WHAT IS CLAIMED IS:

1. A GPC3 CAR comprising an antigen binding domain that selectively binds to the human glypican-3 beta subunit (SEQ ID NO:2) wherein the antigen binding domain is an scFv having at least 90%%, 95%, 99%, or 100% sequence identity to SEQ ID NO:10 or SEQ ID NO:11.

2. The GPC3 CAR of claim 1 wherein the GPC3 CAR comprises a CD3 zeta signaling domain and a costimulatory domain selected from the costimulatory domains of C28 or 4-1BB.

3. The GPC3 CAR of claim 1 wherein the GPC3 CAR has at least 90%, 95%, 99%, or 100% sequence identity to a GPC3 CAR selected from the group consisting of SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, and SEQ ID NO: 40.

4. The GPC3 CAR of claim 1 wherein the GPC3 CAR is selected from the group consisting of SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, and SEQ ID NO: 40.

5. A nucleic acid sequence encoding the GPC3 CAR of any one of claims 1-4.

6. A recombinant vector comprising the nucleic acid sequence of claim 5.

7. The recombinant vector of claim 6 wherein the recombinant vector is a lentiviral vector or a retroviral vector.

8. The recombinant vector of claim 6 or 7 wherein the vector further comprises a nucleic acid sequence encoding an ortho CD122 receptor.

9. The recombinant viral vector of claim 8 wherein the nucleic acid sequence encoding the GPC3 CAR and the and the nucleic acid sequence encoding the ortho CD122 receptor are operably linked to at least one expression control sequence functional in a mammalian T cell.

10. The recombinant viral vector of claim 9 wherein nucleic acid sequence encoding an orthogonal receptor and the nucleic acid sequence encoding the GPC3 CAR the nucleic acid sequence encoding an ortho CD122 receptor are operably linked to single expression control sequence and the wherein the nucleic acid sequences encoding the GPC3 CAR and the ortho CD122 receptor are separated by an IRES or T2A sequence.

11. A recombinantly modified T cell comprising a recombinant viral vector of claim 10.

12. An ortho GPC3 CAR T cell, the cell expressing an ortho CD122 and a GPC3 CAR wherein the ortho CD122 comprises amino acid substitutions at positions 133 and/or 134 numbered in accordance with wild-type hCD122.

13. The ortho GPC3 CAR T cell of claim 12 wherein the GPC3 CAR comprises the amino acid sequence of SEQ ID NO: 37; and (b) the ortho CD122 having the amino acid sequence of SEQ ID NO:4.

14. A method of making an ortho GPC3 CAR T cell, the method comprising the steps of:

a) contacting a sample of peripheral blood mononuclear cells (PBMCs) obtained from a human subject with magnetic beads coated with CD3 and CD28 ligands to provide a population of activated PBMCs;

b) isolating from the activated PBMCs a population of CD8+ and CD4+ T cells;

c) contacting the isolated population of CD8+ and CD4+ T cells with a recombinant lentiviral vector, the lentiviral vector comprising an expression cassette consisting of a nucleic acid sequence encoding from 5' to 3':

- a promoter active in a T cell e.g. the EF1a promoter;
- a nucleic acid sequence encoding a signal peptide
- a nucleic acid sequence encoding a GPC3 CAR;
- a T2A sequence (SEQ ID NO:41)
- a nucleic acid sequence encoding a signal peptide
- a nucleic acid sequence encoding the ortho CD122 of SEQ ID NO:4

such that a fraction of the isolated population CD8+ and CD4+ T cells is transduced with the lentiviral vector; and

d) contacting the population of cells obtained from step (c) with an ortho IL2, the ortho IL2 selected from the group consisting of a human IL2 mutein containing the of amino acid substitutions E15S/H16Q/L19V/D20L/Q22K/M23A; an ortho IL2 of SEQ ID NO 9 (STK-007), or pegylated variant thereof (e.g., STK-009).

15. An ortho GPC3 CAR T cell prepared in accordance with Claim 14.

16. Use of the ortho GPC3 CAR T cell of Claim 15 in the manufacture of a medicament for treating or preventing a neoplastic disease, disorder, or condition in a mammalian subject in need of treatment or prevention, wherein a therapeutically effective amount of the ortho GPC3 CAR T cell of Claim 15 is to be administered to the subject in combination with a therapeutically effective dose of ortho IL.

17. The method of claim 14 wherein the population of cells is enriched for CD8+ or CD4+ T cells prior to contacting the sample with magnetic beads coated with CD3 and CD28 ligands.

18. The method of claim 14 wherein ortho IL2 employed ex vivo in step (a) is different than the orthogonal ligand used in step (b).

19. The method of claim 14 wherein the human subject is to be treated with a lymphodepleting regimen before the PBMCs are obtained.

20. Use of an ortho IL2 in the manufacture of a medicament for treating relapse following ortho GPC3 CAR therapy in a subject, wherein a therapeutically effective amount of an ortho IL2 is to be administered to the subject such that the orthogonal ligand induces the activation and/or proliferation of the ortho GPC3 CAR T cell in the subject.

21. The use of claim 20 wherein the ortho IL2 is STK-009.

22. A method of generating an ortho GPC3 CAR T cell product substantially enriched for a population of ortho GPC3 CAR T cells, the method comprising the steps of:

(a) Contacting a population of cells isolated from a mammalian subject, the population of cells comprising T cells, with a recombinant vector comprising a first nucleic acid sequence encoding a GPC3 CAR and a second nucleic encoding an ortho CD122, the first and second nucleic acid sequences operably linked to an expression control sequence operable in a mammalian T cell, wherein the first and second nucleic acid sequences are separated by an IRES or T2A nucleic acid sequence, such that the cell expresses the GPC3 CAR and the ortho CD122 (ortho GPC3 CAR T cell);

(b) Contacting the isolated population of cells from step (a) ex vivo with a quantity of a ortho IL2 sufficient to induce proliferation of cells transduced by the contacting of step (a),

wherein the contacting with the ortho IL2 is maintained for a period of time period of time such that the fraction of cells expressing the GPC3 CAR and the ortho CD122 comprise at least 10% of the population.

23. The ortho GPC3 CAR T cell of Claim 15 for use in therapy.

24. An ortho IL2 for use in therapy in a subject following ortho GPC3 CAR therapy, wherein the ortho IL2 is STK-009.