A10. The bispecific antibody or the bispecific antibody fragment thereof according to any one of above 1 to 18 and A1 to A5, for use in treatment and/or diagnosis of a disease associated with a GM-CSF.

A11. The bispecific antibody or the bispecific antibody fragment thereof according to above A10, in which the disease associated with a GM-CSF is a disease associated with an autoantibody to a GM-CSF.

A12. Use of the bispecific antibody or the bispecific antibody fragment thereof according to any one of above 1 to 18 and A1 to A5 for the manufacture of a therapeutic and/or diagnostic agent for a diseases associated with a GM-CSF.

A13. The use according to above A12, in which the disease associated with a GM-CSF is a disease associated with an autoantibody to a GM-CSF.

A14. A reagent for detecting or measuring at least one of CD116 and CD131, containing the bispecific antibody or the bispecific antibody fragment thereof according to any one of above 1 to 18 and A1 to A5.

23. A method for purifying a composition containing an antibody, the method including: purifying an antibody containing an Fc region by Protein A column chromatography, in which the antibody is an antibody with an H435F mutation introduced in the Fc region.

24. The bispecific antibody or the bispecific antibody fragment thereof according to any one of above 1 to 18, which binds to an epitope containing W at position 163 and R at position 221 in CD131 (SEQ ID NO: 211) and an epitope containing N at position 156, K at position 158, and T at position 187 in CD116 (SEQ ID NO: 210).

[0018a] In one example, the present disclosure refers to 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.

In one aspect, the present disclosure refers to 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, 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),

wherein the bispecific antibody or the bispecific antibody fragment thereof comprises:

(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-VH2-CH1') 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, (ii) a hinge region; and

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

wherein

a C-terminus of the (VH_1-CH1-VH2-CH1') is bound to an N-terminus of the hinge region in each polypeptide chain,

wherein the bispecific antibody is any one selected from the following:

(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,

(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,

(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,

(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,

(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.

[0018b] In one aspect, the present disclosure refers to a DNA encoding the bispecific antibody or the bispecific antibody fragment thereof as disclosed herein.

[0018c] In one aspect, the present disclosure refers to a recombinant vector comprising the DNA as disclosed herein.

[0018d] In one aspect, the present disclosure refers to a transformant obtained by introducing the recombinant vector as disclosed herein into a host cell.

[0018e] In one aspect, the present disclosure refers to the bispecific antibody or the bispecific

antibody fragment thereof as disclosed herein for use in treating and/or diagnosing a disease associated with a GM-CSF.

[0018f] In one aspect, the present disclosure refers to a method for producing the bispecific antibody or the bispecific antibody fragment thereof as disclosed herein, the method including: culturing the transformant as disclosed herein in a medium; producing and accumulating the bispecific antibody or the bispecific antibody fragment thereof as disclosed herein in a culture; and collecting the bispecific antibody or the bispecific antibody fragment thereof from the culture.

[0018g] In one aspect, the present disclosure refers to use of the bispecific antibody or the bispecific antibody fragment thereof as disclosed herein in the manufacture of a medicament for treating a disease associated with a GM-CSF.

In one aspect, the present disclosure refers to use of the bispecific antibody or the bispecific antibody fragment thereof as disclosed herein in the manufacture of a diagnostic agent for diagnosing a disease associated with a GM-CSF.

ADVANTAGEOUS EFFECTS OF DISCLOSURE

[0019] According to the present disclosure, there is provided a novel bispecific antibody binding to CD116 and CD131, a novel bispecific antibody having an agonist activity to a GM-CSF receptor, a bispecific antibody fragment thereof, a DNA encoding the bispecific antibody or the bispecific antibody fragment thereof, a vector containing the DNA, a hybridoma or transformant producing the bispecific antibody or the bispecific antibody fragment thereof, a method for producing the bispecific antibody or the bispecific antibody fragment thereof, a therapeutic and diagnostic agent containing the bispecific antibody or the bispecific antibody fragment thereof, a therapeutic and diagnostic method using the bispecific antibody or the bispecific antibody fragment thereof, and a detection or measurement reagent containing the

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, 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),

wherein the bispecific antibody or the bispecific antibody fragment thereof comprises:

(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 (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, (ii) a hinge region; and

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

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,

wherein the bispecific antibody is any one selected from the following:

(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,

(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,

(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,

(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,

(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.

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, 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.

4. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 3, wherein the bispecific antibody is any one selected from the following:

(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,

(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,

(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,

(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,

(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.

5. The bispecific antibody or the bispecific antibody fragment thereof according to claim 1 or 3, 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) (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,

(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,

(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,

(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,

(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.

6. The bispecific antibody or the bispecific antibody fragment thereof according to claim 3, 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.

7. The bispecific antibody or the bispecific antibody fragment thereof according to claim 3, 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.

8. A DNA encoding the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 7.

9. A recombinant vector comprising the DNA according to claim 8.

10. A transformant obtained by introducing the recombinant vector according to claim 9 into a host cell.

11. The bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 7 for use in treating and/or diagnosing a disease associated with a GM-CSF.

12. A method for producing the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 7, the method including: culturing the transformant according to claim 10 in a medium; producing and accumulating the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 7 in a culture; and collecting the bispecific antibody or the bispecific antibody fragment thereof from the culture.

13. Use of the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 7 in the manufacture of a medicament for treating a disease associated with a GM-CSF.

14. Use of the bispecific antibody or the bispecific antibody fragment thereof according to any one of claims 1 to 7 in the manufacture of a diagnostic agent for diagnosing a disease associated with a GM-CSF.