

CLAIMS:

1) Use of a BCMAxCD3 bispecific antibody for the manufacture of a medicament for A
~~method of treating~~the treatment of a cancer in a subject, comprising administering a
therapeutically effective amount of a BCMAxCD3 bispecific antibody to the subject to treat
the cancer, wherein the subject is relapsed or refractory to treatment with a prior anti-cancer
therapeutic.

2) The ~~use method~~ of claim ~~2~~1, wherein:

i) 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; and/or

~~3) — The method of claim 2 or 3,~~

~~wherein ii)~~ 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.

4) The ~~use method~~ of ~~any one of claims 1-3 or claim 2~~, wherein:

i) 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-

~~5) — The method of claim 4, optionally~~ 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 method of any one of claims 1-5, wherein ii)~~ 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;

~~7) — The method of any one of claims 1-6, wherein iii)~~ the cancer is a hematological
malignancy;

~~8) — The method of claim 7, optionally~~ wherein the hematological malignancy is a
multiple myeloma;

~~9) — The method of claim 8, such as~~ wherein the multiple myeloma is a high-risk
multiple myeloma;

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

- a) t(4;14)(p16;q32);
- b) t(14;16)(q32;q23);
- c) del17p;
- d) 1qAmp;
- e) t(4;14)(p16;q32) and t(14;16)(q32;q23);
- f) t(4;14)(p16;q32) and del17p;
- g) t(14;16)(q32;q23) and del17p; or
- h) t(4;14)(p16;q32), t(14;16)(q32;q23) and del17p, or any combination thereof; and/or

~~11)~~ ~~The method of any one of claims 1-10, wherein iv)~~ the subject is refractory or relapsed to treatment with the anti-CD38 antibody, lenalinomide, bortezomib, pomalidomide, carfilzomib, elotuzumab, ixazomib, melphalan or thalidomide, or any combination thereof;

~~12)~~ ~~The method of claim 11, optionally~~ wherein the subject is relapsed to treatment with the anti-CD38 antibody.

~~134)~~ The use method of any one of claims 1-~~123~~, wherein:

i) 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;

~~14)~~ ~~The method of any one of claims 1-13,~~

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

~~15)~~ ~~The method of any one of claims 1-14,~~

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

~~16)~~ ~~The method of any one of claims 1-15,~~

iv) wherein the anti-CD38 antibody comprises the HC of SEQ ID NO: 12 and the LC of SEQ ID NO: 13.

~~175)~~ The use method of any one of claims 1-~~123~~, wherein the anti-CD38 antibody 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;

~~18) The method of claim 17,~~

optionally wherein the anti-CD38 antibody of a), b), c) or d) is an IgG1 isotype.

~~196)~~ The use method of any one of claims 1-~~185~~, wherein the subject is a human.

~~207)~~ The use method of any one of claims 1-~~196~~, further comprising ~~administering to the subject~~ one or more anti-cancer therapies to be administered to the subject;

~~21) The method of claim 20, optionally~~ wherein;

i) 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-; and/or

~~22) The method of claim 21, wherein~~

ii) the one or more anti-cancer therapies is selected from the group consisting of lenalidomide, thalidomide, pomalidomide, bortezomib, carfilzomib, elotuzumab, ixazomib, melphalan, prednisone or dexamethasone, or any combination thereof.

~~238)~~ Use of a GPRC5DxCD3 bispecific antibody for the manufacture of a medicament for ~~A method of treating the treatment of a cancer in a subject, comprising administering a therapeutically effective amount of a GPRC5DxCD3 bispecific antibody to the subject to treat the cancer,~~ wherein the subject is relapsed or refractory to treatment with a prior anti-cancer therapeutic.

~~249)~~ The use method of claim ~~238~~, wherein;

i) the GPRC5DxCD3 bispecific antibody 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-; and/or
~~25) The method of claim 23 or 24, wherein-~~ ii) 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.

~~2610)~~ The use method of any ~~one of claims 23-25~~ 8 or claim 9, wherein

i) the GPRC5DxCD3 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:-

~~27) — The method of claim 26, optionally~~ wherein the GPRC5DxCD3 bispecific antibody further comprises proline at position 228, alanine at position 234 and alanine at position 235 in both the HC1 and the HC2;

~~28) — The method of any one of claims 23-27, wherein ii)~~ the GPRC5DxCD3 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;

~~29) — The method of any one of claims 23-28, wherein iii)~~ the cancer is a hematological malignancy or a solid tumor:-

~~30) — The method of claim 29, optionally~~ wherein the cancer is a multiple myeloma, a lymphoma, a melanoma, a plasma cell leukemia, a breast cancer, an endometrial cancer, an ovarian cancer, a lung cancer, stomach cancer, a prostate cancer, a renal carcinoma, a liver cancer, a pancreatic cancer, a colon cancer, an oesophageal cancer, a bladder cancer or a cervical carcinoma:-

~~31) — The method of claim 30, such as~~ wherein the multiple myeloma is a high-risk multiple myeloma:-

~~32) — The method of claim 31, for example~~ wherein the subject having the high-risk multiple myeloma has one or more chromosomal abnormalities comprising:

- a) t(4;14)(p16;q32);
- b) t(14;16)(q32;q23);
- c) del17p;
- d) 1qAmp;
- e) t(4;14)(p16;q32) and t(14;16)(q32;q23);
- f) t(4;14)(p16;q32) and del17p;
- g) t(14;16)(q32;q23) and del17p; or
- h) t(4;14)(p16;q32), t(14;16)(q32;q23) and del17p, or any combination thereof; and/or

~~33) — The method of any one of claims 23-32, wherein iv)~~ the subject is refractory or relapsed to treatment with the anti-CD38 antibody, lenalinomide, bortezomib, pomalidomide, carfilzomib, elotzumab, ixazomib, melphalan or thalidomide, or any combination thereof:-

~~34) — The method of claim 33, optionally~~ wherein the subject is relapsed or refractory to treatment with the anti-CD38 antibody.

~~35~~11) The use method of any one of claims ~~238-34~~10, wherein:

i) 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;

~~36) The method of any one of claims 23-35, wherein:~~

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

;

~~37) The method of any one of claims 23-36, wherein~~ iii) the anti-CD38 antibody is an IgG1 isotype; and/or

~~38) The method of any one of claims 23-37, wherein~~

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

~~39~~12) The use method of any one of claims ~~238-34~~10, wherein the anti-CD38 antibody 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;

~~40) The method of claim 39,~~

optionally wherein the anti-CD38 antibody of a), b), c) or d) is an IgG1 isotype.

~~41~~13) The use method of any one of claims ~~238-40~~12, wherein the subject is a human.

~~42~~14) The use method of any one of claims ~~238-41~~13, further comprising administering to the subject one or more anti-cancer therapies to be administered to the subject, optionally

~~43) The method of claim 42, wherein:~~

i) 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; and/or

~~44) The method of claim 42, wherein~~ ii) 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.