We claim:

1. An anti-guanylyl cyclase C (GCC) chimeric antigen receptor (CAR) comprising an extracellular antigen binding domain that binds to guanylyl cyclase C (GCC), a transmembrane domain, and at least one intracellular signaling domain.

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

   a heavy chain variable region (V_H) with complementarity determining region (CDR) sequences of HYYWS (HCDR1) (SEQ ID NO: 8), RIYPSGSTSYNPSLKS (HCDR2) (SEQ ID NO: 11) and DRSTGWSEWNSDL (HCDR3) (SEQ ID NO: 16);

   a heavy chain variable region (V_H) with complementarity determining region (CDR) sequences of RYWMS (HCDR1) (SEQ ID NO: 9), KIRHDGGEKYYVDSVKG (HCDR2) (SEQ ID NO: 12) and DYTRDV (HCDR3) (SEQ ID NO: 17);

   a heavy chain variable region (V_H) with complementarity determining region (CDR) sequences of RYWMT (HCDR1) (SEQ ID NO: 10), KIKYDGSEKYYADSVKG (HCDR2) (SEQ ID NO: 13) and DYNKDY (HCDR3) (SEQ ID NO: 18);

   a heavy chain variable region (V_H) with complementarity determining region (CDR) sequences of RYWMT (HCDR1) (SEQ ID NO: 10), KIRHDGGEKYYPDSVKG (HCDR2) (SEQ ID NO: 14) and DYNKDL (HCDR3) (SEQ ID NO: 19) or

   a heavy chain variable region (V_H) with complementarity determining region (CDR) sequences of RYWMT (HCDR1) (SEQ ID NO: 10), KIRHDGGEKYYADSVKG (HCDR2) (SEQ ID NO: 15) and DYNKDY (HCDR3) (SEQ ID NO: 18).

3. The anti-GCC CAR of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) that is at least 90% identical to SEQ ID NO: 1 or SEQ ID NO: 20.

4. The anti-GCC CAR of claim 1, wherein the antigen binding domain comprises

   an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 21;

   an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 26;

an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 27; or

an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 28.

5. The anti-GCC CAR of any one of claims 1-4, wherein the antigen binding domain comprises an immunoglobulin variable heavy chain only anti-GCC antigen binding domain.

6. The anti-GCC CAR of any one of claims 1-5, wherein the extracellular anti-GCC antigen binding domain is preceded by a leader nucleotide sequence encoding a leader peptide.

7. The anti-GCC CAR of claim 6, wherein the leader peptide comprises SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 42.

8. The anti-GCC CAR of any one of claims 1-7, further comprising a hinge domain.

9. The anti-GCC CAR of claim 8, wherein the hinge domain is comprises a hinge domain of CD28.

10. The anti-GCC CAR of claim 9, wherein the CD28 hinge domain comprises SEQ ID NO: 29

11. The anti-GCC CAR of any one of claims 8-10, wherein the hinge domain is fused to the transmembrane domain.

12. The anti-GCC CAR of any one of claims 1-11, wherein the transmembrane domain comprises a transmembrane domain of a protein selected from the alpha, beta or zeta chain of the T-cell receptor, CD8, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD83, CD86, CD134, CD137, CD154, and TNFRSF19, and any combination thereof.

13. The anti-GCC CAR of claim 12, wherein the transmembrane domain comprises a CD28 transmembrane domain.

14. The anti-GCC CAR of claim 13, wherein the CD28 transmembrane domain comprises SEQ ID NO: 30.

15. The anti-GCC CAR of any one of claims 1-14, wherein the at least one intracellular signaling domain comprises a costimulatory domain and a primary signaling domain.

16. The anti-GCC CAR of claim 15, wherein the costimulatory domain comprises a functional signaling domain of OX40, CD70, CD27, CD28, CD5, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), DAP10, DAP12, and 4-1BB (CD137), or any combination thereof.

17. The anti-GCC CAR of claim 16, wherein the costimulatory domain comprises a functional signaling domain of CD28.

18. The anti-GCC CAR of claim 17, wherein the CD28 costimulatory domain comprises SEQ ID NO: 32.

19. The anti-GCC CAR of claim 15-18, wherein the primary signaling domain comprises a CD3zeta signaling domain.

20. The anti-GCC CAR of claim 19, wherein the CD3 zeta signaling domain comprises SEQ ID NO: 33.

21. An anti-GCC CAR comprising a sequence selected from the group consisting of SEQ ID NO: 47-52.

22. An isolated polynucleotide encoding the anti-GCC CAR of any one of claims 1-21.

23. The isolated polynucleotide of claim 22, further comprising a truncated sequence of epidermal growth factor receptor (tEGFR).

24. The isolated polynucleotide of claim 23, wherein the tEGFR comprises a nucleic acid sequence that encodes an amino acid sequence that is at least 95%, 96%, 97%, 98%, 99% identical to SEQ ID NO: 43.

25. The isolated polynucleotide of claim 24, wherein the tEGFR comprises a nucleic acid sequence that encodes an amino acid sequence that is identical to SEQ ID NO: 43.

26. The isolated polynucleotide of any one of claims 22-25, further comprising a furin recognition site and downstream 2A self-cleaving peptide sequence, designed for simultaneous bicistronic expression of the tag sequence and the CAR sequence.

27. The isolated polynucleotide of claim 26, wherein the 2A self-cleaving peptide is selected from F2A, P2A, E2A and T2A.

28. The isolated polynucleotide of claim 27, wherein the 2A self-cleaving peptide is P2A.

29. A vector comprising the isolated polynucleotide of any one of claims 22-28.

30. The vector of claim 29, wherein the vector is an adenoviral vector, an adenovirus-associated vector, a DNA vector, a lentiviral vector, a plasmid, a retroviral vector, or an RNA vector.

31. A cell comprising the vector of claim 29 or 30.

32. The cell of claim 31, wherein the cell is a T cell, an allogeneic T cell, an autologous T cell, or a tumor-infiltrating lymphocyte (TIL).

33. A population of cells comprising the anti-GCC CAR of any one of claims 1-20 or the nucleic acid of any one of claims 22-32.

34. A kit comprising the population of cells of claim 33.

35. A pharmaceutical composition comprising a population of the cells of claim 31 or 32.

36. The pharmaceutical composition of claim 35, wherein greater than 70%, 80%, 90%, or 95% of the cells in the population express the anti-GCC CAR.

37. Use of a composition comprising the anti-GCC CAR of any one of claims 1-20 in the manufacture of a medicament for the treatment of cancer comprising the administration of a pharmaceutical composition or population of cells to a subject in need of treatment.

38. The use according to claim 37, wherein the cancer is selected from gastrointestinal cancer, colorectal cancer, colorectal adenocarcinoma, colorectal leiomyosarcoma, colorectal lymphoma, colorectal melanoma, a colorectal neuroendocrine tumor, metastatic colon cancer, stomach cancer, gastric adenocarcinoma, gastric lymphoma, gastric sarcoma, esophageal cancer, squamous cell carcinoma, adenocarcinoma of the esophagus, or pancreatic cancer.

39. The use according to claim 38, wherein the cancer is a gastrointestinal cancer.

40. The use according to claim 39, wherein the gastrointestinal cancer is colon cancer, colorectal cancer, stomach cancer, or esophageal cancer.

41. Use of a composition comprising the anti-GCC CAR of any one of claims 1-21 in the manufacture of a medicament for reducing tumor growth or tumor size comprising the administration of a pharmaceutical composition or population of cells to a subject in need of treatment.