

What is claimed:

- 1) ~~Use of an anti-CD38 antibody for the manufacture of a medicament for treating a cancer in a subject, wherein the medicament is to be administered in combination with a T cell redirecting therapeutic.~~
- 1) ~~Use of a T cell redirecting therapeutic for the manufacture of a medicament for treating a cancer in a subject, wherein the medicament is to be administered in combination with an anti-CD38 antibody.~~
- 1) ~~Use of an anti-CD38 antibody for the manufacture of a medicament for enhancing efficacy of a T cell redirecting therapeutic in a subject having a cancer.~~
- 1) ~~The use of any one of claims 1-3, wherein the anti-CD38 antibody is administered prior to administering the T cell redirecting therapeutic;~~
 - a) ~~the T cell redirecting therapeutic binds BCMA, GPRC5D, CD33, CD123, CD19, PSMA, TMEFF2 or CD20; and/or~~
 - a) ~~the T cell redirecting therapeutic binds CD3, CD3-epsilon (CD3ε), CD8, KIL4, NKG2E, NKG2D, NKG2F, BTNL3, CD186, BTNL8, PD-1, CD195, or NKG2C.~~
- 1) ~~The use of claim 4b), wherein:~~
 - a) ~~the T cell redirecting therapeutic comprises a CD3 binding domain comprising~~
 - i) ~~a heavy chain complementarity determining region 1 (HCDR1) of SEQ ID NO: 33, a HCDR2 of SEQ ID NO: 34, a HCDR3 of SEQ ID NO: 35, a light chain complementarity determining region 1 (LCDR1) of SEQ ID NO: 36, a LCDR2 of SEQ ID NO: 37 and a LCDR3 of SEQ ID NO: 38;~~
 - i) ~~a heavy chain variable region (VH) of SEQ ID NO: 39 and a light chain variable region (VL) of SEQ ID NO: 40;~~
 - i) ~~the HCDR1 of SEQ ID NO: 74, the HCDR2 of SEQ ID NO: 75, the HCDR3 of SEQ ID NO: 76, the LCDR1 of SEQ ID NO: 77, the LCDR2 of SEQ ID NO: 78 and the LCDR3 of SEQ ID NO: 79;~~
 - i) ~~the VH of SEQ ID NO: 80 and the VL of SEQ ID NO: 81;~~
 - i) ~~the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of a CD3 binding domain of SEQ ID NO: 53; or~~
 - i) ~~the VH and the VL of the CD3 binding domain of SEQ ID NO: 53;~~
 - a) ~~the T cell redirecting therapeutic comprises~~
 - i) ~~a BCMA binding domain comprising the HCDR1 of SEQ ID NO: 23, the HCDR2 of SEQ ID NO: 24, the HCDR3 of SEQ ID NO: 25, the LCDR1 of SEQ ID NO: 26, the LCDR2 of SEQ ID NO: 27 and the LCDR3 of SEQ ID NO: 28, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 33, the HCDR2 of SEQ ID NO: 34, the~~

- HCDR3 of SEQ ID NO: 35, the LCDR1 of SEQ ID NO: 36, the LCDR2 of SEQ ID NO: 37 and the LCDR3 of SEQ ID NO: 38; and/or
- i) ~~the BCMA binding domain comprising the VH of SEQ ID NO: 29 and the VL of SEQ ID NO: 30, and the CD3 binding domain comprising the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40,~~
- optionally wherein the T cell redirecting therapeutic comprises a first heavy chain (HC1) of SEQ ID NO: 31, a first light chain (LC1) of SEQ ID NO: 32, a second heavy chain (HC2) of SEQ ID NO: 41, and a second light chain (LC2) of SEQ ID NO: 42;
- a) ~~the T cell redirecting therapeutic comprises~~
- i) ~~a GPRC5D binding domain comprising the HCDR1 of SEQ ID NO: 43, the HCDR2 of SEQ ID NO: 44, the HCDR3 of SEQ ID NO: 45, the LCDR1 of SEQ ID NO: 46, the LCDR2 of SEQ ID NO: 47 and the LCDR3 of SEQ ID NO: 48, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 33, the HCDR2 of SEQ ID NO: 34, the HCDR3 of SEQ ID NO: 35, the LCDR1 of SEQ ID NO: 36, the LCDR2 of SEQ ID NO: 37 and the LCDR3 of SEQ ID NO: 38; and/or~~
- i) ~~the GPRC5D binding domain comprising the VH of SEQ ID NO: 49 and the VL of SEQ ID NO: 50, and the CD3 binding domain comprising the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40,~~
- optionally wherein the T cell redirecting therapeutic comprises the HC1 of SEQ ID NO: 51, the LC1 of SEQ ID NO: 52, the HC2 of SEQ ID NO: 41, and the LC2 of SEQ ID NO: 42;
- a) ~~the T cell redirecting therapeutic comprises~~
- i) ~~a CD33 binding domain comprising the HCDR1 of SEQ ID NO: 84, the HCDR2 of SEQ ID NO: 85, the HCDR3 of SEQ ID NO: 86, the LCDR1 of SEQ ID NO: 87, the LCDR2 of SEQ ID NO: 88 and the LCDR3 of SEQ ID NO: 89, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 74, the HCDR2 of SEQ ID NO: 75, the HCDR3 of SEQ ID NO: 76, the LCDR1 of SEQ ID NO: 77, the LCDR2 of SEQ ID NO: 78 and the LCDR3 of SEQ ID NO: 79; and/or~~
- i) ~~the CD33 binding domain comprising the VH of SEQ ID NO: 90 and the VL of SEQ ID NO: 91, and the CD3 binding domain comprising the VH of SEQ ID NO: 80 and the VL of SEQ ID NO: 81,~~
- optionally wherein the T cell redirecting therapeutic comprises the HC1 of SEQ ID NO: 92, the LC1 of SEQ ID NO: 93, the HC2 of SEQ ID NO: 82 and the LC2 of SEQ ID NO: 83;
- a) ~~the T cell redirecting therapeutic comprises~~
- i) ~~a CD123 binding domain comprising the HCDR1 of SEQ ID NO: 94, the HCDR2 of SEQ ID NO: 95, the HCDR3 of SEQ ID NO: 96, the LCDR1 of SEQ ID NO: 9, the LCDR2 of SEQ ID NO: 10, and the LCDR3 of SEQ ID NO: 59, and a CD3 binding domain~~

- comprising the HCDR1 of SEQ ID NO: 33, the HCDR2 of SEQ ID NO: 34, the HCDR3 of SEQ ID NO: 35, the LCDR1 of SEQ ID NO: 36, the LCDR2 of SEQ ID NO: 37 and the LCDR3 of SEQ ID NO: 38; and/or
- i) the CD123 binding domain comprising the VH of SEQ ID NO: 100 and the VL of SEQ ID NO: 61, and the CD3 binding domain comprising the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40,
- optionally wherein the T cell redirecting therapeutic comprises the HC1 of SEQ ID NO: 102, the LC1 of SEQ ID NO: 63, the HC2 of SEQ ID NO: 41 and the LC2 of SEQ ID NO: 42;
- a) the T cell redirecting therapeutic comprises
- i) a CD19 binding domain comprising the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of the CD19 binding domain of SEQ ID NO: 53 and a CD3 binding domain comprising the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of the CD3 binding domain of SEQ ID NO 53; and/or
- i) the amino acid sequence of SEQ ID NO: 53;
- a) the T cell redirecting therapeutic comprises
- i) a PSMA binding domain comprising the HCDR1 of SEQ ID NO: 54, the HCDR2 or SEQ ID NO: 55, the HCDR3 or SEQ ID NO: 56, the LCDR1 or SEQ ID NO: 9, the LCDR2 or SEQ ID NO: 10 and the LCDR3 of SEQ ID NO: 59, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 33, the HCDR2 of SEQ ID NO: 34, the HCDR3 of SEQ ID NO: 35, the LCDR1 of SEQ ID NO: 36, the LCDR2 of SEQ ID NO: 37 and the LCDR3 of SEQ ID NO: 38; and/or
- i) the PSMA binding domain comprising the VH of SEQ ID NO: 60 and the VL of SEQ ID NO: 61, and the CD3 binding domain comprising the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40,
- optionally wherein the T cell redirecting therapeutic comprises the HC1 of SEQ ID NO: 62, the LC1 of SEQ ID NO: 63, the HC2 of SEQ ID NO: 41 and the LC2 of SEQ ID NO: 42; or
- a) the T cell redirecting therapeutic comprises
- i) a TMEFF2 binding domain comprising the HCDR1 of SEQ ID NO: 64, the HCDR2 of SEQ ID NO: 65, the HCDR3 of SEQ ID NO: 66, the LCDR1 of SEQ ID NO: 67, the LCDR2 of SEQ ID NO: 68 and the LCDR3 of SEQ ID NO: 69, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 74, the HCDR2 of SEQ ID NO: 75, the HCDR3 or SEQ ID NO: 76, the LCDR1 or SEQ ID NO: 77, the LCDR2 or SEQ ID NO: 78 and the LCDR3 of SEQ ID NO: 79; and/or
- i) the TMEFF2 binding domain comprising the VH of SEQ ID NO: 70 and the VL of SEQ ID NO: 71, and the CD3 binding domain comprising the VH of SEQ ID NO: 80 and the VL of SEQ ID NO: 81,

optionally wherein the T cell redirecting therapeutic comprises the HC1 of SEQ ID NO: 72, the LC1 of SEQ ID NO: 73, the HC2 of SEQ ID NO: 82 and the LC2 of SEQ ID NO: 83.

1) ~~The use of any one of claims 1-5, wherein the T cell redirecting therapeutic is a multispecific antibody, a chimeric antigen receptor (CAR), or a T cell comprising the CAR, optionally wherein the multispecific antibody:~~

- a) ~~is an IgG1, an IgG2, an IgG3 or an IgG4 isotype, for example wherein the multispecific antibody comprises one or more Fc substitutions that reduces binding of the multispecific antibody to a Fcγ receptor (FcγR), optionally wherein the one or more Fc substitutions is selected from the group consisting of F234A/L235A on IgG4, L234A/L235A on IgG1, V234A/G237A/ P238S/H268A/V309L/A330S/P331S on IgG2, F234A/L235A on IgG4, S228P/F234A/ L235A on IgG4, N297A on all Ig isotypes, V234A/G237A on IgG2, K214T/E233P/ L234V/L235A/G236-deleted/A327G/P331A/D365E/L358M on IgG1, H268Q/V309L/A330S/P331S on IgG2, S267E/L328F on IgG1, L234F/L235E/D265A on IgG1, L234A/L235A/G237A/P238S/H268A/A330S/P331S on IgG1, S228P/F234A/L235A/G237A/P238S on IgG4 and S228P/F234A/L235A/G236-deleted/G237A/P238S on IgG4, wherein residue numbering is according to the EU index, for example wherein the multispecific antibody further comprises a S228P substitution; and/or~~
- a) ~~comprises one or more asymmetric substitutions in a first CH3 domain or in a second CH3 domain, or in both the first CH3 domain and the second CH3 domain, optionally wherein the one or more asymmetric substitutions is selected from the group consisting of F450L/K409R, wild type/F409L_R409K, T366Y/F405A, T366W/F405W, F405W/Y407A, T394W/Y407T, T394S/Y407A, T366W/T394S, F405W/T394S and T366W/T366S_L368A_Y407V, L351Y_F405A_Y407V/T394W, T366I_K392M_T394W/F405A_Y407V, T366L_K392M_T394W/F405A_Y407V, L351Y_Y407A/T366A_K409F, L351Y_Y407A/T366V_K409F, Y407A/T366A_K409F and T350V_L351Y_F405A_Y407V/T350V_T366L_K392L_T394W.~~

1) ~~The use of any one of claims 1-6, wherein:~~

- a) ~~the subject has a newly diagnosed cancer;~~
- a) ~~the subject is relapsed or refractory to a prior anti-cancer therapy; and/or~~
- a) ~~the cancer is a hematological malignancy or a solid tumor, optionally wherein:~~
 - i) ~~the hematological malignancy is a multiple myeloma, a smoldering multiple myeloma, a monoclonal gammopathy of undetermined significance (MGUS), an acute lymphoblastic leukemia (ALL), a diffuse large B-cell lymphoma (DLBCL), a Burkitt's lymphoma (BL), a follicular lymphoma (FL), a mantle-cell lymphoma (MCL), Waldenstrom's macroglobulinemia, a plasma cell leukemia, a light chain amyloidosis (AL), a precursor B-cell lymphoblastic leukemia, a precursor B-cell lymphoblastic leukemia, an acute~~

myeloid leukemia (AML), a myelodysplastic syndrome (MDS), a chronic lymphocytic leukemia (CLL), a B-cell malignancy, a chronic myeloid leukemia (CML), a hairy cell leukemia (HCL), a blastic plasmacytoid dendritic cell neoplasm, Hodgkin's lymphoma, non-Hodgkin's lymphoma, a marginal zone B-cell lymphoma (MZL) or a mucosa-associated lymphatic tissue lymphoma (MALT), plasma cell leukemia, anaplastic large-cell lymphoma (ALCL), leukemia or lymphoma, for example wherein:

I. the multiple myeloma is a newly diagnosed multiple myeloma, optionally wherein the multiple myeloma is a high-risk multiple myeloma, for example wherein the subject having the high-risk multiple myeloma has one or more chromosomal abnormalities comprising:

A. ~~t(4;14)(p16;q32);~~

A. ~~t(14;16)(q32;q23);~~

A. ~~del17p;~~

A. ~~1qAmp;~~

A. ~~t(4;14)(p16;q32) and t(14;16)(q32;q23);~~

A. ~~t(4;14)(p16;q32) and del17p;~~

A. ~~t(14;16)(q32;q23) and del17p; or~~

A. ~~t(4;14)(p16;q32), t(14;16)(q32;q23) and del17p, or any combination thereof; or~~

I. the multiple myeloma is a relapsed or a refractory multiple myeloma optionally wherein:

A. the multiple myeloma is a high-risk multiple myeloma, for example wherein the subject having the high-risk multiple myeloma has one or more chromosomal abnormalities comprising:

a. ~~t(4;14)(p16;q32);~~

a. ~~t(14;16)(q32;q23);~~

a. ~~del17p;~~

a. ~~1qAmp;~~

a. ~~t(4;14)(p16;q32) and t(14;16)(q32;q23);~~

a. ~~t(4;14)(p16;q32) and del17p;~~

a. ~~t(14;16)(q32;q23) and del17p; or~~

a. ~~t(4;14)(p16;q32), t(14;16)(q32;q23) and del17p, or any combination thereof; or~~

A. the multiple myeloma is relapsed or refractory to treatment with the anti-CD38 antibody, lenalidomide, bortezomib, pomalidomide, carfilzomib, elotuzumab, ixazomib, melphalan or thalidomide, or any combination thereof;

- I. ~~the AML is AML with at least one genetic abnormality, AML with multilineage dysplasia, therapy-related AML, undifferentiated AML, AML with minimal maturation, AML with maturation, acute myelomonocytic leukemia, acute monocytic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia, acute basophilic leukemia, acute panmyelosis with fibrosis or myeloid sarcoma, optionally wherein the at least one genetic abnormality is a translocation between chromosomes 8 and 21, a translocation or an inversion in chromosome 16, a translocation between chromosomes 15 and 17, changes in chromosome 11, or mutation in fms-related tyrosine kinase 3 (FLT3), nucleophosmin (NPM1), isocitrate dehydrogenase 1 (IDH1), isocitrate dehydrogenase 2 (IDH2), DNA (cytosine 5) methyltransferase 3 (DNMT3A), CCAAT/enhancer binding protein alpha (CEBPA), U2 small nuclear RNA auxiliary factor 1 (U2AF1), enhancer of zeste 2 polycomb repressive complex 2 subunit (EZH2), structural maintenance of chromosomes 1A (SMC1A) or structural maintenance of chromosomes 3 (SMC3), for example wherein the at least one genetic abnormality is a translocation t(8; 21)(q22; q22), an inversion inv(16)(p13; q22), a translocation t(16; 16)(p13; q22), a translocation t(15; 17)(q22; q12), a mutation FLT3-ITD, mutations R132H or R100Q/R104V/F108L/R119Q/I130V in IDH1 or mutations R140Q or R172 in IDH2; or~~
- I. ~~the ALL is B-cell lineage ALL, T-cell lineage ALL, adult ALL or pediatric ALL, optionally wherein the subject with ALL has a Philadelphia chromosome or is resistant or has acquired resistance to treatment with a BCR-ABL kinase inhibitor; or~~
- i) ~~the solid tumor is a prostate cancer, a lung cancer, a liver cancer, cervical cancer, a colon cancer, a breast cancer, an ovarian cancer, an endometrial cancer, a pancreatic cancer, a melanoma, a glioblastoma, an esophageal cancer, a gastric cancer, a stomach cancer, a renal carcinoma, a colon cancer, a bladder cancer, a cervical carcinoma, a melanoma, a hepatocellular carcinoma, a renal cell carcinoma, an urothelial carcinoma, a head and neck cancer, a glioma or a glioblastoma, optionally wherein the prostate cancer is a relapsed, a refractory, a malignant or a castration-resistant prostate cancer, or any combination thereof.~~
- 1) ~~The use of any one of claims 1-7, wherein:~~
- a) ~~the anti-CD38 antibody:~~
- i) ~~comprises the HCDR1 of SEQ ID NO: 6, the HCDR2 of SEQ ID NO: 7, the HCDR3 of SEQ ID NO: 8, the LCDR1 of SEQ ID NO: 9, the LCDR2 of SEQ ID NO: 10 and the LCDR3 of SEQ ID NO: 11, optionally wherein:~~
- I. ~~the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;~~

- I. —the anti-CD38 antibody is an IgG1 isotype; and/or
- I. —the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13; or
- i) —comprises
 - I. —the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;
 - I. —the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;
 - I. —the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or
 - I. —the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21;
 optionally wherein the anti-CD38 antibody is an IgG1 isotype;
- a) —the T cell redirecting therapeutic is a BCMAxCD3 bispecific antibody, a GPRC5DxCD3 bispecific antibody, a CD33xCD3 bispecific antibody, a CD19xCD3 bispecific antibody, a CD123xCD3 bispecific antibody, a PSMAxCD3 bispecific antibody, or a TMEFF2xCD3 bispecific antibody;
- a) —wherein the use further comprises administering to the subject one or more anti-cancer therapies, optionally wherein the one or more anti-cancer therapies is selected from the group consisting of an autologous stem cell transplant (ASCT), radiation, surgery, a chemotherapeutic agent, an immunomodulatory agent and a targeted cancer therapy, for example wherein the one or more anti-cancer therapies is selected from the group consisting of lenalidomide, thalidomide, pomalidomide, bortezomib, carfilzomib, elotuzumab, ixazomib, melphalan, dexamethasone, vincristine, cyclophosphamide, hydroxydaunorubicin, prednisone, rituximab, imatinib, dasatinib, nilotinib, bosutinib, ponatinib, bafetinib, saracatinib, tozasertib or danusertib, cytarabine, daunorubicin, idarubicin, mitoxantrone, hydroxyurea, decitabine, cladribine, fludarabine, topotecan, etoposide 6-thioguanine, corticosteroid, methotrexate, 6-mercaptopurine, azacitidine, arsenic trioxide and all-trans retinoic acid, or any combination thereof; and/or
- a) —the anti-CD38 antibody:
 - i) —is:
 - I. —administered at a dose of between about 8 mg/kg and about 16 mg/kg; and/or
 - I. —administered or provided for administration in a pharmaceutical composition comprising between about 20 mg/mL to about 120 mg/mL of the anti-CD38 antibody in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mannitol and about 0.04% w/v polysorbate 20 (PS-20); at pH about 5.5; or
 - i) —is administered or provided for administration in a pharmaceutical composition comprising about 1,800 mg of the anti-CD38 antibody and about 30,000 U of rHuPH20, optionally wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising about 120 mg/mL of the anti-CD38 antibody

and about 2,000 U/mL of rHuPH20, for example wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising

- I. between about 5 mM and about 15 mM histidine;
- I. between about 100 mM and about 300 mM sorbitol;
- I. between about 0.01% w/v and about 0.04 % w/v PS-20; and
- I. between about 1 mg/mL and about 2 mg/mL methionine, at a pH of about 5.5-5.6,

optionally wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising

A. about 1,800 mg of the anti-CD38 antibody;

A. about 30,000 U of rHuPH20;

A. about 10 mM histidine;

A. about 300 mM sorbitol;

A. about 0.04 % (w/v) PS-20; and

A. about 1 mg/mL methionine, at a pH of about 5.6,

for example wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising

a. about 120 mg/mL of the anti-CD38 antibody;

a. about 2,000 U/mL of rHuPH20;

a. about 10 mM histidine;

a. about 300 mM sorbitol;

a. about 0.04 % (w/v) PS-20; and

a. about 1 mg/mL methionine, at a pH of about 5.6.

91) Use of a BCMAxCD3 bispecific antibody for the manufacture of a medicament for ~~treating the~~ treatment of a cancer in a subject, wherein the medicament is to be administered in combination with an anti-CD38 antibody, wherein the cancer is a multiple myeloma, and wherein:

a) the BCMAxCD3 bispecific antibody comprises a BCMA binding domain and a CD3 binding domain, wherein the BCMA binding domain comprises the VH of SEQ ID NO: 29 and the VL of SEQ ID NO: 30, and wherein the CD3 binding domain comprises the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40; and

b) the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.

102) Use of an anti-CD38 antibody for the manufacture of a medicament for ~~treating the treatment~~ of a cancer in a subject, wherein the medicament is to be administered in combination with a BCMAxCD3 bispecific antibody, wherein the cancer is a multiple myeloma, and wherein:

a) the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;
and

- b) the BCMAxCD3 bispecific antibody comprises a BCMA binding domain and a CD3 binding domain, wherein the BCMA binding domain comprises the VH of SEQ ID NO: 29 and the VL of SEQ ID NO: 30, and the CD3 binding domain comprises the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40.
- 3) Use of a BCMAxCD3 bispecific antibody and an anti-CD38 antibody for the manufacture of a medicament for ~~treating~~ the treatment of a cancer in a subject, wherein the cancer is a multiple myeloma, and wherein:
- a) the BCMAxCD3 bispecific antibody comprises a BCMA binding domain and a CD3 binding domain, wherein the BCMA binding domain comprises the VH of SEQ ID NO: 29 and the VL of SEQ ID NO: 30, and the CD3 binding domain comprises the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40; and
- b) the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.
- ~~414)~~ The use of ~~any one of claims 1-39 or 40~~, wherein
- a) the anti-CD38 antibody is ~~to be~~ administered to the subject prior to ~~administering~~ the BCMAxCD3 bispecific antibody ~~being administered~~; and/or
- ~~b) the BCMAxCD3 bispecific antibody comprises a BCMA binding domain comprising the HCDR1 of SEQ ID NO: 23, the HCDR2 of SEQ ID NO: 24, the HCDR3 of SEQ ID NO: 25, the LCDR1 of SEQ ID NO: 26, the LCDR2 of SEQ ID NO: 27 and the LCDR3 of SEQ ID NO: 28, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 33, the HCDR2 of SEQ ID NO: 34, the HCDR3 of SEQ ID NO: 35, the LCDR1 of SEQ ID NO: 36, the LCDR2 of SEQ ID NO: 37 and the LCDR3 of SEQ ID NO: 38, optionally wherein the BCMA binding domain comprises the VH of SEQ ID NO: 29 and the VL of SEQ ID NO: 30, and the CD3 binding domain comprises the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40;~~
- e) the BCMAxCD3 bispecific antibody is an IgG4 isotype and comprises phenylalanine at position 405 and arginine at position 409 in the HC1 and leucine at position 405 and lysine at position 409 in the HC2, wherein residue numbering is according to the EU Index, ~~optionally~~
- 5) The use of claim 4e), wherein the BCMAxCD3 bispecific antibody further comprises proline at position 228, alanine at position 234 and alanine at position 235 in both the HC1 and the HC2,;
- 6) The use of claim 5, ~~for example~~ wherein the BCMAxCD3 bispecific antibody comprises the HC1 of SEQ ID NO: 31, the LC1 of SEQ ID NO: 32, the HC2 of SEQ ID NO: 41 and the LC2 of SEQ ID NO: 42,;
- ~~d) the cancer is a BCMA-expressing cancer;~~
- e) 7) The use of any one of claims 1-6, wherein the subject is relapsed or refractory to treatment with the anti-CD38 antibody, lenalidomide, bortezomib, pomalidomide, carfilzomib, elotuzumab, ixazomib, melphalan or thalidomide, or any combination thereof,;

~~8) The use of claim 7, optionally wherein the subject is relapsed or refractory to treatment with the anti-CD38 antibody; and/or,~~

~~f) the cancer is a hematological malignancy, optionally wherein the hematological malignancy is a multiple myeloma, myeloma, a DLBCL, a CLL, Waldenstrom's hypergammaglobulinaemia or non Hodgkin's lymphoma, for example wherein:~~

9) The use of any one of claims 1-8, wherein:

ag) the multiple myeloma:

10. I. ~~is a newly diagnosed multiple myeloma; or~~

II. ~~is a relapsed or a refractory multiple myeloma; and/or~~

bh) the multiple myeloma is a high-risk multiple myeloma;

10) The use of claim 9b), for example wherein the subject having the high-risk multiple myeloma has one or more chromosomal abnormalities comprising:

I. t(4;14)(p16;q32);

II. t(14;16)(q32;q23);

III. del17p;

IV. 1qAmp;

V. t(4;14)(p16;q32) and t(14;16)(q32;q23);

VI. t(4;14)(p16;q32) and del17p;

VII. t(14;16)(q32;q23) and del17p; or

VIII. t(4;14)(p16;q32), t(14;16)(q32;q23) and del17p, or any combination thereof.

11) The use of any one of claims 1-10, wherein:

~~a) the anti-CD38 antibody comprises the HCDR1 of SEQ ID NO: 6, the HCDR2 of SEQ ID NO: 7, the HCDR3 of SEQ ID NO: 8, the LCDR1 of SEQ ID NO: 9, the LCDR2 of SEQ ID NO: 10 and the LCDR3 of SEQ ID NO: 11;~~

~~a) the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;~~

ae) the anti-CD38 antibody is an IgG1 isotype; and/or

be) the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13;

~~e) the anti-CD38 antibody comprises~~

~~i) the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;~~

~~i) the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;~~

~~i) the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or~~

~~i) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21;~~

~~optionally wherein the anti-CD38 antibody is an IgG1 isotype;~~

12) The use of any one of claims 1-11, wherein:

ae) the anti-CD38 antibody is to be administered at a dose of between about 8 mg/kg and about 16 mg/kg; and/or

- ~~b~~d) wherein the BCMAxCD3 bispecific antibody and the anti-CD38 antibody are to be administered by an intravenous injection or wherein the BCMAxCD3 bispecific antibody is to be administered by an intravenous injection and the anti-CD38 antibody is to be administered by a subcutaneous injection;
- 13e) The use of any one of claims 1-12, wherein the subject is a human;
- 14f) The use of any one of claims 1-13, wherein the use further comprises ~~administering to the subject~~ one or more anti-cancer therapies to be administered to the subject;
- 15) The use of claim 14, optionally wherein the one or more anti-cancer therapies is selected from the group consisting of:
- i) an autologous stem cell transplant (ASCT), radiation, surgery, a chemotherapeutic agent, an immunomodulatory agent and a targeted cancer therapy; or
 - ii) lenalidomide, thalidomide, pomalidomide, bortezomib, carfilzomib, elotozumab, ixazomib, melphalan, prednisone or dexamethasone, or any combination thereof.
- 16) The use of any one of claims 1-15, wherein:
- a)g) the anti-CD38 antibody is to be administered or provided for administration in a pharmaceutical composition comprising between about 20 mg/mL to about 120 mg/mL of the anti-CD38 antibody in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mannitol and about 0.04% w/v polysorbate-20 (PS-20); at pH about 5.5; and/or
 - b)h) the anti-CD38 antibody is to be administered or provided for administration in a pharmaceutical composition comprising about 1,800 mg of the anti-CD38 antibody and about 30,000 U of rHuPH20;
- 17) The use of claim 16b), optionally wherein the anti-CD38 antibody is to be administered or provided for administration in a pharmaceutical composition comprising about 120 mg/mL of the anti-CD38 antibody and about 2,000 U/mL of rHuPH20;
- 18) The use of claim 17, for example wherein the anti-CD38 antibody is to be administered or provided for administration in a pharmaceutical composition comprising
- i) between about 5 mM and about 15 mM histidine;
 - ii) between about 100 mM and about 300 mM sorbitol;
 - iii) between about 0.01% w/v and about 0.04 % w/v PS-20; and
 - iv) between about 1 mg/mL and about 2 mg/mL methionine, at a pH of about 5.5-5.6,
- 19) The use of claim 18, optionally wherein the anti-CD38 antibody is to be administered or provided for administration in a pharmaceutical composition comprising
- I. about 1,800 mg of the anti-CD38 antibody;
 - II. about 30,000 U of rHuPH20;
 - III. about 10 mM histidine;
 - IV. about 300 mM sorbitol;

V. about 0.04 % (w/v) PS-20; and

VI. about 1 mg/mL methionine, at a pH of about 5.6;

20) The use of claim 19, for example wherein the anti-CD38 antibody is to be administered or provided for administration in a pharmaceutical composition comprising

A. about 120 mg/mL of the anti-CD38 antibody;

B. about 2,000 U/mL of rHuPH20;

C. about 10 mM histidine;

D. about 300 mM sorbitol;

E. about 0.04 % (w/v) PS-20; and

F. about 1 mg/mL methionine, at a pH of about 5.6.

2143) A pharmaceutical composition comprising a BCMAxCD3 bispecific antibody comprising a BCMA binding domain comprising the VH of SEQ ID NO: 29 and the VL of SEQ ID NO: 30 and a CD3 binding domain comprising the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40, and an anti-CD38 antibody comprising the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5.

2244) The pharmaceutical composition of claim 2143, wherein:

a) the BCMAxCD3 bispecific antibody comprises the HC1 of SEQ ID NO: 31, the LC1 of SEQ ID NO: 32, the HC2 of SEQ ID NO: 41 and the LC2 of SEQ ID NO: 42 and the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13; and/or

b) the pharmaceutical composition is a non-fixed combination.

23) The pharmaceutical composition of claim 22b), optionally comprising:

ai) from about 20 mg/mL to about 120 mg/mL of the anti-CD38 antibody in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mannitol and about 0.04% w/v polysorbate-20 (PS-20); at pH about 5.5; or

bii) about 1,800 mg of the anti-CD38 antibody and about 30,000 U of rHuPH20;

24) The pharmaceutical composition of claim 23b), optionally comprising about 120 mg/mL of the anti-CD38 antibody and about 2,000 U/mL of rHuPH20;

25) The pharmaceutical composition of claim 24, for example wherein the pharmaceutical composition further comprises one or more excipients;

26) The pharmaceutical composition of claim 25, optionally wherein the one or more excipients is histidine, methionine, sorbitol or polysorbate-20 (PS-20), or any combination thereof;

27) The pharmaceutical composition of claim 26, for example wherein the pharmaceutical composition comprises

I. between about 100 mg/mL and about 120 mg/mL of the anti-CD38 antibody;

II. between about 5 mM and about 15 mM histidine;

III. between about 100 mM and about 300 mM sorbitol;

IV. between about 0.01% w/v and about 0.04 % w/v PS-20; and

V. between about 1 mg/mL and about 2 mg/mL methionine, at a pH of about 5.5-5.6,

28) The pharmaceutical composition of claim 27, optionally wherein the pharmaceutical composition:

- A. comprises about 10 mM histidine;
- B. comprises about 300 mM sorbitol;
- C. comprises about 0.04% (w/v) PS-20;
- D. comprises about 1 mg/mL methionine;
- E. comprises
 - a. about 1,800 mg of the anti-CD38 antibody;
 - b. about 30,000 U of rHuPH20;
 - c. about 10 mM histidine;
 - d. about 300 mM sorbitol;
 - e. about 0.04 % (w/v) PS-20; and
 - f. about 1 mg/mL methionine, at a pH of about 5.6; and/or
- F. comprises
 - a. about 120 mg/mL of the anti-CD38 antibody;
 - b. about 2,000 U/mL of rHuPH20;
 - c. about 10 mM histidine;
 - d. about 300 mM sorbitol;
 - e. about 0.04 % (w/v) PS-20; and
 - f. about 1 mg/mL methionine, at a pH of about 5.6.

2945) A kit comprising the pharmaceutical composition of any one of claims 21-28~~13 or 14~~.

~~16) Use of a T-cell redirecting therapeutic that binds GPRC5D for the manufacture of a medicament for treating a cancer in a subject, wherein the medicament is to be administered in combination with an anti-CD38 antibody.~~

~~17) Use of an anti-CD38 antibody for the manufacture of a medicament for treating a cancer in a subject, wherein the medicament is to be administered in combination with a T-cell redirecting therapeutic that binds GPRC5D.~~

~~18) The use of claim 16 or 17, wherein:~~

- ~~a) the anti-CD38 antibody is administered to subject prior to administering the T-cell redirecting therapeutic that binds GPRC5D;~~
- ~~a) the subject is relapsed or refractory to treatment with a prior anti-cancer therapeutic;~~
- ~~a) the cancer is a GPRC5D-expressing cancer, optionally wherein the GPRC5D-expressing cancer is:~~

- i) ~~a hematological malignancy, optionally wherein the hematological malignancy is a leukemia, a lymphoma, or a multiple myeloma, for example wherein the multiple myeloma is:~~
 - I. ~~a newly diagnosed multiple myeloma; or~~
 - I. ~~a relapsed or refractory multiple myeloma,~~
~~optionally wherein the multiple myeloma is a high-risk multiple myeloma, for example wherein the subject having the high-risk multiple myeloma has one or more chromosomal abnormalities comprising:~~
 - A. ~~t(4;14)(p16;q32);~~
 - A. ~~t(14;16)(q32;q23);~~
 - A. ~~del17p;~~
 - A. ~~1qAmp;~~
 - A. ~~t(4;14)(p16;q32) and t(14;16)(q32;q23);~~
 - A. ~~t(4;14)(p16;q32) and del17p;~~
 - A. ~~t(14;16)(q32;q23) and del17p; or~~
 - A. ~~t(4;14)(p16;q32), t(14;16)(q32;q23) and del17p, or any combination thereof; or~~
- i) ~~a solid tumor, optionally wherein the solid tumor is an ovarian cancer, a lung cancer, a stomach cancer, a prostate cancer, a renal carcinoma, a liver cancer, a pancreatic cancer, a colon cancer, an oesophageal cancer, a bladder cancer, a cervical carcinoma or a malignant melanoma;~~
- a) ~~the subject is relapsed or refractory to treatment with the anti-CD38 antibody, lenalidomide, bortezomib, pomalidomide, carfilzomib, clotozumab, ixazomib, melphalan or thalidomide, or any combination thereof, for example wherein the subject is relapsed or refractory to treatment with the anti-CD38 antibody;~~
- e) ~~the T-cell redirecting therapeutic binds CD3, CD3-epsilon (CD3ε), CD8, KI2L4, NKG2E, NKG2D, NKG2F, BTNL3, CD186, BTNL8, PD-1, CD195, or NKG2C;~~
- e) ~~the T-cell redirecting therapeutic comprises a GPRC5D binding domain comprising the HCDR1 of SEQ ID NO: 43, the HCDR2 of SEQ ID NO: 44, the HCDR3 of SEQ ID NO: 45, the LCDR1 of SEQ ID NO: 46, the LCDR2 of SEQ ID NO: 47 and the LCDR3 of SEQ ID NO: 48, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 33, the HCDR2 of SEQ ID NO: 34, the HCDR3 of SEQ ID NO: 35, the LCDR1 of SEQ ID NO: 36, the LCDR2 of SEQ ID NO: 37 and the LCDR3 of SEQ ID NO: 38;~~
- e) ~~the GPRC5D binding domain comprises the VH of SEQ ID NO: 49 and the VL of SEQ ID NO: 50 and the CD3 binding domain comprises the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40;~~

- e) ~~the T-cell redirecting therapeutic that binds GPRC5C is a multispecific antibody, a CAR or a T cell expressing the CAR, optionally wherein the multispecific antibody:~~
 - i) ~~is an IgG1, an IgG2, an IgG3 or an IgG4 isotype, optionally wherein the multispecific antibody comprises one or more Fc substitutions that reduces binding of the multispecific antibody to a Fcγ receptor (FcγR), for example wherein the one or more Fc substitutions is selected from the group consisting of F234A/L235A on IgG4, L234A/L235A on IgG1, V234A/G237A/ P238S/H268A/V309L/A330S/P331S on IgG2, F234A/L235A on IgG4, S228P/F234A/ L235A on IgG4, N297A on all Ig isotypes, V234A/G237A on IgG2, K214T/E233P/ L234V/L235A/G236-deleted/A327G/P331A/D365E/L358M on IgG1, H268Q/V309L/A330S/P331S on IgG2, S267E/L328F on IgG1, L234F/L235E/D265A on IgG1, L234A/L235A/G237A/P238S/H268A/A330S/P331S on IgG1, S228P/F234A/L235A/G237A/P238S on IgG4 and S228P/F234A/L235A/G236-deleted/G237A/P238S on IgG4, wherein residue numbering is according to the EU index, optionally wherein the multispecific antibody further comprises a S228P substitution; and/or~~
 - i) ~~comprises one or more asymmetric substitutions in a first CH3 domain or in a second CH3 domain, or in both the first CH3 domain and the second CH3 domain, optionally wherein the one or more asymmetric substitutions is selected from the group consisting of F450L/K409R, wild-type/F409L_R409K, T366Y/F405A, T366W/F405W, F405W/Y407A, T394W/Y407T, T394S/Y407A, T366W/T394S, F405W/T394S and T366W/T366S_L368A_Y407V, L351Y_F405A_Y407V/T394W, T366I_K392M_T394W/F405A_Y407V, T366L_K392M_T394W/F405A_Y407V, L351Y_Y407A/T366A_K409F, L351Y_Y407A/T366V_K409F, Y407A/T366A_K409F and T350V_L351Y_F405A_Y407V/T350V_T366L_K392L_T394W;~~
- e) ~~the multispecific antibody comprises the HC1 of SEQ ID NO: 51, the LC1 of SEQ ID NO: 52, the HC2 of SEQ ID NO: 41 and the LC2 of SEQ ID NO: 42;~~
- e) ~~the anti-CD38 antibody comprises the HCDR1 of SEQ ID NO: 6, the HCDR2 of SEQ ID NO: 7, the HCDR3 of SEQ ID NO: 8, the LCDR1 of SEQ ID NO: 9, the LCDR2 of SEQ ID NO: 10 and the LCDR3 of SEQ ID NO: 11;~~
- e) ~~the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;~~
- e) ~~the anti-CD38 antibody is an IgG1 isotype;~~
- e) ~~the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13;~~
- e) ~~the anti-CD38 antibody comprises~~
 - i) ~~the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;~~
 - i) ~~the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;~~
 - i) ~~the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or~~

- i) the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21, optionally wherein the anti-CD38 antibody is an IgG1 isotype;
- e) the anti-CD38 antibody is administered at a dose of between about 8 mg/kg and about 16 mg/kg;
- e) the T-cell redirecting therapeutic that binds GPRC5D and the anti-CD38 antibody are administered by an intravenous injection;
- e) the T-cell redirecting therapeutic that binds GPRC5D is administered by an intravenous injection and the anti-CD38 antibody is administered by a subcutaneous injection;
- e) the subject is a human;
- e) the T-cell redirecting therapeutic that binds GPRC5D is a GPRC5D×CD3 bispecific antibody;
- e) the use further comprises administering to the subject one or more anti-cancer therapies, optionally wherein the one or more anti-cancer therapies is selected from the group consisting of:
 - i) an autologous stem cell transplant (ASCT), radiation, surgery, a chemotherapeutic agent, an immunomodulatory agent and a targeted cancer therapy; or
 - i) lenalidomide, thalidomide, pomalidomide, bortezomib, carfilzomib, elotuzumab, ixazomib, melphalan, dexamethasone or prednisone;
- e) the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising between about 20 mg/mL to about 120 mg/mL of the anti-CD38 antibody in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mannitol and about 0.04% w/v polysorbate 20 (PS-20); at pH about 5.5; and/or
- e) the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising about 1,800 mg of the anti-CD38 antibody and about 30,000 U of rHuPH20, optionally wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising about 120 mg/mL of the anti-CD38 antibody and about 2,000 U/mL of rHuPH20, for example wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising
 - i) between about 100 mg/mL and about 120 mg/mL of the anti-CD38 antibody;
 - i) between about 5 mM and about 15 mM histidine;
 - i) between about 100 mM and about 300 mM sorbitol;
 - i) between about 0.01% w/v and about 0.04 % w/v PS-20; and
 - i) between about 1 mg/mL and about 2 mg/mL methionine, at a pH of about 5.5-5.6, optionally wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising
 - I. about 1,800 mg of the anti-CD38 antibody;

I. ~~about 30,000 U of rHuPH20;~~

I. ~~about 10 mM histidine;~~

I. ~~about 300 mM sorbitol;~~

I. ~~about 0.04 % (w/v) PS-20; and~~

I. ~~about 1 mg/mL methionine, at a pH of about 5.6;~~

~~optionally wherein the anti-CD38 antibody is administered or provided for administration in a pharmaceutical composition comprising~~

~~A. about 120 mg/mL of the anti-CD38 antibody;~~

~~A. about 2,000 U/mL of rHuPH20;~~

~~A. about 10 mM histidine;~~

~~A. about 300 mM sorbitol;~~

~~A. about 0.04 % (w/v) PS-20; and~~

~~A. about 1 mg/mL methionine, at a pH of about 5.6.~~

19) ~~A pharmaceutical combination comprising a GPRC5D $\times$ CD3 bispecific antibody comprising a GPRC5D binding domain comprising the HCDR1 of SEQ ID NO: 43, the HCDR2 of SEQ ID NO: 44, the HCDR3 of SEQ ID NO: 45, the LCDR1 of SEQ ID NO: 46, the LCDR2 of SEQ ID NO: 47 and the LCDR3 of SEQ ID NO: 48, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 33, the HCDR2 of SEQ ID NO: 34, the HCDR3 of SEQ ID NO: 35, the LCDR1 of SEQ ID NO: 36, the LCDR2 of SEQ ID NO: 37 and the LCDR3 of SEQ ID NO: 38 and an anti-CD38 antibody comprising the HCDR1 of SEQ ID NO: 6, the HCDR2 of SEQ ID NO: 7, the HCDR3 of SEQ ID NO: 8, the LCDR1 of SEQ ID NO: 9, the LCDR2 of SEQ ID NO: 10 and the LCDR3 of SEQ ID NO: 11.~~

20) ~~The pharmaceutical combination of claim 19, wherein:~~

~~a) the GPRC5D binding domain comprises the VH of SEQ ID NO: 49 and the VL of SEQ ID NO: 50 and the CD3 binding domain comprises the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40, and the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5, optionally wherein the GPRC5C $\times$ CD3 bispecific antibody comprises the HC1 of SEQ ID NO: 51, the LC1 of SEQ ID NO: 52, the HC2 of SEQ ID NO: 41 and the LC2 of SEQ ID NO: 42, and the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13; and/or~~

~~a) the pharmaceutical combination is a non-fixed combination, optionally wherein the pharmaceutical composition comprises:~~

~~i) from about 20 mg/mL to about 120 mg/mL of the anti-CD38 antibody in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mannitol and about 0.04% w/v polysorbate-20 (PS-20); at pH about 5.5; or~~

i) ~~about 1,800 mg of the anti-CD38 antibody and about 30,000 U of rHuPH20, optionally comprising about 120 mg/mL of the anti-CD38 antibody and about 2,000 U/mL of rHuPH20, for example wherein the pharmaceutical composition further comprises one or more excipients, optionally wherein the one or more excipients is histidine, methionine, sorbitol or polysorbate 20 (PS-20), or any combination thereof, for example wherein the pharmaceutical composition~~

~~I. comprises~~

~~A. between about 100 mg/mL and about 120 mg/mL of the anti-CD38 antibody;~~

~~A. between about 5 mM and about 15 mM histidine;~~

~~A. between about 100 mM and about 300 mM sorbitol;~~

~~A. between about 0.01% w/v and about 0.04 % w/v PS-20; and~~

~~A. between about 1 mg/mL and about 2 mg/mL methionine, at a pH of about 5.5-5.6,~~

~~optionally wherein the pharmaceutical composition:~~

~~a. comprises about 10 mM histidine;~~

~~a. comprises about 300 mM sorbitol; and/or~~

~~a. comprises~~

~~1. about 120 mg/mL of the anti-CD38 antibody;~~

~~1. about 2,000 U/mL of rHuPH20;~~

~~1. about 10 mM histidine;~~

~~1. about 300 mM sorbitol;~~

~~1. about 0.04 % (w/v) PS-20; and~~

~~6. about 1 mg/mL methionine, at a pH of about 5.6;~~

~~I. comprises about 0.04% (w/v) PS-20;~~

~~I. comprises about 1 mg/mL methionine; and/or~~

~~I. comprises~~

~~A. about 1,800 mg of the anti-CD38 antibody;~~

~~A. about 30,000 U of rHuPH20;~~

~~A. about 10 mM histidine;~~

~~A. about 300 mM sorbitol;~~

~~A. about 0.04 % (w/v) PS-20; and~~

~~A. about 1 mg/mL methionine, at a pH of about 5.6.~~

~~21) A kit comprising the pharmaceutical combination of claim 19 or 20.~~

~~22) Use of a T-cell redirecting therapeutic that binds CD19 for the manufacture of a medicament for treating a cancer in a subject, wherein the medicament is to be administered in combination with an anti-CD38 antibody.~~

- 23) ~~Use of an anti-CD38 antibody for the manufacture of a medicament for treating a cancer in a subject, wherein the medicament is to be administered in combination with a T-cell redirecting therapeutic that binds CD19.~~
- 24) ~~The use of claim 22 or 23, wherein the anti-CD38 antibody is administered to the subject prior to administering the T-cell redirecting therapeutic that binds CD19.~~
- 25) ~~—Use of an anti-CD38 antibody for the manufacture of a medicament for enhancing efficacy of a T-cell redirecting therapeutic that binds CD19 in a subject having a cancer, wherein the medicament is administered prior to administering the T-cell redirecting therapeutic that binds CD19.~~
- 26) ~~The use of any one of claims 22-25, wherein:~~
- ~~a) the subject is refractory or relapsed to treatment with a prior anti-cancer therapeutic;~~
 - ~~a) the cancer is:~~
 - ~~i) a hematological malignancy, optionally wherein the hematological malignancy is lymphoma, a B-cell malignancy, Hodgkin's lymphoma, non-Hodgkin's lymphoma, a DLBCL, a FL, a MCL, a marginal zone B-cell lymphoma (MZL), a mucosa-associated lymphatic tissue lymphoma (MALT), a CLL, an ALL, an AML, Waldenstrom's Macroglobulinemia or a T-cell lymphoma; or~~
 - ~~i) a solid tumor, optionally wherein the solid tumor is a lung cancer, a liver cancer, a cervical cancer, a colon cancer, a breast cancer, an ovarian cancer, a pancreatic cancer, a melanoma, a glioblastoma, a prostate cancer, an esophageal cancer or a gastric cancer;~~
 - ~~a) the T-cell redirecting therapeutic binds CD3 epsilon (CD3ε), CD8, K12L4, NKG2E, NKG2D, NKG2F, BTNL3, CD186, BTNL8, PD-1, CD195, or NKG2C;~~
 - ~~a) the T-cell redirecting therapeutic that binds CD19 comprises a CD19 binding domain of blinatumomab, axicabtagene ciloleucel, tisagenlecleucel-t, inebilizumab, lisocabtagene maraleucel, XmAb-5574, CIK-CAR-CD19, ICTCAR-011, IM-19, JCAR-014, loncastuximab tesirine, MB-CART2019.1, OXS-1550, PBCAR-0191, PCAR-019, PCAR-119, Senl-001, TI-1007, XmAb-5871, PTG-01, PZ01, Senl-1904A, Senl-1904B, UCART-19, CSG-CD19, DI-B4, ET-190, GC-007F or GC-022;~~
 - ~~a) the T-cell redirecting therapeutic that binds CD19 comprises blinatumomab, axicabtagene ciloleucel, tisagenlecleucel-t, inebilizumab, lisocabtagene maraleucel, XmAb-5574, CIK-CAR-CD19, ICTCAR-011, IM-19, JCAR-014, loncastuximab tesirine, MB-CART2019.1, OXS-1550, PBCAR-0191, PCAR-019, PCAR-119, Senl-001, TI-1007, XmAb-5871, PTG-01, PZ01, Senl-1904A, Senl-1904B, UCART-19, CSG-CD19, DI-B4, ET-190, GC-007F or GC-022;~~
 - ~~a) the T-cell redirecting therapeutic that binds CD19 is a multispecific antibody, a CAR or a T-cell expressing the CAR;~~
 - ~~a) the anti-CD38 antibody;~~

- i) ~~comprises:~~
 - I. ~~the HCDR1 of SEQ ID NO: 6, the HCDR2 of SEQ ID NO: 7, the HCDR3 of SEQ ID NO: 8, the LCDR1 of SEQ ID NO: 9, the LCDR2 of SEQ ID NO: 10 and the LCDR3 of SEQ ID NO: 11;~~
 - I. ~~the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5;~~
 - I. ~~the anti-CD38 antibody is an IgG1 isotype; and/or~~
 - I. ~~the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13; or~~
 - i) ~~comprises~~
 - I. ~~the VH of SEQ ID NO: 14 and the VL of SEQ ID NO: 15;~~
 - I. ~~the VH of SEQ ID NO: 16 and the VL of SEQ ID NO: 17;~~
 - I. ~~the VH of SEQ ID NO: 18 and the VL of SEQ ID NO: 19; or~~
 - I. ~~the VH of SEQ ID NO: 20 and the VL of SEQ ID NO: 21,~~
~~optionally wherein the anti-CD38 antibody is an IgG1 isotype;~~
 - a) ~~the anti-CD38 antibody is administered at a dose of between about 8 mg/kg and about 16 mg/kg;~~
 - a) ~~the T-cell redirecting therapeutic that binds CD19 and the anti-CD38 antibody are administered by an intravenous injection or wherein the T-cell redirecting therapeutic that binds CD19 is administered by an intravenous injection and the anti-CD38 antibody is administered by a subcutaneous injection;~~
 - a) ~~the subject is a human.~~
 - a) ~~the T-cell redirecting therapeutic that binds CD19 is a CD19×CD3 bispecific antibody; and/or~~
 - a) ~~the use further comprises administering to the subject one or more anti-cancer therapies, optionally wherein the one or more anti-cancer therapies is selected from the group consisting of an autologous stem cell transplant (ASCT), radiation, surgery, a chemotherapeutic agent, an immunomodulatory agent and a targeted cancer therapy.~~
- 27) A pharmaceutical combination comprising a CD19×CD3 bispecific antibody comprising blinatumomab of SEQ ID NO: 53 an anti-CD38 antibody comprising the HCDR1 of SEQ ID NO: 6, the HCDR2 of SEQ ID NO: 7, the HCDR3 of SEQ ID NO: 8, the LCDR1 of SEQ ID NO: 9, the LCDR2 of SEQ ID NO: 10 and the LCDR3 of SEQ ID NO: 11.
- 28) The pharmaceutical combination of claim 27, wherein:
- a) ~~the anti-CD38 antibody comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 5,~~
~~optionally wherein the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13; and/or~~

- a) ~~the pharmaceutical combination is a non-fixed combination, optionally wherein the pharmaceutical combination comprises:~~
- i) ~~from about 20 mg/mL to about 120 mg/mL of the anti-CD38 antibody in about 25 mM acetic acid, about 60 mM sodium chloride, about 140 mannitol and about 0.04% w/v polysorbate 20 (PS-20); at pH about 5.5; or~~
 - i) ~~about 1,800 mg of the anti-CD38 antibody and about 30,000 U of rHuPH20, optionally comprising about 120 mg/mL of the anti-CD38 antibody and about 2,000 U/mL of rHuPH20, for example wherein the pharmaceutical combination further comprises one or more excipients, optionally wherein the one or more excipients is histidine, methionine, sorbitol or polysorbate 20 (PS-20), or any combination thereof, for example wherein the pharmaceutical combination comprises~~
 - I. ~~between about 100 mg/mL and about 120 mg/mL of the anti-CD38 antibody;~~
 - I. ~~between about 5 mM and about 15 mM histidine;~~
 - I. ~~between about 100 mM and about 300 mM sorbitol;~~
 - I. ~~between about 0.01% w/v and about 0.04 % w/v PS-20; and~~
 - I. ~~between about 1 mg/mL and about 2 mg/mL methionine, at a pH of about 5.5-5.6, optionally wherein the pharmaceutical combination:~~
 - A. ~~comprises about 10 mM histidine;~~
 - A. ~~comprises about 300 mM sorbitol;~~
 - A. ~~comprises about 0.04% (w/v) PS-20;~~
 - A. ~~comprises about 1 mg/mL methionine;~~
 - A. ~~comprises~~
 - a. ~~about 1,800 mg of the anti-CD38 antibody;~~
 - a. ~~about 30,000 U of rHuPH20;~~
 - a. ~~about 10 mM histidine;~~
 - a. ~~about 300 mM sorbitol;~~
 - a. ~~about 0.04 % (w/v) PS-20; and~~
 - a. ~~about 1 mg/mL methionine, at a pH of about 5.6; and/or~~
 - A. ~~comprises~~
 - a. ~~about 120 mg/mL of the anti-CD38 antibody;~~
 - a. ~~about 2,000 U/mL of rHuPH20;~~
 - a. ~~about 10 mM histidine;~~
 - a. ~~about 300 mM sorbitol;~~
 - a. ~~about 0.04 % (w/v) PS-20; and~~
 - a. ~~about 1 mg/mL methionine, at a pH of about 5.6.~~

29) A kit comprising the pharmaceutical composition of claim 27 or 28.