: 10, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 20, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 30, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 40, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 50, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 60; and/or wherein:-

~~3. The~~ the antibody or antigen binding fragment ~~of claim 1 or 2~~, comprises

- (i) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 61 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 71, or
- (ii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 62 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 72, or
- (iii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 63 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 73, or
- (iv) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 64 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 74, or
- (v) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 65 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 75, or
- (vi) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 66 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 76, or
- (vii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 67 and a VL domain comprising

- an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 77, or
- (viii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 68 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 78, or
 - (ix) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 69 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 79, or
 - (x) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 70 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 80, or
 - (xi) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 117 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 123, or
 - (xii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 118 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 123, or
 - (xiii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 119 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 123, or
 - (xiv) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 120 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 123, or
 - (xv) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 121 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 123, or

- (xvi) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 122 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 123, or
- (xvii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 117 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 124, or
- (xviii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 118 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 124, or
- (xix) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 119 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 124, or
- (xx) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 120 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 124, or
- (xxi) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 121 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 124, or
- (xxii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 122 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 124, or
- (xxiii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 117 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 125, or
- (xxiv) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 118 and a VL domain comprising

an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 125, or

- (xxv) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 119 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 125, or
- (xxvi) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 120 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 125, or
- (xxvii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 121 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 125, or
- (xxviii) a VH domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 122 and a VL domain comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 125.

~~4-3.~~ 3. The antibody or antigen binding fragment of any one of claims 1-~~3~~2, ~~comprises~~ comprising

- (i) a VH domain comprising the amino acid sequence of SEQ ID NO: 61 and a VL domain comprising the amino acid sequence of SEQ ID NO: 71, or
- (ii) a VH domain comprising the amino acid sequence of SEQ ID NO: 62 and a VL domain comprising the amino acid sequence of SEQ ID NO: 72, or
- (iii) a VH domain comprising the amino acid sequence of SEQ ID NO: 63 and a VL domain comprising the amino acid sequence of SEQ ID NO: 73, or
- (iv) a VH domain comprising the amino acid sequence of SEQ ID NO: 64 and a VL domain comprising the amino acid sequence of SEQ ID NO: 74, or
- (v) a VH domain comprising the amino acid sequence of SEQ ID NO: 65 and a VL domain comprising the amino acid sequence of SEQ ID NO: 75, or
- (vi) a VH domain comprising the amino acid sequence of SEQ ID NO: 66 and a VL domain comprising the amino acid sequence of SEQ ID NO: 76, or

- (vii) a VH domain comprising the amino acid sequence of SEQ ID NO: 67 and a VL domain comprising the amino acid sequence of SEQ ID NO: 77, or
- (viii) a VH domain comprising the amino acid sequence of SEQ ID NO: 68 and a VL domain comprising the amino acid sequence of SEQ ID NO: 78, or
- (ix) a VH domain comprising the amino acid sequence of SEQ ID NO: 69 and a VL domain comprising the amino acid sequence of SEQ ID NO: 79, or
- (x) a VH domain comprising the amino acid sequence of SEQ ID NO: 70 and a VL domain comprising the amino acid sequence of SEQ ID NO: 80, or
- (xi) a VH domain comprising the amino acid sequence of SEQ ID NO: 117 and a VL domain comprising the amino acid sequence of SEQ ID NO: 123, or
- (xii) a VH domain comprising the amino acid sequence of SEQ ID NO: 118 and a VL domain comprising the amino acid sequence of SEQ ID NO: 123, or
- (xiii) a VH domain comprising the amino acid sequence of SEQ ID NO: 119 and a VL domain comprising the amino acid sequence of SEQ ID NO: 123, or
- (xiv) a VH domain comprising the amino acid sequence of SEQ ID NO: 120 and a VL domain comprising the amino acid sequence of SEQ ID NO: 123, or
- (xv) a VH domain comprising the amino acid sequence of SEQ ID NO: 121 and a VL domain comprising the amino acid sequence of SEQ ID NO: 123, or
- (xvi) a VH domain comprising the amino acid sequence of SEQ ID NO: 122 and a VL domain comprising the amino acid sequence of SEQ ID NO: 123, or
- (xvii) a VH domain comprising the amino acid sequence of SEQ ID NO: 117 and a VL domain comprising the amino acid sequence of SEQ ID NO: 124, or
- (xviii) a VH domain comprising the amino acid sequence of SEQ ID NO: 118 and a VL domain comprising the amino acid sequence of SEQ ID NO: 124, or
- (xix) a VH domain comprising the amino acid sequence of SEQ ID NO: 119 and a VL domain comprising the amino acid sequence of SEQ ID NO: 124, or
- (xx) a VH domain comprising the amino acid sequence of SEQ ID NO: 120 and a VL domain comprising the amino acid sequence of SEQ ID NO: 124, or
- (xxi) a VH domain comprising the amino acid sequence of SEQ ID NO: 121 and a VL domain comprising the amino acid sequence of SEQ ID NO: 124, or
- (xxii) a VH domain comprising the amino acid sequence of SEQ ID NO: 122 and a VL domain comprising the amino acid sequence of SEQ ID NO: 124, or
- (xxiii) a VH domain comprising the amino acid sequence of SEQ ID NO: 117 and a VL domain comprising the amino acid sequence of SEQ ID NO: 125, or

- (xxiv) a VH domain comprising the amino acid sequence of SEQ ID NO: 118 and a VL domain comprising the amino acid sequence of SEQ ID NO: 125, or
- (xxv) a VH domain comprising the amino acid sequence of SEQ ID NO: 119 and a VL domain comprising the amino acid sequence of SEQ ID NO: 125, or
- (xxvi) a VH domain comprising the amino acid sequence of SEQ ID NO: 120 and a VL domain comprising the amino acid sequence of SEQ ID NO: 125, or
- (xxvii) a VH domain comprising the amino acid sequence of SEQ ID NO: 121 and a VL domain comprising the amino acid sequence of SEQ ID NO: 125, or
- (xxviii) a VH domain comprising the amino acid sequence of SEQ ID NO: 122 and a VL domain comprising the amino acid sequence of SEQ ID NO: 125; and/or wherein the:-

~~5.~~—The antibody or antigen binding fragment of any one of claims 1-4, wherein the antibody or antigen binding fragment is a Fab fragment, a Fab' fragment, a F(ab')₂ fragment, a single chain variable fragment (scFv), or a disulfide stabilized variable fragment (dsFv).

~~6.~~ 4. The antibody or antigen binding fragment of any one of claims 1-~~5~~3, comprising an amino acid sequence having at least 80% identity to any one of SEQ ID NOs: 81-90, 128, and 129; and/or wherein the antibody is an IgG or a humanized antibody.

~~7.~~—The antibody of any one of claims 1-6, wherein the antibody is an IgG.

~~8.~~—The antibody of any one of claims 1-7, wherein the antibody is a humanized antibody.

~~9.~~5. A nucleic acid molecule encoding the antibody or antigen binding fragment of any one of claims 1-~~8~~4.

~~10.~~6. A vector comprising the nucleic acid molecule of claim-~~9~~5.

~~11.~~7. A host cell transformed with the vector of claim-~~10~~6.

~~12.~~8. A composition comprising a therapeutically effective amount of the antibody or antigen binding fragment of any one of claims 1-~~8~~4, the nucleic acid molecule of claim-~~9~~5, or the vector of claim-~~10~~6, and a pharmaceutically acceptable carrier.

~~13- 9.~~ Use of the composition of claim 8 in the manufacture of a medicament ~~A method of for treating a patient who has cancer that expresses GPC3, comprising administering to the patient the composition of claim 12, wherein the composition is to be administered to the patient,~~ wherein optionally the cancer is selected from the group consisting of hepatocellular carcinoma (HCC), melanoma, ovarian clear cell carcinoma (OCCC), yolk sac tumor (YST), neuroblastoma, hepatoblastoma, nephroblastoma (Wilms' tumor), squamous cell carcinoma of the lung, testicular nonseminomatous germ cell tumor, liposarcoma, cervical intraepithelial neoplasia, adenoma of the adrenal gland, schwannoma, embryonal tumor, gastric carcinoma, colorectal carcinoma, and thyroid cancer.

~~14- 10.~~ A method of detecting GPC3 in a tissue sample, comprising contacting the tissue sample with the antibody or antigen binding fragment of any one of claims 1-~~8~~4; and detecting binding of the antibody to the tissue sample, wherein an increase in binding of the antibody to the tissue sample as compared to binding of the antibody to a control sample detects GPC3 in the tissue sample; and/or -

~~15.~~ ~~The method of claim 14,~~ wherein the antibody is directly labeled with a detectable marker.

~~16- 11.~~ The method of claim ~~14-10 or 15,~~ further comprising contacting a second antibody that specifically binds the antibody with the tissue sample, and detecting the binding of the second antibody, wherein an increase in binding of the second antibody to the tissue sample as compared to binding of the second antibody to a control sample detects GPC3 in the tissue sample; and/or -

~~17.~~ ~~The method of any one of claims 14-16,~~ wherein the tissue sample comprises cells of hepatocellular carcinoma (HCC), melanoma, ovarian clear cell carcinoma (OCCC), yolk sac tumor (YST), neuroblastoma, hepatoblastoma, nephroblastoma (Wilms' tumor), squamous cell carcinoma of the lung, adenocarcinoma of the lung, large-cell lung carcinoma, small cell lung cancer, testicular nonseminomatous germ cell tumor, liposarcoma, cervical intraepithelial neoplasia, adenoma of the adrenal gland, schwannoma, embryonal tumor, gastric carcinoma, colorectal carcinoma, thyroid cancer, and/or esophageal cancer.

~~18.~~ 12. A chimeric antigen receptor (CAR), comprising a polypeptide comprising:
(a) an extracellular antigen binding domain comprising the antibody or antigen binding fragment of any one of claims 1-~~84~~;

(b) a transmembrane domain; and

(c) an intracellular signaling domain.

~~19.~~ The CAR of claim 18, wherein the antibody or antigen binding fragment is an scFv.

~~20.~~ 13. The CAR of claim ~~12-18~~ or 19, further comprising a signal peptide located at the N-terminus of the polypeptide; and/or:-

~~21.~~ The CAR of claim ~~20~~, wherein the signal peptide is derived from a molecule selected from the group consisting of CD8 α , GM-CSF receptor α , and IgG1 heavy chain; and/or wherein the antibody or antigen binding fragment is an scFv.

~~22.~~ 14. The CAR of any one of claims ~~18-21~~ 12-13, further comprising a hinge domain located between the C-terminus of the extracellular antigen binding domain and the N-terminus of the transmembrane domain; and/or:-

~~23.~~ The CAR of claim ~~22~~, wherein the hinge domain is derived from CD8 α ; and/or:-

~~24.~~ The CAR of any one of claims ~~18-23~~, wherein the transmembrane domain is derived from a molecule selected from the group consisting of CD8 α , CD4, CD28, CD137, CD80, CD86, CD152 and PD1.

~~25.~~ 15. The CAR of any one of claims ~~18-24~~ 12-14, wherein the intracellular signaling domain comprises a co-stimulatory signaling domain; and/or:-

~~26.~~ The CAR of claim ~~25~~, wherein the co-stimulatory signaling domain is derived from a co-stimulatory molecule selected from the group consisting of CD27, CD28, CD137, OX40, CD30, CD40, CD3, HVEM, ICOS, Myd88, LFA-1, ICOS, CD2, CD7, LIGHT, NKG2C, B7-H3, Ligands of CD83 and a combination thereof.

~~27-~~ 16. The CAR of any one of claims ~~18-26~~ 12-15, wherein the intracellular signaling domain comprises a primary intracellular signaling domain of an immune effector cell; and/or -

~~28.~~ ~~The CAR of claim 27,~~ wherein the primary intracellular signaling domain is derived from CD3 ζ .

~~29-~~ 17. The CAR of any one of claims ~~18-28~~ 12-16, comprising a polypeptide comprising

- (i) the amino acid sequence of SEQ ID NO: 91, or
- (ii) the amino acid sequence of SEQ ID NO: 92, or
- (iii) the amino acid sequence of SEQ ID NO: 93, or
- (iv) the amino acid sequence of SEQ ID NO: 94, or
- (v) the amino acid sequence of SEQ ID NO: 95, or
- (vi) the amino acid sequence of SEQ ID NO: 96, or
- (vii) the amino acid sequence of SEQ ID NO: 97, or
- (viii) the amino acid sequence of SEQ ID NO: 98, or
- (ix) the amino acid sequence of SEQ ID NO: 99, or
- (x) the amino acid sequence of SEQ ID NO: 100, or
- (xi) the amino acid sequence of SEQ ID NO: 107, or
- (xii) the amino acid sequence of SEQ ID NO: 108, or
- (xiii) the amino acid sequence of SEQ ID NO: 109, or
- (xiv) the amino acid sequence of SEQ ID NO: 110, or
- (xv) the amino acid sequence of SEQ ID NO: 111, or
- (xvi) the amino acid sequence of SEQ ID NO: 112, or
- (xvii) the amino acid sequence of SEQ ID NO: 113, or
- (xviii) the amino acid sequence of SEQ ID NO: 114, or
- (xix) the amino acid sequence of SEQ ID NO: 115, or
- (xx) the amino acid sequence of SEQ ID NO: 116, or
- (xxi) the amino acid sequence of SEQ ID NO: 130, or
- (xxii) the amino acid sequence of SEQ ID NO: 131.

~~30-~~ 18. A polypeptide comprising the CAR of any one of claims ~~18-29~~ 12-17, wherein the polypeptide further comprises p40 subunit of IL-12 and/or CCL-19.

~~31.~~ The polypeptide of claim ~~30~~; and/or wherein p40 subunit of IL-12 is human p40 subunit of IL-12 comprising the amino acid sequence of SEQ ID NO: 135, and wherein CCL-19 is human CCL-19 comprising the amino acid sequence of SEQ ID NO: 136.

~~32.~~19. The polypeptide of claim ~~30~~18 or claim ~~31~~, wherein p40 subunit of IL-12 and CCL-19 are linked by a first self-cleaving peptide; and/or -

~~33.~~ The polypeptide of claim ~~32~~, wherein the first self-cleaving peptide is a 2A self-cleaving peptide T2A fragment comprising the amino acid sequence of SEQ ID NO: 139; and/or

~~34.~~ The polypeptide of any one of claims ~~30-33~~, wherein p40 subunit of IL-12 and CCL-19 are present in a domain comprising the amino acid sequence of SEQ ID NO: 134.

~~35.~~20. The polypeptide of claim ~~34~~19, wherein the CAR is linked to the domain by a second self-cleaving peptide; and/or -

~~36.~~ The polypeptide of claim ~~35~~, wherein the second self-cleaving peptide is a 2A self-cleaving peptide P2A fragment comprising the amino acid sequence of SEQ ID NO: 138.

~~37.~~21. The polypeptide of any one of claims ~~30-36~~18-20, comprising the amino acid sequence of SEQ ID NO: 133.

~~38.~~22. A nucleic acid molecule encoding the CAR of any one of claims ~~18-29~~12-17 or the polypeptide of any one of claims ~~30-37~~18-21.

~~39.~~23. A vector comprising the nucleic acid molecule of claim ~~38~~22; and/or -

~~40.~~ The vector of claim ~~39~~, wherein the vector is a viral vector or a non-viral vector.

~~41.~~24. A host cell transformed with the vector of claim ~~39~~ or ~~40~~23; and/or

~~42.~~ The host cell of claim 41, wherein the host cell is an immune effector cell selected from a group consisting of T cell, NK cell, peripheral blood mononuclear cell (PBMC), hematopoietic stem cell, pluripotent stem cell, an embryonic stem cell, and a combination thereof.

~~43.~~ 25. An immune effector cell expressing (i) the CAR of any one of claims ~~18-29~~ 12-17, (ii) exogenously introduced p40, and (iii) exogenously introduced CCL-19.

~~44.~~ 26. A composition comprising a therapeutically effective amount of the host cell of claim ~~41~~ or claim ~~42~~ 24, or the immune effector cell of claim ~~43~~ 25, and a pharmaceutically acceptable carrier.

~~45.~~ 27. Use of the composition of claim 26 in the manufacture of medicament for A method of treating a patient who has cancer that expresses GPC3, wherein comprising administering to the patient the composition of claim 44 is to be administered to the patient, wherein the cancer is optionally selected from the group consisting of hepatocellular carcinoma (HCC), melanoma, ovarian clear cell carcinoma (OCCC), yolk sac tumor (YST), neuroblastoma, hepatoblastoma, nephroblastoma (Wilms' tumor), squamous cell carcinoma of the lung, adenocarcinoma of the lung, large-cell lung carcinoma, small cell lung cancer, testicular nonseminomatous germ cell tumor, liposarcoma, cervical intraepithelial neoplasia, adenoma of the adrenal gland, schwannoma, embryonal tumor, gastric carcinoma, colorectal carcinoma, thyroid cancer, and esophageal cancer.

~~46~~ 28. The ~~method-use~~ of claim ~~45~~ 27, wherein the host cell or the immune effector cell is obtained from the patient; or

~~47.~~ The ~~method of claim 45~~, wherein the host cell or the immune effector cell is obtained from a healthy donor.

~~48.~~ The antibody or antigen binding fragment of any one of claims ~~1-8~~, wherein the GPC3 comprises the amino acid sequence of at least one selected from GenBank Accession numbers: NM_001164617 and NP_001158089, NM_004484 and NP_004475, NM_001164618 and NP_001158090, and NM_001164619 and NP_001158091.

~~49. The CAR of any one of claims 18-29 or the polypeptide of any one of claims 30-37, wherein the GPC3 comprises the amino acid sequence of at least one selected from GenBank Accession numbers: NM_001164617 and NP_001158089, NM_004484 and NP_004475, NM_001164618 and NP_001158090, and NM_001164619 and NP_001158091.~~