

Claims:

- 1) Use of an antibody that specifically binds CD38 in the manufacture of a medicament for the treatment of a subject having a solid tumor.
- 2) The use of claim 1, wherein the antibody that specifically binds CD38 elicits an immune response in the patient.
- 3) The use of claim 2, wherein the immune response is an effector T cell (Teff) response.
- 4) The use of claim 3, wherein the Teff response is mediated by CD4⁺ T cells or CD8⁺ T cells.
- 5) The use of claim 4, wherein the Teff response is mediated by the CD8⁺ T cells.
- 6) The use of claim 3, wherein the Teff response is an increase in the number of the CD8⁺ T cells, increased CD8⁺ T cell proliferation, increased T cell clonal expansion, increased CD8⁺ memory cell formation, increased antigen-dependent antibody production, increased cytokine production, increased chemokine production or increased interleukin production.
- 7) The use of claim 1, wherein the antibody that specifically binds CD38 inhibits function of an immune suppressor cell.
- 8) The use of claim 7, wherein the immune suppressor cell is a regulatory T cell (Treg).
- 9) The use of claim 8, wherein the Treg is a CD3⁺CD4⁺CD25⁺CD127^{dim} T cell.
- 10) The use of claim 9, wherein the Treg expresses CD38.
- 11) The use of claim 10, wherein the Treg function is inhibited by killing the Treg.
- 12) The use of claim 11, wherein killing the Treg is mediated by antibody-dependent cell cytotoxicity (ADCC).
- 13) The use of claim 7, wherein the immune suppressor cell is a myeloid-derived suppressor cell (MDSC).
- 14) The use of claim 13, wherein the MDSC is a CD11b⁺HLADR⁻CD14⁻CD33⁺CD15⁺ cell.
- 15) The use of claim 14, wherein the CD11b⁺HLADR⁻CD14⁻CD33⁺CD15⁺ cell expresses CD38.
- 16) The use of claim 15, wherein the MDSC function is inhibited by killing the MDSC.
- 17) The use of claim 16, wherein killing of MDSC is mediated by ADCC.
- 18) The use of claim 7, wherein the immune suppressor cell is a regulatory B cell (Breg).
- 19) The use of claim 18, wherein the Breg is a CD19⁺CD24⁺CD38⁺ cell.
- 20) The use of claim 19, wherein the Breg function is inhibited by killing the Breg.
- 21) The use of claim 20, wherein killing the Breg is mediated by ADCC.

- 22) The use of claim 7, wherein the immune suppressor cell resides in bone marrow or in peripheral blood.
- 23) The use of any of the claims 1-22, wherein the solid tumor is a melanoma, a lung cancer, a squamous non-small cell lung cancer (NSCLC), a non-squamous NSCLC, a colorectal cancer, a prostate cancer, a castration-resistant prostate cancer, a stomach cancer, an ovarian cancer, a gastric cancer, a liver cancer, a pancreatic cancer, a thyroid cancer, a squamous cell carcinoma of the head and neck, a carcinoma of the esophagus or gastrointestinal tract, a breast cancer, a fallopian tube cancer, a brain cancer, an urethral cancer, a genitourinary cancer, an endometriosis, a cervical cancer or a metastatic lesion of the cancer.
- 24) The use of any of the claims 1-23, wherein the solid tumor lacks detectable CD38 expression.
- 25) The use of any of the claims 1-24, wherein the antibody that specifically binds CD38 is a non-agonistic antibody.
- 26) The use of claim 25, wherein the non-agonistic antibody induces proliferation of a sample of peripheral blood mononuclear cells *in vitro* in a statistically insignificant manner.
- 27) The use of any of the claims 1-26, wherein the antibody that specifically binds CD38 competes for binding to CD38 with an antibody comprising a heavy chain variable region (VH) of SEQ ID NO: 4 and a light chain variable region (VL) of SEQ ID NO: 5.
- 28) The use of claim 27, wherein the antibody that specifically binds CD38 binds at least to the region SKRNIQFSCCKNIYR (SEQ ID NO: 2) and the region EKVQTLEAWVIHGG (SEQ ID NO: 3) of human CD38 (SEQ ID NO: 1).
- 29) The use of any of the claims 1-28, wherein the antibody that specifically binds CD38 comprises a heavy chain complementarity determining region (HCDR) 1, a HCDR2, a HCDR3, a light chain complementarity determining region (LCDR) 1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NOs: 6, 7, 8, 9, 10 and 11, respectively.
- 30) The use of any of the claims 1-29, wherein the antibody that specifically binds CD38 comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
- 31) The use of any of the claims 1-26, wherein the antibody that specifically binds CD38 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:
- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;

- c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
- 32) The use of claim 31, wherein the antibody that specifically binds CD38 comprises:
- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
- 33) The use of any of the claims 1-32, wherein the antibody that specifically binds CD38 is to be administered in combination with a second therapeutic agent.
- 34) The use of claim 33, wherein the second therapeutic agent is a chemotherapeutic agent, a targeted anti-cancer therapy, a standard of care drug for treatment of solid tumor, or an immune checkpoint inhibitor.
- 35) The use of claim 34, wherein the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-PD-L2 antibody, an anti-LAG3 antibody, an anti-TIM3 antibody, or an anti-CTLA-4 antibody.
- 36) The use of claim 35, wherein the immune checkpoint inhibitor is an anti-PD-1 antibody.
- 37) The use of claim 36, wherein the anti-PD-1 antibody comprises
- a) the VH of SEQ ID NO: 22 and the VL of SEQ ID NO: 23;
 - b) the VH of SEQ ID NO: 24 and the VL of SEQ ID NO: 25;
 - c) the VH of SEQ ID NO: 32 and the VL of SEQ ID NO: 33; or
 - d) the VH of SEQ ID NO: 34 and the VL of SEQ ID NO: 35.
- 38) The use of claim 35, wherein the immune checkpoint inhibitor is an anti-PD-L1 antibody.
- 39) The use of claim 38, wherein the anti-PD-L1 antibody comprises
- a) the VH of SEQ ID NO: 26 and the VL of SEQ ID NO: 27;
 - b) the VH of SEQ ID NO: 28 and the VL of SEQ ID NO: 29; or
 - c) the VH of SEQ ID NO: 30 and the VL of SEQ ID NO: 31.
- 40) The use of claim 35, wherein the immune checkpoint inhibitor is an anti-PD-L2 antibody.
- 41) The use of claim 35, wherein the immune checkpoint inhibitor is an anti-LAG3 antibody.
- 42) The use of claim 35, wherein the immune checkpoint inhibitor is an anti-TIM-3 antibody.
- 43) The use of claim 42, wherein the anti-TIM-3 antibody comprises

- a) the VH of SEQ ID NO: 36 and the VL of SEQ ID NO: 37; or
 - b) the VH of SEQ ID NO: 38 and the VL of SEQ ID NO: 39.
- 44) The use of any of the claims 33-43, wherein the second therapeutic agent is to be administered simultaneously, sequentially or separately.
 - 45) The use of any of the claims 1-44, wherein the antibody that specifically binds CD38 is to be administered intravenously.
 - 46) The use of any of the claims 1-44, wherein the antibody that specifically binds CD38 is to be administered subcutaneously in a pharmaceutical composition comprising the antibody that specifically binds CD38 and a hyaluronidase.
 - 47) The use of claim 46, wherein the hyaluronidase is rHuPH20 of SEQ ID NO: 40.
 - 48) The use of any of the claims 1-47, wherein the patient is to be treated or has been treated with radiation therapy.
 - 49) The use of any of the claims 1-47, wherein the patient has had or will undergo surgery.
 - 50) A method of suppressing activity of an immune suppressor cell, comprising contacting the immune suppressing cell with an antibody that specifically binds CD38.
 - 51) The method of claim 50, wherein the immune suppressor cell is a Treg.
 - 52) The method of claim 51, wherein the Treg is a CD3⁺CD4⁺CD25⁺CD127^{dim} T cell.
 - 53) The method of claim 50, wherein the immune suppressor cell is a MDSC.
 - 54) The method of claim 53, wherein the MDSC is a CD11b⁺HLADR⁻CD14⁻CD33⁺CD15⁺ cell.
 - 55) The method of claim 50, wherein the immune suppressor cell is a Breg.
 - 56) The method of claim 55, wherein the Breg is a CD19⁺CD24⁺CD38⁺ cell.
 - 57) The method of any of the claims 50-56, wherein the antibody that specifically binds CD38 is a non-agonistic antibody.
 - 58) The method of claim 57, wherein the non-agonistic antibody induces proliferation of a sample of peripheral blood mononuclear cells *in vitro* in a statistically insignificant manner.
 - 59) The method of any of the claims 50-58, wherein the antibody that specifically binds CD38 competes for binding to CD38 with an antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
 - 60) The method of claim 59, wherein the antibody that specifically binds CD38 binds at least to the region SKRNIQFSCCKNIYR (SEQ ID NO: 2) and the region EKVQTLEAWVIHGG (SEQ ID NO: 3) of human CD38 (SEQ ID NO: 1).

- 61) The method of any of the claims 50-60, wherein the antibody that specifically binds CD38 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 6, 7, 8, 9, 10 and 11, respectively.
- 62) The method of claim 61, wherein the antibody that specifically binds CD38 comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
- 63) The method of any of the claims 50-58, wherein the antibody that specifically binds CD38 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:
- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
- 64) The method of claim 63, wherein the antibody that specifically binds CD38 comprises:
- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
- 65) Use of an antibody that specifically binds CD38 in the manufacture of a medicament for enhancing an immune response in patient.
- 66) The use of claim 65, wherein the patient has a cancer or a viral infection.
- 67) The use of claim 65 or 66, wherein the antibody that specifically binds CD38 is a non-agonistic antibody.
- 68) The use of claim 67, wherein the non-agonistic antibody induces proliferation of a sample of peripheral blood mononuclear cells *in vitro* in a statistically insignificant manner.
- 69) The use of any of the claims 65-68, wherein the antibody that specifically binds CD38 competes for binding to CD38 with an antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
- 70) The use of any of the claims 65- 69, wherein the antibody that specifically binds CD38 binds at least to the region SKRNIQFSCIYR (SEQ ID NO: 2) and the region EKVQTLEAWVIHGG (SEQ ID NO: 3) of human CD38 (SEQ ID NO: 1).
- 71) The use of any of the claims 65-70, wherein the antibody that specifically binds CD38 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 6, 7, 8, 9, 10 and 11, respectively.

- 72) The use of any of the claims 65-70, wherein the antibody that specifically binds CD38 comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
- 73) The use of any of the claims 65-68, wherein the antibody that specifically binds CD38 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:
- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
- 74) The use of claim 73, wherein the antibody that specifically binds CD38 comprises:
- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
- 75) Use of an antibody that specifically binds CD38 in the manufacture of a medicament for the treatment of a viral infection.
- 76) The use of claim 75, wherein the antibody that specifically binds CD38 is a non-agonistic antibody.
- 77) The use of claim 75 or 76, wherein the non-agonistic antibody induces proliferation of a sample of peripheral blood mononuclear cells *in vitro* in a statistically insignificant manner.
- 78) The use of any of the claims 75-77, wherein the antibody that specifically binds CD38 competes for binding to CD38 with an antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
- 79) The use of any of the claims 75-78, wherein the antibody that specifically binds CD38 binds at least to the region SKRNIQFSCIYR (SEQ ID NO: 2) and the region EKVQTLEAWVIHGG (SEQ ID NO: 3) of human CD38 (SEQ ID NO: 1).
- 80) The use of any of the claims 75-79, wherein the antibody that specifically binds CD38 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 6, 7, 8, 9, 10 and 11, respectively.
- 81) The use of any of the claims 75-80, wherein the antibody that specifically binds CD38 comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
- 82) The use of any of the claims 75-77, wherein the antibody that specifically binds CD38 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:

- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.
- 83) The use of claim 82, wherein the antibody that specifically binds CD38 comprises:
- a) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - b) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - c) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - d) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21.