

We claim:

1. A guanylyl cyclase C (GCC) binding agent comprising:
 - a heavy chain variable region (V_H) with complementarity determining region (CDR) sequences of HYWWS (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), KIRHDGGGEKYYVDSVKG (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), KIRHDGGGEKYYPDSVKG (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), KIRHDGGGEKYYADSVKG (HCDR2) (SEQ ID NO: 15) and DYNKDY (HCDR3) (SEQ ID NO: 18).
2. The GCC binding agent of claim 1, comprising
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 1 or SEQ ID NO: 20;
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 21;
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 26;
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 27; or
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 28.

3. A guanylyl cyclase C (GCC) binding agent comprising:
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 1 or SEQ ID NO: 20;
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 21;
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 26;
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 27; or
 - an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 28.
4. The GCC binding agent of any one of the preceding claims, wherein the V_H region comprises an amino acid sequence that is at least 95% identical to any one of SEQ ID Nos:1, 20, 21, 26, 27, or 28.
5. The GCC binding agent of any one of the preceding claims, wherein the V_H region comprises an amino acid sequence that is identical to any one of SEQ ID NOs:1, 20, 21, 26, 27, or 28.
6. The GCC binding agent of any one of the preceding claims, wherein the GCC binding agent is selected from the group consisting of an IgA antibody, IgG antibody, IgE antibody, IgM antibody, bi- or multi- specific antibody, Fab fragment, Fab' fragment, F(ab')₂ fragment, Fd' fragment, Fd fragment, isolated CDRs or sets thereof; single-chain variable fragment (scFv), polypeptide-Fc fusion, single domain antibody (sdAb), camelid antibody; masked antibody, Small Modular ImmunoPharmaceuticals ("SMIPsTM"), single chain, Tandem diabody, VHHs, Anticalin, Nanobody, humabody, minibodies, BiTE, ankyrin repeat protein, DARPIN, Avimer, DART, TCR-like antibody, Adnectin, Affilin, Trans-body; Affibody, TrimerX, MicroProtein, Fynomer, Centyrin; and KALBITOR.
7. The GCC binding agent of any one of the preceding claims, wherein the GCC binding agent is a single domain antibody (sdAb).

8. The GCC binding agent of any one of the preceding claims, wherein the GCC binding agent is a heavy chain only antibody.
9. The GCC binding agent of any one of the preceding claims, wherein the binding agent binds GCC with a K_D between about 0.3 nanomolar (nM) and about 10 nM.
10. The GCC binding agent of any one of the preceding claims, wherein the binding agent binds GCC on target cells with an EC_{50} between about 0.5 nM and about 8 nM.
11. ~~Use of a composition A method of treating a cancer comprising administering the GCC binding agent~~ of any one of the preceding claims in the manufacture of a medicament for the treatment of cancer ~~into~~ a subject in need thereof ~~of treatment~~.
12. The use according to ~~method of~~ claim 11, 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.
13. The use according to ~~method of~~ claim 11, wherein the cancer is a gastrointestinal cancer.
14. The use according to ~~method of~~ claim 13, wherein the gastrointestinal cancer is colon cancer, colorectal cancer, stomach cancer, or esophageal cancer.
15. A pharmaceutical composition comprising a GCC binding agent and a pharmaceutically acceptable carrier, wherein the GCC binding agent comprises:
 - a heavy chain variable region (V_H) with complementarity determining region (CDR) sequences of HYWWS (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), KIRHDGGGEKYYVDSVKG (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), KIRHDGGGEKYYPDSVKG (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), KIRHDGGGEKYYADSVKG (HCDR2) (SEQ ID NO: 15) and DYNKDY (HCDR3) (SEQ ID NO: 18).

16. Use of a composition~~A method of treating a cancer~~ comprising ~~administering an~~ GCC binding agent in the manufacture of a medicament for the treatment of cancer into a subject in need thereof of treatment, wherein the GCC binding agent 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), KIRHDGGGEKYYVDSVKG (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), KIRHDGGGEKYYPDSVKG (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), KIRHDGGGEKYYADSVKG (HCDR2) (SEQ ID NO: 15) and DYNKDY (HCDR3) (SEQ ID NO: 18).

17. A nucleic acid encoding a VH amino acid sequence that is identical to any one of SEQ ID Nos: 1, 20, 21, 26, 27, or 28.
18. A vector comprising the isolated nucleic acid sequence of claim 17.
19. An isolated cell comprising the vector of claim 18.
20. An anti-guanylyl cyclase C (GCC) chimeric antigen receptor (CAR), wherein the anti-GCC CAR comprises an anti-GCC binding agent of any one of claims 1-10.
21. Use of an anti-GCC CAR comprising an anti-GCC binding agent of any one of claims 1-10 in the manufacture of a medicament for~~A method of~~ inducing an immune response in a subject, comprising
contacting cells with an anti-guanylyl cyclase C (GCC) chimeric antigen receptor (CAR),~~wherein the anti-GCC CAR comprises an anti-GCC binding agent of any one of claims 1-~~
~~10.~~
22. A method of inducing cytotoxicity comprising
contacting cells with an anti-guanylyl cyclase C (GCC) chimeric antigen receptor (CAR), wherein the anti-GCC CAR comprises an anti-GCC binding agent of any one of claims 1-10.
23. A method of detecting the presence of cancer in a mammal, comprising:
(a) contacting a sample comprising one or more cells from the mammal with the anti-GCC binding agent of any one of claims 1-10, thereby forming a complex, and
(b) detecting the complex, wherein detection of the complex is indicative of the presence of cancer in the mammal.
24. The method of claim 23, wherein the contacting is *in vitro* or *in vivo* with respect to the mammal.

25. The method of claim 24, wherein the contacting is *in vitro*.