

sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 16; or (iii) the VH comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 48, and the VL comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 53; or (iv) the VH comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 49, and the VL comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 52; or (v) the VH comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 57, and the VL comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 64; or (vi) the VH comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 58, and the VL comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 63. Thus, in one aspect, the present disclosure provides an antibody that binds to GPRC5D, wherein the antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), (i) wherein the VH comprises an amino acid sequence of SEQ ID NO: 13, and the VL comprises an amino acid sequence of SEQ ID NO: 14; or (ii) wherein the VH comprises an amino acid sequence of SEQ ID NO: 48, and the VL comprises an amino acid sequence of SEQ ID NO: 53; or (iii) wherein the VH comprises an amino acid sequence of SEQ ID NO: 49, and the VL comprises an amino acid sequence of SEQ ID NO: 52. In another example (i) the VH comprises the amino acid sequence of SEQ ID NO: 13, and the VL comprises the amino acid sequence of SEQ ID NO: 14; or (ii) the VH comprises the amino acid sequence of SEQ ID NO: 15, and the VL comprises the amino acid sequence of SEQ ID NO: 16; or (iii) the VH comprises

antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 15, and the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 16; or (iii) the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 48, and the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 53; or (iv) the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 49, and the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 52; or (v) the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 57, and the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 64; or (vi) the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 58, and the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 63. Thus, in another aspect, the present disclosure provides a bispecific antigen binding molecule, comprising (a) a first antigen binding moiety that binds to a first antigen, wherein the first antigen is GPRC5D and the first antigen binding moiety comprises a heavy chain variable region (VH) comprising an amino acid sequence of SEQ ID NO: 13, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 14; or an amino acid sequence of SEQ ID NO: 48, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 53; or an amino acid

sequence of SEQ ID NO: 49, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 52; and (b) a second antigen binding moiety which specifically binds to a second antigen. In an example, (i) the VH of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 13, and the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 14; or (ii) the VH of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 15, and the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 16; or (iii) the VH of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 48, and the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 53; or (iv) the VH of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 49, and the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 52; or (v) the VH of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 57, and the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 64; or (vi) the VH of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 58, and the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID

antigen binding moiety. In another example, the third antigen moiety is identical to the first antigen binding moiety. In another example, the bispecific antigen binding molecule comprises an Fc domain composed of a first and a second subunit. In another example, the first, the second and, where present, the third antigen binding moiety are each a Fab molecule; and wherein either
5 (i) the second antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the first antigen binding moiety and the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain, or (ii) the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the second antigen binding moiety and the
10 second antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain; and wherein the third antigen binding moiety, where present, is fused at the C-terminus of the Fab heavy chain to the N-terminus of the second subunit of the Fc domain. In another example, the Fc domain is an IgG, particularly an IgG₁, Fc domain. In yet another example, the Fc domain is a human Fc domain. In another example, an
15 amino acid residue in the CH3 domain of the first subunit of the Fc domain is replaced with an amino acid residue having a larger side chain volume, thereby generating a protuberance within the CH3 domain of the first subunit which is positionable in a cavity within the CH3 domain of the second subunit, and an amino acid residue in the CH3 domain of the second subunit of the Fc domain is replaced with an amino acid residue having a smaller side chain volume, thereby
20 generating a cavity within the CH3 domain of the second subunit within which the protuberance within the CH3 domain of the first subunit is positionable. In another example, the Fc domain comprises one or more amino acid substitution that reduces binding to an Fc receptor and/or effector function. This means, that the binding to an Fc receptor may be reduced, or the effector function may be reduced, or the binding to an Fc receptor and the effector function may be
25 reduced.

In another aspect the disclosure provides one or more isolated polynucleotide encoding the antibody or bispecific antigen binding molecule as described herein. The disclosure provides one or more vector, particularly expression vector, comprising the polynucleotide(s) as described herein. In another aspect the disclosure provides one or more vector comprising the
30 polynucleotide(s) as described herein. In another aspect the disclosure provides a host cell comprising the polynucleotide(s) as described herein or the vector(s) as described herein. In some examples the host cell is a eukaryotic cell, particularly a mammalian cell.

In the disclosure a method of producing an antibody that binds to GPRC5D is provided comprising the steps of a) culturing the host cell as described herein under conditions

suitable for the expression of the antibody and b) optionally recovering the antibody. In another aspect the disclosure provides a method of producing an antibody that binds to GPRC5D, comprising the step of culturing the host cell as described herein under conditions suitable for the expression of the antibody. The disclosure provides an antibody that binds to GPRC5D,
5 produced by the method as described herein. Another aspect of the disclosure relates to a pharmaceutical composition comprising the antibody or bispecific antigen binding molecule as described herein and a pharmaceutically acceptable carrier. Another aspect of the disclosure relates to the antibody or bispecific antigen binding molecule as described herein or the pharmaceutical composition as described herein for use as a medicament. Another aspect of the
10 disclosure relates the antibody or bispecific antigen binding molecule as described herein or the pharmaceutical composition as described herein for use in the treatment of a disease. In an example, the disease is cancer, particularly multiple myeloma. Alternatively, the disease is an autoimmune disease, such as systemic lupus erythematosus and/or rheumatoid arthritis.

The disclosure provides the use of the antibody or bispecific antigen binding molecule as
15 described herein in the manufacture of a medicament for the treatment of a disease. The disease is particularly cancer, more particularly multiple myeloma. Alternatively, the disease is an autoimmune disease, such as systemic lupus erythematosus and/or rheumatoid arthritis. Thus, in another aspect, the present disclosure provides use of the antibody or bispecific antigen binding molecule as described herein in the manufacture of a medicament for the treatment of a disease,
20 wherein said disease is cancer, an autoimmune disease, or multiple myeloma.

The disclosure relates to a method of treating a disease, particularly cancer, more particularly multiple myeloma, in an individual, comprising administering to said individual a therapeutically effective amount of a composition comprising the antibody or bispecific antigen binding molecule as described herein in a pharmaceutically acceptable form. Alternatively, the disease is
25 an autoimmune disease, such as systemic lupus erythematosus and/or rheumatoid arthritis. In any of the above examples the individual preferably is a mammal, particularly a human.

Brief Description of the Drawings

Figures 1A-Z. Exemplary configurations of the bispecific antigen binding molecules of the invention. (Fig.1A, Fig.2D) Illustration of the “1+1 CrossMab” molecule.
30 (Fig.1B, Fig.1E) Illustration of the “2+1 IgG Crossfab” molecule with alternative

Claims

1. An antibody that binds to GPRC5D, wherein the antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL),
 - (i) wherein the VH comprises an amino acid sequence of SEQ ID NO: 13, and the VL comprises
5 an amino acid sequence of SEQ ID NO: 14; or
 - (ii) wherein the VH comprises an amino acid sequence of SEQ ID NO: 48, and the VL comprises an amino acid sequence of SEQ ID NO: 53; or
 - (iii) wherein the VH comprises an amino acid sequence of SEQ ID NO: 49, and the VL comprises an amino acid sequence of SEQ ID NO: 52.
- 10 2. The antibody of claim 1, wherein the antibody is an IgG antibody.
3. The antibody of claim 2, wherein the antibody is an IgG1 antibody.
4. The antibody of any one of claims 1 to 3, wherein the antibody is a full-length antibody.
5. The antibody of any one of claims 1 to 3, wherein the antibody is an antibody fragment
selected from the group of an Fv molecule, a scFv molecule, a Fab molecule, and a F(ab')₂
15 molecule.
6. The antibody of any one of claims 1 to 5, wherein the antibody is a multispecific antibody.
7. A bispecific antigen binding molecule, comprising
 - (a) a first antigen binding moiety that binds to a first antigen,
20 wherein the first antigen is GPRC5D and the first antigen binding moiety comprises a heavy chain variable region (VH) comprising an amino acid sequence of SEQ ID NO: 13, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 14; or an amino acid sequence of SEQ ID NO: 48, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 53; or an amino acid sequence of SEQ
25 ID NO: 49, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence of SEQ ID NO: 52; and
 - (b) a second antigen binding moiety which specifically binds to a second antigen.

8. The bispecific antigen binding molecule of claim 7, wherein the second antigen is CD3.
9. The bispecific antigen binding molecule of claim 8, wherein the second antigen is CD3ε.
10. The bispecific antigen binding molecule of claim 8 or 9, wherein the second antigen binding moiety comprises a VH comprising a HCDR 1 of SEQ ID NO: 29, a HCDR 2 of SEQ ID NO: 30, and a HCDR 3 of SEQ ID NO: 31, and a VL comprising a LCDR 1 of SEQ ID NO: 32, a LCDR 2 of SEQ ID NO: 33 and a LCDR 3 of SEQ ID NO: 34.
11. The bispecific antigen binding molecule of claim 10, wherein the VH of the second antigen binding moiety comprises an amino acid sequence that is at least 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 35, and the VL of the second antigen binding moiety comprises an amino acid sequence that is at least 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 36.
12. The bispecific antigen binding molecule of any one of claims 7 to 11, wherein the first and/or the second antigen binding moiety is a Fab molecule.
13. The bispecific antigen binding molecule of any one of claims 7 to 12, wherein the second antigen binding moiety is a Fab molecule wherein the variable domains VL and VH or the constant domains CL and CH1 of the Fab light chain and the Fab heavy chain are replaced by each other.
14. The bispecific antigen binding molecule of claim 13, wherein the variable domains VL and VH of the Fab light chain and the Fab heavy chain are replaced by each other.
15. The bispecific antigen binding molecule of any one of claims 7 to 14, wherein the first antigen binding moiety is a Fab molecule wherein in the constant domain CL the amino acid at position 124 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat) and the amino acid at position 123 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat), and in the constant domain CH1 the amino acid at position 147 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index) and the amino acid at position 213 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index).

16. The bispecific antigen binding molecule of any one of claims 7 to 15, wherein the first and the second antigen binding moiety are fused to each other.

17. The bispecific antigen binding molecule of claim 16, wherein the first and the second antigen binding moiety are fused to each other via a peptide linker.

5 18. The bispecific antigen binding molecule of any one of claims 7 to 17, wherein the first and the second antigen binding moiety are each a Fab molecule and wherein either (i) the second antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the first antigen binding moiety, or (ii) the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the
10 second antigen binding moiety.

19. The bispecific antigen binding molecule of any one of claims 7 to 18, comprising a third antigen binding moiety.

20. The bispecific antigen binding molecule of claim 19, wherein the third antigen binding moiety is identical to the first antigen binding moiety.

15 21. The bispecific antigen binding molecule of any one of claims 7 to 20, comprising an Fc domain composed of a first and a second subunit.

22. The bispecific antigen binding molecule of claim 21, wherein the first, the second and, where present, the third antigen binding moiety are each a Fab molecule;
and wherein either (i) the second antigen binding moiety is fused at the C-terminus of the Fab
20 heavy chain to the N-terminus of the Fab heavy chain of the first antigen binding moiety and the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain, or (ii) the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the second antigen binding moiety and the second antigen binding moiety is fused at the C-terminus of the Fab
25 heavy chain to the N-terminus of the first subunit of the Fc domain;
and wherein the third antigen binding moiety, where present, is fused at the C-terminus of the Fab heavy chain to the N-terminus of the second subunit of the Fc domain.

23. The bispecific antigen binding molecule of claim 21 or 22, wherein the Fc domain is an IgG Fc domain.

24. The bispecific antigen binding molecule of claim 23, wherein the Fc domain is an IgG₁ Fc domain.

25. The bispecific antigen binding molecule of any one of claims 21 to 24, wherein the Fc domain is a human Fc domain.

5 26. The bispecific antigen binding molecule of any one of claims 21 to 25, wherein an amino acid residue in the CH3 domain of the first subunit of the Fc domain is replaced with an amino acid residue having a larger side chain volume, thereby generating a protuberance within the CH3 domain of the first subunit which is positionable in a cavity within the CH3 domain of the second subunit, and an amino acid residue in the CH3 domain of the second subunit of the Fc
10 domain is replaced with an amino acid residue having a smaller side chain volume, thereby generating a cavity within the CH3 domain of the second subunit within which the protuberance within the CH3 domain of the first subunit is positionable,

wherein the amino acid residue having a larger side chain volume is selected from the group consisting of arginine, phenylalanine, tyrosine and tryptophan, and

15 wherein the amino acid residue having a smaller side chain volume is selected from the group consisting of alanine, serine, threonine and valine.

27. The bispecific antigen binding molecule of any one of claims 21 to 26, wherein the Fc domain comprises one or more amino acid substitution that reduces binding to an Fc receptor and/or effector function.

20 28. One or more isolated polynucleotide encoding the antibody or bispecific antigen binding molecule of any one of claims 1 to 26.

29. One or more vector comprising the polynucleotide(s) of claim 28.

30. The one or more vector of claim 29, wherein the one of more vector is an expression vector.

25 31. A host cell comprising the polynucleotide(s) of claim 28 or the vector(s) of claim 29 or 30.

32. A method of producing an antibody that binds to GPRC5D, comprising the step of culturing the host cell of claim 31 under conditions suitable for the expression of the antibody.

33. The method of claim 32, further comprising a step of recovering the antibody.

34. A pharmaceutical composition comprising the antibody or bispecific antigen binding molecule of any one of claims 1 to 27 and a pharmaceutically acceptable carrier.

35. The antibody or bispecific antigen binding molecule of any one of claims 8 to 27 or the
5 pharmaceutical composition of claim 34 for use as a medicament.

36. The antibody or bispecific antigen binding molecule of any one of claims 8 to 27 or the pharmaceutical composition of claim 34 for use in the treatment of a disease.

37. The antibody, bispecific antigen binding molecule or pharmaceutical composition for use according to claim 36, wherein the disease is cancer or an autoimmune disease.

10 38. The antibody, bispecific antigen binding molecule or pharmaceutical composition for use according to claim 37, wherein the disease is multiple myeloma.

39. Use of the antibody or bispecific antigen binding molecule of any one of claims 8 to 27 in the manufacture of a medicament for the treatment of a disease, wherein said disease is cancer, an autoimmune disease, or multiple myeloma.