

CLAIMS

What is claimed:

- 1) A method of treating a cancer in a subject in need thereof, comprising administering a therapeutically effective amount of a BCMAxCD3 bispecific antibody or antigen binding fragment thereof, to the subject to treat the cancer, wherein the subject is relapsed or refractory to treatment with a prior anti-cancer treatment.
- 2) The method of claim 1, wherein the BCMAxCD3 bispecific antibody or antigen binding fragment thereof comprises a BCMA binding domain comprising the HCDR1 of SEQ ID NO: 4, the HCDR2 of SEQ ID NO: 5, the HCDR3 of SEQ ID NO: 6, the LCDR1 of SEQ ID NO: 7, the LCDR2 of SEQ ID NO: 8 and the LCDR3 of SEQ ID NO: 9, and a CD3 binding domain comprising the HCDR1 of SEQ ID NO: 14, the HCDR2 of SEQ ID NO: 15, the HCDR3 of SEQ ID NO: 16, the LCDR1 of SEQ ID NO: 17, the LCDR2 of SEQ ID NO: 18 and the LCDR3 of SEQ ID NO: 19.
- 3) The method of claim 2, wherein the BCMA binding domain comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO: 10 and a light chain variable region (VL) having the amino acid sequence of SEQ ID NO: 11, and the CD3 binding domain comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO: 20 and a light chain variable region (VL) having the amino acid sequence of SEQ ID NO: 21.
- 4) The method of claim 2, wherein 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 2, 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 claim 2, wherein the BCMAxCD3 bispecific antibody comprises a first heavy chain (HC1) having the amino acid sequence of SEQ ID NO: 12, the a first light chain (LC1) having the amino acid sequence of SEQ ID NO: 13, a second heavy chain (HC2) having the amino acid sequence of SEQ ID NO: 22 and a second light chain (LC2) having the amino acid sequence of SEQ ID NO: 23.
- 7) The method of claim 2, wherein the BCMAxCD3 bispecific antibody is teclistamab.
- 8) The method of claim 2, wherein the BCMAxCD3 bispecific antibody is administered intravenously or subcutaneously.
- 9) The method of claim 8, wherein the BCMAxCD3 bispecific antibody is administered intravenously at a dose of about 0.2 µg/kg weekly to about 1500 µg/kg weekly, such as about 35 µg/kg weekly to about 850 µg/kg weekly, 270 µg/kg to about 720 µg/kg weekly, or 19.2-720 µg/kg weekly; or about 0.1 to 100 µg/kg biweekly, such as about 0.2 to 50 µg/kg biweekly, or 0.3-19.2 µg/kg biweekly.
- 10) The method of claim 8, wherein the BCMAxCD3 bispecific antibody is administered subcutaneously at a dose of about 0.2 µg/kg weekly to about 3000 µg/kg weekly, such as about 80 - 3000 µg/kg weekly, about 100 µg/kg weekly to about 1800 µg/kg weekly, about 720 µg/kg to 1500 µg/kg weekly, such as about 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700 or 1800 µg/kg weekly.
- 11) The method of claim 2, wherein the BCMAxCD3 bispecific antibody is administered for a time sufficient to achieve complete response, stringent complete response, very good partial response, partial response, minimal response or stable disease status, and can be continued until disease progression or lack of patient benefit.
- 12) The method of claim 11, wherein the BCMAxCD3 bispecific antibody is administered for a time sufficient to achieve complete response that is characterized by negative minimal residual disease (MRD) status, preferably negative MRD status at 10^{-6} cells, as determined by next generation sequencing (NGS).

- 13) The method of claim 2, wherein the cancer is a hematological malignancy.
- 14) The method of claim 2, wherein the hematological malignancy is a multiple myeloma.
- 15) The method of claim 2, wherein the subject is refractory or relapsed to treatment with an anti-CD38 antibody, selinexor, venetoclax, lenalinomide, bortezomib, pomalidomide, carfilzomib, elotozumab, ixazomib, melphalan or thalidomide, or any combination thereof.
- 16) The method of claim 2, wherein the subject is a human subject, preferably the prior anti-cancer treatment comprises administering to the human subject at least one of a proteasome inhibitor and immunomodulatory drug, such as bortezomib, carfilzomib, lenalidomide, or pomalidomide.
- 17) The method of claim 2, further comprising administering to the subject one or more additional anti-cancer therapies.
- 18) The method of claim 17, wherein the one or more additional anti-cancer therapies are selected from the group consisting of an autologous stem cell transplant (ASCT), radiation, surgery, a chemotherapeutic agent, a CAR-T therapy, an immunomodulatory agent and a targeted cancer therapy.
- 19) The method of claim 18, wherein the one or more anti-cancer therapies are selected from the group consisting of selinexor, venetoclax, lenalidomide, thalidomide, pomalidomide, bortezomib, carfilzomib, elotozumab, ixazomib, melphalan, prednisone or dexamethasone, or any combination thereof.
- 20) The method of claim 2, wherein the treatment achieves an overall response rate of at least 60%, such as 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more in the treated subjects.

- 21) The method of claim 2, wherein the treatment achieves 15% or more, such as 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, 25% or more complete response in the treated subjects.