

What is claimed is:

1. An isolated antibody or antigen-binding fragment thereof that binds glucocorticoid-induced tumor necrosis factor receptor (GITR), wherein the antibody or antigen-binding fragment exhibits one or more properties selected from the group consisting of:
 - (i) binds monomeric human GITR at 37°C with a K_D of less than about 5.0 nM as measured by surface plasmon resonance;
 - (ii) binds monomeric human GITR at 37 °C with a $t_{1/2}$ of greater than about 12 minutes;
 - (iii) binds dimeric human GITR at 37°C with a K_D of less than about 950 pM as measured by surface plasmon resonance;
 - (iv) binds dimeric human GITR at 37°C with a $t_{1/2}$ of greater than about 7 minutes; and
 - (v) binds human GITR transfected human embryonic kidney 293 (HEK-293) D9 cells with an EC_{50} of less than about 260 pM.
2. The antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment activates human GITR.
3. An isolated antibody or antigen-binding fragment thereof that binds glucocorticoid-induced tumor necrosis factor receptor (GITR), wherein the antibody or antigen-binding fragment activates human GITR in the absence of Fc anchoring.
4. The antibody or antigen-binding fragment of claim 3, wherein the antibody or antigen-binding fragment activates human GITR at an activation percentage greater than about 25% at an EC_{50} of less than about 3 nM as determined by NFkB reporter assay
5. The antibody or antigen-binding fragment of claim 3 or 4, wherein the antibody or antigen-binding fragment activates human GITR with an EC_{50} of less than about 1.0 nM as determined by NFkB reporter assay.
6. An isolated antibody or antigen-binding fragment thereof that binds glucocorticoid-induced tumor necrosis factor receptor (GITR), wherein the antibody or antigen-binding fragment exhibits T-cell proliferative activity in the absence of Fc anchoring as determined in naïve human CD4+ T-cell proliferation assay.
7. The antibody or antigen-binding fragment of claim 6, wherein the antibody or antigen-binding fragment exhibits T-cell proliferative activity in the absence of Fc anchoring

with an EC_{50} of about 8 nM or less as determined in naïve human CD4+ T-cell proliferation assay.

8. The antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment activates human GITR in the presence of Fc anchoring.

9. An isolated antibody or antigen-binding fragment thereof that binds glucocorticoid-induced tumor necrosis factor receptor (GITR), wherein the antibody or antigen-binding fragment exhibits T-cell proliferative activity in the presence of Fc anchoring at least about 2 fold above background as determined in naïve human CD4+ T-cell proliferation assay.

10. The antibody or antigen-binding fragment of claim 9, wherein the antibody or antigen-binding fragment exhibits T-cell proliferative activity in the presence of Fc anchoring with an EC_{50} of less than about 34 nM as determined by naïve human CD4+ T-cell proliferation assay.

11. The antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment blocks hGITR ligand (hGITRL)-mediated receptor stimulation.

12. The antibody or antigen-binding fragment of claim 11, wherein the antibody or antigen-binding fragment blocks hGITRL-mediated receptor stimulation in the absence of Fc anchoring.

13. An isolated antibody or antigen-binding fragment thereof that binds glucocorticoid-induced tumor necrosis factor receptor (GITR), wherein the antibody or antigen-binding fragment blocks hGITRL-mediated receptor stimulation in the absence of Fc anchoring at a blocking percentage greater than about 54% at an IC_{50} of less than about 4.0 nM as determined by NF κ B reporter assay.

14. An isolated antibody or antigen-binding fragment thereof that binds glucocorticoid-induced tumor necrosis factor receptor (GITR), wherein the antibody or antigen-binding fragment comprises: (a) the complementarity determining regions (CDRs) of a heavy chain variable region (HCVR) having an amino acid sequence as set forth in Table 1; and (b) the CDRs of a light chain variable region (LCVR) having an amino acid sequence as set forth in Table 1.

15. The isolated antibody or antigen-binding fragment of claim 14, wherein the antibody or antigen-binding fragment comprises an HCVR having an amino acid sequence as set forth in Table 1 and a LCVR having an amino acid sequence as set forth in Table 1.

16. The isolated antibody or antigen-binding fragment of claim 14, wherein the antibody or antigen-binding fragment comprises:

- (i) a HCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 100, 164, 196, 244, 292, 340, and 348;
- (ii) a HCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 102, 166, 198, 246, 294, 342, and 350;
- (iii) a HCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 104, 168, 200, 248, 296, 344, 352;
- (iv) a LCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 108, 172, 204, 252, 300, and 404
- (v) a LCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 110, 174, 206, 254, 302, and 406, and
- (vi) a LCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 112, 176, 208, 256, 304, and 408.

17. The isolated antibody or antigen-binding fragment of claim 14, wherein the antibody or antigen-binding fragment comprises:

- (i) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 100; an HCDR2 comprising SEQ ID NO: 102; an HCDR3 comprising SEQ ID NO: 104; a light chain complementarity determining region (LCDR)-1 comprising SEQ ID NO: 108; an LCDR2 comprising SEQ ID NO: 110; and an LCDR3 comprising SEQ ID NO: 112;
- (ii) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 164; an HCDR2 comprising SEQ ID NO: 166; an HCDR3 comprising SEQ ID NO: 168; a light chain complementarity determining region (LCDR)-1 comprising SEQ ID NO: 172; an LCDR2 comprising SEQ ID NO: 174; and an LCDR3 comprising SEQ ID NO: 176;
- (iii) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 196; an HCDR2 comprising SEQ ID NO: 198; an HCDR3 comprising SEQ ID NO: 200; a light chain complementarity determining region (LCDR)-1 comprising

SEQ ID NO: 204; an LCDR2 comprising SEQ ID NO: 206; and an LCDR3 comprising SEQ ID NO: 208;

(iv) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 244; an HCDR2 comprising SEQ ID NO: 246; an HCDR3 comprising SEQ ID NO: 248; a light chain complementarity determining region (LCDR)-1 comprising SEQ ID NO: 252; an LCDR2 comprising SEQ ID NO: 254; and an LCDR3 comprising SEQ ID NO: 256;

(v) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 292; an HCDR2 comprising SEQ ID NO: 294; an HCDR3 comprising SEQ ID NO: 296; a light chain complementarity determining region (LCDR)-1 comprising SEQ ID NO: 300; an LCDR2 comprising SEQ ID NO: 302; and an LCDR3 comprising SEQ ID NO: 304;

(vi) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 340; an HCDR2 comprising SEQ ID NO: 342; an HCDR3 comprising SEQ ID NO: 344; a light chain complementarity determining region (LCDR)-1 comprising SEQ ID NO: 404; an LCDR2 comprising SEQ ID NO: 406; and an LCDR3 comprising SEQ ID NO: 408; or

(vii) a heavy chain complementarity determining region (HCDR)-1 comprising SEQ ID NO: 348; an HCDR2 comprising SEQ ID NO: 350; an HCDR3 comprising SEQ ID NO: 352; a light chain complementarity determining region (LCDR)-1 comprising SEQ ID NO: 404; an LCDR2 comprising SEQ ID NO: 406; and an LCDR3 comprising SEQ ID NO: 408.

18. An isolated antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof competes for binding to GITR with a reference antibody comprising an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOS: 98/106; 162/170; 194/202; 242/250; 290/298; 338/402; and 346/102.

19. An isolated antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof binds to the same epitope on GITR as a reference antibody comprising an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOS: 98/106; 162/170; 194/202; 242/250; 290/298; 338/402; and 346/102.

20. A pharmaceutical composition comprising the antibody or antigen-binding fragment of any of claims 1-19 and a pharmaceutically acceptable carrier or diluent.

21. A method for treating cancer in a subject comprising administering the composition of claim 20.

22. A method of modulating anti-tumor immune response in a subject comprising administering to the subject the antibody that binds GITR of any of claims 1-19 or antigen-binding fragment thereof.

23. The method of claim 20, further comprising administering an antibody or antigen-binding fragment thereof that binds to a second T-cell activating receptor.

24. The method of claim 21, wherein the T-cell activating receptor is CD28, OX40, CD137, CD27, or HVEM.

25. The method of any of claims 19-24, further comprising administering an antibody or antigen-binding fragment thereof that binds to a T-cell inhibitory receptor.

26. The method of claim 25, wherein the T-cell inhibitory receptor is CTLA-4, PD-1, TIM-3, BTLA, VISTA, or LAG-3.

27. The method of any of claims 20-26, further comprising administering radiation therapy to said subject.

28. The method of any of claims 20-27, further comprising administering one or more chemotherapeutic agent.

29. The method of claim 26, wherein the T-cell inhibitory receptor is PD1.

30. The method of claim 29, wherein the antibody that binds to a T-cell receptor is REGN 2810.

31. The method of any of claims 22-30, wherein the antibody that binds GITR is an antibody of claim 17.