CLAIMS

1. A bispecific antibody or a bispecific antibody fragment thereof comprising:
a first antigen-binding domain; and
a second antigen-binding domain, wherein
the first antigen-binding domain is the antigen-binding domain binding to CD131, and the second antigen-binding domain is the antigen-binding domain binding to CD116.

2. The bispecific antibody or the bispecific antibody fragment thereof according to claim 1, which has an agonist activity to a granulocyte macrophage-colony stimulating factor (hereinafter abbreviated as GM-CSF) receptor.

3. The bispecific antibody or the bispecific antibody fragment thereof according to claim 1 or 2, wherein the first antigen-binding domain and the second antigen-binding domain each comprise a heavy chain variable region (hereinafter abbreviated as VH) and a light chain variable region (hereinafter abbreviated as VL).

4. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 3, comprising one or two first antigen-binding domains and one or two second antigen-binding domains.

5. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 4, wherein the antigen-binding domain binding to CD131 is any one selected from the following (1a) to (1e):
(1a) an antigen-binding domain comprising a VH comprising complementarity determining regions (hereinafter abbreviated as CDRs) 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 61 to 63, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 64 to 66, respectively,
(1b) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 67 to 69, respectively, and a VL comprising CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOs: 70 to 72, respectively,
(1c) an antigen-binding domain comprising a VH containing CDRs 1 to 3

comprising the amino acid sequences represented by SEQ ID NOs: 73 to 75, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 76 to 78, respectively,

(1d) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 79 to 81, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 82 to 84, respectively, and

(1e) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively.

6. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 5, wherein the antigen-binding domain binding to CD131 is any one selected from the following (1A) to (1E):

(1A) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 21 and a VL comprising the amino acid sequence represented by SEQ ID NO: 22,

(1B) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 23 and a VL comprising the amino acid sequence represented by SEQ ID NO: 24,

(1C) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 25 and a VL comprising the amino acid sequence represented by SEQ ID NO: 26,

(1D) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 27 and a VL comprising the amino acid sequence represented by SEQ ID NO: 28, and

(1E) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 29 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30.

7. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 6, wherein the antigen-binding domain binding to CD116 is any one

selected from the following (2a) to (2q) and (2r-1) to (2r-12):

(2a) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 31 to 33, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 34 to 36, respectively,

(2b) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 37 to 39, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 40 to 42, respectively,

(2c) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NO: 43 to 45, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NO: 46 to 48, respectively,

(2d) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 49 to 51, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 52 to 54, respectively,

(2e) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 55 to 57, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 58 to 60, respectively,

(2f) an antigen-binding domain comprising a VH containing CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 104 to 106, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2g) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 107 to 109, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2h) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 110 to 112, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2i) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 113 to 115, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2j) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 116 to 118, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2k) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 119 to 121, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2l) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 122 to 124, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2m) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 125 to 127, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2n) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 128 to 130, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2o) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 131 to 133, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2p) an antigen-binding domain comprising a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 134 to 136, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2q) an antigen-binding domain comprising a VH comprising CDRs 1 to 3

comprising the amino acid sequences represented by SEQ ID NOs: 137 to 139, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-1) an antigen-binding domain comprising a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute arginine at position 9 in the amino acid sequence represented by SEQ ID NO: 138 with lysine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-2) an antigen-binding domain comprising a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute glycine at position 17 in the amino acid sequence represented by SEQ ID NO: 138 with aspartic acid is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-3) an antigen-binding domain comprising a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute arginine at position 9 in the amino acid sequence represented by SEQ ID NO: 138 with threonine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-4) an antigen-binding domain comprising a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute phenylalanine at position 2 in the amino acid sequence represented by SEQ ID NO: 138 with leucine and arginine at position 9 with threonine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-5) an antigen-binding domain comprising a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute phenylalanine at position 2 in the amino acid

sequence represented by SEQ ID NO: 138 with serine and arginine at position 9 with threonine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-6) an antigen-binding domain comprising a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with valine, serine at position 3 with alanine, and methionine at position 4 with leucine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-7) an antigen-binding domain comprising a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with phenylalanine and serine at position 3 with alanine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-8) an antigen-binding domain comprising a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute serine at position 3 in the amino acid sequence represented by SEQ ID NO: 137 with alanine and methionine at position 4 with leucine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-9) an antigen-binding domain comprising a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with tyrosine and serine at position 3 with alanine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-10) an antigen-binding domain comprising a VH comprising CDR1 comprising

the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 139 with glutamic acid is introduced, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(2r-11) an antigen-binding domain comprising a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 139 with glutamic acid, tyrosine at position 5 with tryptophan, and tyrosine at position 6 with methionine, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and

(2r-12) an antigen-binding domain comprising a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with phenylalanine, serine at position 3 with alanine, and methionine at position 4 with leucine, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively.

8. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 7, wherein the antigen-binding domain binding to CD116 is any one selected from the following (2A) to (2Y) and (2Z-1) to (2Z-20):

(2A) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 11 and a VL comprising the amino acid sequence represented by SEQ ID NO: 12,

(2B) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 13 and a VL comprising the amino acid sequence represented by SEQ ID NO: 14,

(2C) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 15 and a VL comprising the amino acid sequence represented by SEQ ID NO: 16,

(2D) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 17 and a VL comprising the amino acid sequence represented by SEQ ID NO: 18,

(2E) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 19 and a VL comprising the amino acid sequence represented by SEQ ID NO: 20,

(2F) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 92 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2G) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 93 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2H) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 94 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2I) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 95 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2J) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 96 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2K) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 97 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2L) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 98 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2M) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 99 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2N) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 100 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2O) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 101 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2P) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 102 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Q) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 103 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2R) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 176 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2S) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 177 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2T) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 178 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2U) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 179 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2V) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 182 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2W) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 183 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2X) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 184 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Y) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 185 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-1) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 190 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-2) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 191 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-3) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 192 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-4) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 193 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-5) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 194 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-6) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 195 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-7) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 196 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-8) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 197 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-9) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 198 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-10) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 199 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-11) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 200 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-12) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 201 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-13) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 202 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-14) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 203 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-15) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 204 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-16) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 205 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-17) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 206 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-18) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 207 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(2Z-19) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 208 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and

(2Z-20) an antigen-binding domain comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 209 and a VL comprising the amino acid sequence represented by SEQ ID NO: 30.

9. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 8, wherein

the first antigen-binding domain and the second antigen-binding domain are each Fab (hereinafter abbreviated as a first Fab and a second Fab, respectively),

the first Fab comprises a heavy chain (VH_1-CH1) comprising a VH and CH1

domain, and a light chain (VL-CL), and

the second Fab comprises a heavy chain (VH_2-CH1') comprising a VH and CH1 domain, and a light chain (VL-CL).

10. The bispecific antibody or the bispecific antibody fragment thereof according to claim 9, comprising:

one first Fab and a hinge region;

one second Fab and a hinge region; and

wherein

a C-terminus of the heavy chain in the first Fab is bound to an N-terminus of the hinge region and a C-terminus of the heavy chain in the second Fab is bound to an N-terminus of the hinge region.

11. The bispecific antibody or the bispecific antibody fragment thereof according to claim 9, comprising:

a first polypeptide and a hinge region;

a second polypeptide and a hinge region; and

wherein

a C-terminus of the first polypeptide is bound to an N-terminus of the hinge region and a C-terminus of the second polypeptide is bound to an N-terminus of the hinge region,

the first polypeptide comprises at least the first Fab (VH_1-CH1, VL-CL) and optionally the second Fab (VH_2-CH1', VL-CL) positioned at the N- or C-terminus of the first Fab, and

the second polypeptide comprises at least the second Fab (VH_2-CH1', VL-CL) and optionally the first Fab (VH_1-CH1, VL-CL) positioned at the N- or C-terminus of the second Fab.

12. The bispecific antibody or the bispecific antibody fragment thereof according to claim 9, comprising:

(a) two polypeptide chains each comprising (i) a heavy chain from the first Fab and a heavy chain from the second Fab (VH_1-CH1-VH_2-CH1') in which the C-terminus of the heavy chain in the first Fab and the N-terminus of the heavy chain in the second Fab bind to each other directly or via a linker, (ii) a hinge region; and

wherein

a C-terminus of the (VH_1-CH1-VH_2-CH1') is bound to an N-terminus of the hinge region in each polypeptide chain, and

(b) four light chains (VL-CL).

13. The bispecific antibody or the bispecific antibody fragment thereof according to claim 12, wherein each polypeptide chain further comprises:

a Fc region, wherein a N-terminus of each Fc region is bound to a C-terminus of the hinge region of each polypeptide chain.

14. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 13, wherein

the bispecific antibody is any one selected from the following (x1) to (x12) and (x13-1) to (x13-12):

(x1) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 104 to 106, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x2) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 107 to 109, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x3) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences

represented by SEQ ID NOs: 110 to 112, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x4) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 113 to 115, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x5) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 116 to 118, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x6) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 119 to 121, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x7) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 122 to 124, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively

(x8) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid

sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 125 to 127, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x9) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 128 to 130, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x10) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 131 to 133, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x11) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 134 to 136, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x12) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 137 to 139, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-1) a bispecific antibody in which the first antigen-binding domain comprises a

VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute arginine at position 9 in the amino acid sequence represented by SEQ ID NO: 138 with lysine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-2) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute glycine at position 17 in the amino acid sequence represented by SEQ ID NO: 138 with aspartic acid is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-3) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute arginine at position 9 in the amino acid sequence represented by SEQ ID NO: 138 with threonine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-4) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding

domain comprises a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute phenylalanine at position 2 in the amino acid sequence represented by SEQ ID NO: 138 with leucine and arginine at position 9 with threonine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-5) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising an amino acid sequence in which a modification to substitute phenylalanine at position 2 in the amino acid sequence represented by SEQ ID NO: 138 with serine and arginine at position 9 with threonine is introduced, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-6) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with valine, serine at position 3 with alanine, and methionine at position 4 with leucine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-7) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising an amino acid sequence in which a

modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with phenylalanine and serine at position 3 with alanine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-8) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute serine at position 3 in the amino acid sequence represented by SEQ ID NO: 137 with alanine and methionine at position 4 with leucine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-9) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with tyrosine and serine at position 3 with alanine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-10) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising an amino acid sequence in which a modification to substitute

leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 139 with glutamic acid is introduced, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively,

(x13-11) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising the amino acid sequence represented by SEQ ID NO: 137, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 139 with glutamic acid, tyrosine at position 5 with tryptophan, and tyrosine at position 6 with methionine is introduced, and a VL comprising CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and

(x13-12) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 85 to 87, respectively, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively, and the second antigen-binding domain comprises a VH comprising CDR1 comprising an amino acid sequence in which a modification to substitute leucine at position 2 in the amino acid sequence represented by SEQ ID NO: 137 with phenylalanine, serine at position 3 with alanine, and methionine at position 4 with leucine is introduced, CDR2 comprising the amino acid sequence represented by SEQ ID NO: 138, and CDR3 comprising the amino acid sequence represented by SEQ ID NO: 139, and a VL comprising CDRs 1 to 3 comprising the amino acid sequences represented by SEQ ID NOs: 88 to 90, respectively.

15. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 14, wherein the bispecific antibody is any one selected from the following (y1) to (y12) and (y13-1) to (y13-20):

(y1) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID

NO: 175, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y2) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 176, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y3) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 177, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y4) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 178, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y5) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 179, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y6) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 180, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y7) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 181, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y8) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL

comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 182, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y9) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 183, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y10) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 184, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y11) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 185, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y12) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 186, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-1) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 190, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-2) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 191, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-3) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 192, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-4) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 193, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-5) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 194, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-6) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 195, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-7) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 196, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-8) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 197, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-9) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-

binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 198, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-10) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 199, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-11) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 200, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-12) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 201, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-13) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 202, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-14) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 203, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-15) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 204, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-16) a bispecific antibody in which the first antigen-binding domain comprises

a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 205, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-17) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 206, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-18) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 207, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30,

(y13-19) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 208, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and

(y13-20) a bispecific antibody in which the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 209, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30.

16. The bispecific antibody or the bispecific antibody fragment thereof according to claim 12 or 13, wherein the polypeptide chain is the polypeptide chain (VH_1-CH1-VH_2-CH') in which the C-terminus of the heavy chain (VH_1-CH1) in the first Fab and the N-terminus of the heavy chain (VH_2-CH1') in the second Fab bind to each other directly or via a linker, and (VH_1-CH1-VH_2) in the polypeptide chain is any one selected from the following (v1) to (v12) and (v13-1) to (v13-20):

(v1) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by

SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 175 in order from an N-terminus,

(v2) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 176 in order from an N-terminus,

(v3) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 177 in order from an N-terminus,

(v4) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 178 in order from an N-terminus,

(v5) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 179 in order from an N-terminus,

(v6) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 180 in order from an N-terminus,

(v7) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 181 in order from an N-terminus,

(v8) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 182 in order from an N-terminus,

(v9) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID

NO: 183 in order from an N-terminus,

(v10) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 184 in order from an N-terminus,

(v11) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 185 in order from an N-terminus,

(v12) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 186 in order from an N-terminus,

(v13-1) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 190 in order from an N-terminus,

(v13-2) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 191 in order from an N-terminus,

(v13-3) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 192 in order from an N-terminus,

(v13-4) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 193 in order from an N-terminus,

(v13-5) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 194 in order from an N-terminus,

(v13-6) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 195 in order from an N-terminus,

(v13-7) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 196 in order from an N-terminus,

(v13-8) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 197 in order from an N-terminus,

(v13-9) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 198 in order from an N-terminus,

(v13-10) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 199 in order from an N-terminus,

(v13-11) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 200 in order from an N-terminus,

(v13-12) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 201 in order from an N-terminus,

(v13-13) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 202 in order from an N-terminus,

(v13-14) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence

represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 203 in order from an N-terminus,

(v13-15) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 204 in order from an N-terminus,

(v13-16) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 205 in order from an N-terminus,

(v13-17) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 206 in order from an N-terminus,

(v13-18) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 207 in order from an N-terminus,

(v13-19) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 208 in order from an N-terminus, and

(v13-20) (VH_1-CH1-VH_2) comprising a VH_1 comprising the amino acid sequence represented by SEQ ID NO: 29, a CH1 comprising the amino acid sequence represented by SEQ ID NO: 144, and a VH_2 comprising the amino acid sequence represented by SEQ ID NO: 209 in order from an N-terminus.

17. The bispecific antibody or the bispecific antibody fragment thereof according to claim 13, wherein the first antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 29, and a VL comprising the amino acid sequence represented by SEQ ID NO: 30, and the second antigen-binding domain comprises a VH comprising the amino acid sequence represented by SEQ ID NO: 186, and a VL comprising

the amino acid sequence represented by SEQ ID NO: 30.

18. The bispecific antibody or the bispecific antibody fragment thereof according to claim 13, wherein the VH_1 comprises the amino acid sequence represented by SEQ ID NO: 29, the CH1 comprises the amino acid sequence represented by SEQ ID NO: 144, and the VH_2 comprises the amino acid sequence represented by SEQ ID NO: 186,

the CH1', the hinge region and the Fc region (CH2-CH3) comprise the amino acid sequence represented by SEQ ID NO: 155, and

each light chain comprises a VL comprising the amino acid sequence represented by SEQ ID NO: 30.

19. A DNA encoding the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 18.

20. A recombinant vector comprising the DNA according to claim 19.

21. A transformant obtained by introducing the recombinant vector according to claim 20 into a host cell.

22. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 18 for use in treating and/or diagnosing a disease associated with a GM-CSF.

23. A method for producing the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 18, the method including: culturing the transformant according to claim 21 in a medium; producing and accumulating the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 18 in a culture; and collecting the bispecific antibody or the bispecific antibody fragment thereof from the culture.

24. Use of the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 18 in the manufacture of a medicament for treating and/or diagnosing a disease associated with a GM-CSF.