consisting of any one of the amino acid sequences selected from the following (a1) to (a11), or an antigen-binding site functionally equivalent thereto, and the antigen-binding site of the second polypeptide comprises an antigen-binding site which comprises an H chain variable region consisting of any one of the amino acid sequences selected from the following (b1) to (b11), or an antigen-binding site functionally equivalent thereto:

(a1) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 35 (H chain variable region of Q1);

(a2) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 36 (H chain variable region of Q31);

(a3) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 37 (H chain variable region of ~~Q1~~Q64);

(a4) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 38 (H chain variable region of Q85);

(a5) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 39 (H chain variable region of Q153);

(a6) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 40 (H chain variable region of Q354);

(a7) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 41 (H chain variable region of Q360);

(a8) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 42 (H chain variable region of Q405);

(a9) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 43 (H chain variable region of Q458);

(a10) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 44 (H chain variable region of Q460);

(a11) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 45 (H chain variable region of Q499);

(b1) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 46 (H chain variable region of J232);

(b2) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 47 (H chain variable region of J259);

(b3) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 48 (H chain variable region of J268);

(b4) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 49 (H chain variable region of J300);

(b5) an antigen-binding site comprising an H chain variable region amino acid sequence of

J326: SEQ ID NO: 51
J327: SEQ ID NO: 52
J339: SEQ ID NO: 53
J344: SEQ ID NO: 54
J346: SEQ ID NO: 55
J142: SEQ ID NO: 172

More specifically, the present invention provides multispecific antigen-binding molecules, wherein the antigen-binding site of the first polypeptide comprises an antigen-binding site which comprises an H chain variable region consisting of any one of the amino acid sequences selected from the following (a1) to (a11), or an antigen-binding site functionally equivalent thereto, and the antigen-binding site of the second polypeptide comprises an antigen-binding site which comprises an H chain variable region consisting of any one of the amino acid sequences selected from the following (b1) to (b11), or an antigen-binding site functionally equivalent thereto:

(a1) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 35 (H chain variable region of Q1);
(a2) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 36 (H chain variable region of Q31);
(a3) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 37 (H chain variable region of ~~Q1~~Q64);
(a4) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 38 (H chain variable region of Q85);
(a5) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 39 (H chain variable region of Q153);
(a6) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 40 (H chain variable region of Q354);
(a7) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 41 (H chain variable region of Q360);
(a8) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 42 (H chain variable region of Q405);
(a9) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 43 (H chain variable region of Q458);
(a10) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 44 (H chain variable region of Q460);
(a11) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 45 (H chain variable region of Q499);

CLAIMS

1. A bispecific antibody comprising a first polypeptide, a second polypeptide, a third polypeptide, and a fourth polypeptide, wherein the bispecific antibody is any one of the following (a) to (u):

(a) a bispecific antibody (Q1-G4k/J268-G4h/L45-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 75, 76, and 77, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 114, 115, and 116, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 141, 142, and 143, respectively;

(b) a bispecific antibody (Q1-G4k/J321-G4h/L45-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 75, 76, and 77, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 120, 121, and 122, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 141, 142, and 143, respectively;

(c) a bispecific antibody (Q31-z7/J326-z107/L2-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 78, 79, and 80, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 123, 124, and 125, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 138, 139, and 140, respectively;

(d) a bispecific antibody (Q64-z55/J344-z107/L45-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 81, 82, and 83, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 132, 133, and 134, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 141, 142, and 143, respectively;

(e) a bispecific antibody (Q64-z7/J326-z107/L334-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 81, 82, and 83, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 123, 124, and 125, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 150, 151, and 152, respectively;

(f) a bispecific antibody (Q64-z7/J344-z107/L406-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 81, 82, and 83, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that

comprise SEQ ID NOs: 132, 133, and 134, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 159, 160, and 161, respectively;

(g) a bispecific antibody (Q85-G4k/J268-G4h/L406-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 84, 85, and 86, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 114, 115, and 116, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 159, 160, and 161, respectively;

(h) a bispecific antibody (Q85-G4k/J321-G4h/L334-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 84, 85, and 86, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 120, 121, and 122, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 150, 151, and 152, respectively;

(i) a bispecific antibody (Q153-G4k/J232-G4h/L406-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 87, 88, and 89, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 108, 109, and 110, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 159, 160, and 161, respectively;

(j) a bispecific antibody (Q354-z106/J259-z107/L324-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 90, 91, and 92, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 111, 112, and 113, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 147, 148, and 149, respectively;

(k) a bispecific antibody (Q360-G4k/J232-G4h/L406-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 93, 94, and 95, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 108, 109, and 110, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 159, 160, and 161, respectively;

(l) a bispecific antibody (Q360-z118/J300-z107/L334-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 93, 94, and 95, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 117, 118, and 119, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3

that comprise SEQ ID NOs: 150, 151, and 152, respectively;

(m) a bispecific antibody (Q405-G4k/J232-G4h/L248-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 96, 97, and 98, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 108, 109, and 110, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 144, 145, and 146, respectively;

(n) a bispecific antibody (Q458-z106/J346-z107/L408-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 99, 100, and 101, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise t SEQ ID NOs: 135, 136, and 137, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 162, 163, and 164, respectively;

(o) a bispecific antibody (Q460-z121/J327-z119/L334-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 102, 103, and 104, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 126, 127, and 128, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 150, 151, and 152, respectively;

(p) a bispecific antibody (Q499-z118/J327-z107/L334-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 105, 106, and 107, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 126, 127, and 128, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 150, 151, and 152, respectively;

(q) a bispecific antibody (Q499-z118/J327-z107/L377-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 105, 106, and 107, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 126, 127, and 128, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 153, 154, and 155, respectively;

(r) a bispecific antibody (Q499-z118/J346-z107/L248-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 105, 106, and 107, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 135, 136, and 137, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 144, 145, and 146, respectively;

(s) a bispecific antibody (Q499-z121/J327-z119/L404-k), wherein the first polypeptide is

an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 105, 106, and 107, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 126, 127, and 128, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 156, 157, and 158, respectively;

(t) a bispecific antibody (Q499-z121/J339-z119/L377-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 105, 106, and 107, respectively, the second polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 129, 130, and 131, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 153, 154, and 155, respectively; and

(u) a bispecific antibody (Q153-G4k/J142-G4h/L180-k), wherein the first polypeptide is an H chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 87, 88, and 89, respectively, the second polypeptide is an H chainθ comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs:174, 175, and 176, respectively, and the third polypeptide and the fourth polypeptide are a commonly shared L chain comprising CDRs 1, 2, and 3 that comprise SEQ ID NOs: 177, 178, and 179, respectively.

2. The bispecific antibody of claim 1, which is any one of the following (a) to (u):

(a) a bispecific antibody (Q1-G4k/J268-G4h/L45-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 35, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 48, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 57;

(b) a bispecific antibody (Q1-G4k/J321-G4h/L45-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 35, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 50, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 57;

(c) a bispecific antibody (Q31-z7/J326-z107/L2-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 36, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 51, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 56;

(d) a bispecific antibody (Q64-z55/J344-z107/L45-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 37, the second polypeptide H chain comprises a variable region comprising SEQ ID NO:54, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 57;

(e) a bispecific antibody (Q64-z7/J326-z107/L334-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 37, the second polypeptide

H chain comprises a variable region comprising SEQ ID NO: 51, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 60;

(f) a bispecific antibody (Q64-z7/J344-z107/L406-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 37, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 54, and the third and fourth polypeptide L chains each comprises a variable region comprising SEQ ID NO: 63;

(g) a bispecific antibody (Q85-G4k/J268-G4h/L406-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 38, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 48, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 63;

(h) a bispecific antibody (Q85-G4k/J321-G4h/L334-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 38, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 50, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 60;

(i) a bispecific antibody (Q153-G4k/J232-G4h/L406-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 39, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 46, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 63;

(j) a bispecific antibody (Q354-z106/J259-z107/L324-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 40, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 47, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 59;

(k) a bispecific antibody (Q360-G4k/J232-G4h/L406-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 41, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 46, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 63;

(l) a bispecific antibody (Q360-z118/J300-z107/L334-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 41, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 49, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 60;

(m) a bispecific antibody (Q405-G4k/J232-G4h/L248-k), wherein the first polypeptide H

chain comprises a variable region comprising SEQ ID NO: 42, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 46, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 58;

(n) a bispecific antibody (Q458-z106/J346-z107/L408-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 43, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 55, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 64;

(o) a bispecific antibody (Q460-z121/J327-z119/L334-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 44, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 52, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 60;

(p) a bispecific antibody (Q499-z118/J327-z107/L334-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 45, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 52, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 60;

(q) a bispecific antibody (Q499-z118/J327-z107/L377-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 45, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 52, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 61;

(r) a bispecific antibody (Q499-z118/J346-z107/L248-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 45, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 55, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 58;

(s) a bispecific antibody (Q499-z121/J327-z119/L404-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 45, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 52, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 62;

(t) a bispecific antibody (Q499-z121/J339-z119/L377-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 45, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 53, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO:

61; and

(u) a bispecific antibody (Q153-G4k/J142-G4h/L180-k), wherein the first polypeptide H chain comprises a variable region comprising SEQ ID NO: 39, the second polypeptide H chain comprises a variable region comprising SEQ ID NO: 172, and the third and fourth polypeptide L chains each comprise a variable region comprising SEQ ID NO: 173.

3. The bispecific antibody of claim 2, which is any one of the following (a) to (u):

(a) a bispecific antibody (Q1-G4k/J268-G4h/L45-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71;

(b) a bispecific antibody (Q1-G4k/J321-G4h/L45-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71;

(c) a bispecific antibody (Q31-z7/J326-z107/L2-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 66, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(d) a bispecific antibody (Q64-z55/J344-z107/L45-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 67, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO:72;

(e) a bispecific antibody (Q64-z7/J326-z107/L334-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 66, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(f) a bispecific antibody (Q64-z7/J344-z107/L406-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 66, the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(g) a bispecific antibody (Q85-G4k/J268-G4h/L406-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71;

(h) a bispecific antibody (Q85-G4k/J321-G4h/L334-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71;

(i) a bispecific antibody (Q153-G4k/J232-G4h/L406-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71;

(j) a bispecific antibody (Q354-z106/J259-z107/L324-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 68, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(k) a bispecific antibody (Q360-G4k/J232-G4h/L406-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71;

(l) a bispecific antibody (Q360-z118/J300-z107/L334-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 69, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(m) a bispecific antibody (Q405-G4k/J232-G4h/L248-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71;

(n) a bispecific antibody (Q458-z106/J346-z107/L408-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 68, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(o) a bispecific antibody (Q460-z121/J327-z119/L334-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 70, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 73;

(p) a bispecific antibody (Q499-z118/J327-z107/L334-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 69, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(q) a bispecific antibody (Q499-z118/J327-z107/L377-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 69, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(r) a bispecific antibody (Q499-z118/J346-z107/L248-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 69, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 72;

(s) a bispecific antibody (Q499-z121/J327-z119/L404-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 70, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 73;

(t) a bispecific antibody (Q499-z121/J339-z119/L377-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 70, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 73; and

(u) a bispecific antibody (Q153-G4k/J142-G4h/L180-k), wherein the first polypeptide H chain comprises a constant region consisting of SEQ ID NO: 65, and the second polypeptide H chain comprises a constant region consisting of SEQ ID NO: 71,

wherein each of the third and fourth polypeptide L chains comprises a constant region consisting of SEQ ID NO: 74.

4. The bispecific antibody of claim 3, which is any one of the following (a) to (u):

(a) a bispecific antibody (Q1-G4k/J268-G4h/L45-k), wherein the first polypeptide is an H

chain consisting of the amino acid sequence of SEQ ID NO: 1, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 4, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 9;

(b) a bispecific antibody (Q1-G4k/J321-G4h/L45-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 1, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 5, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 9;

(c) a bispecific antibody (Q31-z7/J326-z107/L2-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 2, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 6, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 8;

(d) a bispecific antibody (Q64-z55/J344-z107/L45-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 3, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 7, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 9;

(e) a bispecific antibody (Q64-z7/J326-z107/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 10, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 6, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(f) a bispecific antibody (Q64-z7/J344-z107/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 10, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 7, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(g) a bispecific antibody (Q85-G4k/J268-G4h/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 11, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 4, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(h) a bispecific antibody (Q85-G4k/J321-G4h/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 11, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 5, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO:

30;

(i) a bispecific antibody (Q153-G4k/J232-G4h/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 12, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 21, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(j) a bispecific antibody (Q354-z106/J259-z107/L324-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 13, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 22, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 29;

(k) a bispecific antibody (Q360-G4k/J232-G4h/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 14, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 21, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(l) a bispecific antibody (Q360-z118/J300-z107/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 15, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 23, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(m) a bispecific antibody (Q405-G4k/J232-G4h/L248-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 16, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 21, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 28;

(n) a bispecific antibody (Q458-z106/J346-z107/L408-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 17, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 27, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 34;

(o) a bispecific antibody (Q460-z121/J327-z119/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 18, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 25, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(p) a bispecific antibody (Q499-z118/J327-z107/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 19, the second

polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 24, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(q) a bispecific antibody (Q499-z118/J327-z107/L377-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 19, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 24, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 31;

(r) a bispecific antibody (Q499-z118/J346-z107/L248-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 19, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 27, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 28;

(s) a bispecific antibody (Q499-z121/J327-z119/L404-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 20, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 25, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 32;

(t) a bispecific antibody (Q499-z121/J339-z119/L377-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 20, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 26, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 31; and

(u) a bispecific antibody (Q153-G4k/J142-G4h/L180-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 12, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 170, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 171.

5. A nucleic acid encoding the bispecific antibody of any one of claims 1 to 4.

6. A vector inserted with the nucleic acid of claim 5.

7. A cell comprising the nucleic acid of claim 5 or the vector of claim 6.

8. A method for producing the bispecific antibody of any one of claims 1 to 4 by culturing the cell of claim 7.

9. A pharmaceutical composition comprising the bispecific antibody of any one of claims 1 to 4, and a pharmaceutically acceptable carrier.

10. The composition of claim 9, which is a pharmaceutical composition used for prevention and/or treatment of bleeding, a disease accompanying bleeding, or a disease caused by bleeding.

11. The composition of claim 10, wherein the bleeding, the disease accompanying bleeding, or the disease caused by bleeding is a disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII.

12. The composition of claim 11, wherein the disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is hemophilia A.

13. The composition of claim 11, wherein the disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is a disease showing emergence of an inhibitor against blood coagulation factor VIII and/or activated blood coagulation factor VIII.

14. The composition of claim 11, wherein the disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is acquired hemophilia.

15. The composition of claim 11, wherein the disease that develops and/or progresses due to a decrease in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is von Willebrand disease.

16. Use of the bispecific antibody of any one of claims 1 to 4 for the manufacture of a pharmaceutical composition for preventing and/or treating bleeding, a disease accompanying bleeding, or a disease caused by bleeding.

17. A kit for use in the prevention and/or treatment of bleeding, a disease accompanying bleeding, or a disease caused by bleeding, which comprises the bispecific antibody of any one of claims 1 to 4, or the composition of any one of claims 9 to 15.

CLAIMS

1. A multispecific antigen-binding molecule that functionally substitutes for blood coagulation factor VIII, which comprises a first antigen-binding site that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and a second antigen-binding site that recognizes blood coagulation factor X, wherein the functional substitution for blood coagulation factor VIII results from an activated blood coagulation factor X (F.Xa) generation-promoting activity higher than the activity of a bispecific antibody (hA69-KQ/hB26-PF/hAL-AQ) which comprises an H chain comprising SEQ ID NOs: 165 and 166, and a commonly shared L chain comprising SEQ ID NO: 167.

2. The multispecific antigen-binding molecule of claim 1, which comprises a first polypeptide comprising a first antigen-binding site that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX and a third polypeptide comprising a third antigen-binding site that recognizes blood coagulation factor IX and/or activated blood coagulation factor IX, as well as a second polypeptide comprising a second antigen-binding site that recognizes blood coagulation factor X and a fourth polypeptide comprising a fourth antigen-binding site that recognizes blood coagulation factor X.

3. The multispecific antigen-binding molecule of claim 2, wherein the first polypeptide and the third polypeptide each comprises an antigen-binding site of an H chain or L chain of an antibody against blood coagulation factor IX or activated blood coagulation factor IX, respectively; and the second polypeptide and the fourth polypeptide each comprises an antigen-binding site of an H chain or L chain of an antibody against blood coagulation factor X, respectively.

4. The multispecific antigen-binding molecule of claim 3, wherein the antigen-binding site of the first polypeptide comprises an antigen-binding site which comprises H chain CDRs consisting of any one of the amino acid sequences selected from the following (a1) to (a11), or an antigen-binding site functionally equivalent thereto, and the antigen-binding site of the second polypeptide comprises an antigen-binding site which comprises H chain CDRs consisting of any one of the amino acid sequences selected from the following (b1) to (b11), or an antigen-binding site functionally equivalent thereto:

(a1) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 75, 76, and 77 (H chain CDRs of Q1), respectively;

(a2) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 78, 79, and 80 (H chain CDRs of Q31), respectively;

(a3) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 81, 82, and 83 (H chain CDRs of Q64), respectively;

(a4) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 84, 85, and 86 (H chain CDRs of Q85), respectively;

(a5) an antigen-binding site comprising the H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 87, 88, and 89 (H chain CDRs of Q153), respectively;

(a6) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 90, 91, and 92 (H chain CDRs of Q354), respectively;

(a7) an antigen-binding site comprising the H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 93, 94, and 95 (H chain CDRs of Q360), respectively;

(a8) an antigen-binding site comprising the of H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 96, 97, and 98 (H chain CDRs of Q405), respectively;

(a9) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 99, 100, and 101 (H chain CDRs of Q458), respectively;

(a10) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 102, 103, and 104 (H chain CDRs of Q460), respectively;

(a11) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 105, 106, and 107 (H chain CDRs of Q499), respectively;

(b1) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 108, 109, and 110 (H chain CDRs of J232), respectively;

(b2) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 111, 112, and 113 (H chain CDRs of J259), respectively;

(b3) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 114, 115, and 116 (H chain CDRs of J268), respectively;

(b4) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 117, 118, and 119 (H chain CDRs of J300), respectively;

(b5) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 120, 121, and 122 (H chain CDRs of J321), respectively;

(b6) an antigen-binding site comprising the H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 123, 124, and 125 (H chain CDRs of J326), respectively;

(b7) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 126, 127, and 128 (H chain CDRs of J327), respectively;

(b8) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 129, 130, and 131 (H chain CDRs of J339), respectively;

(b9) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 132, 133, and 134 (H chain CDRs of J344), respectively;

(b10) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 135, 136, and 137 (H chain CDRs of J346), respectively; and

(b11) an antigen-binding site comprising an H chain CDR 1, 2, and 3 amino acid sequences of SEQ ID NOs: 174, 175, and 176 (H chain CDRs of J142), respectively.

5. The multispecific antigen-binding molecule of claim 3, wherein the antigen-binding site of the first polypeptide comprises an antigen-binding site which comprises an H chain variable region consisting of any one of the amino acid sequences selected from the following (a1) to (a11), or an antigen-binding site functionally equivalent thereto, and the antigen-binding site of the second polypeptide comprises an antigen-binding site which comprises an H chain variable region consisting of any one of the amino acid sequences selected from the following (b1) to (b11), or an antigen-binding site functionally equivalent thereto:

(a1) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 35 (H chain variable region of Q1);

(a2) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 36 (H chain variable region of Q31);

(a3) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 37 (H chain variable region of Q1);

(a4) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 38 (H chain variable region of Q85);

(a5) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 39 (H chain variable region of Q153);

(a6) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 40 (H chain variable region of Q354);

(a7) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 41 (H chain variable region of Q360);

(a8) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 42 (H chain variable region of Q405);

(a9) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 43 (H chain variable region of Q458);

(a10) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 44 (H chain variable region of Q460);

(a11) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 45 (H chain variable region of Q499);

(b1) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 46 (H chain variable region of J232);

(b2) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 47 (H chain variable region of J259);

(b3) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 48 (H chain variable region of J268);

(b4) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 49 (H chain variable region of J300);

(b5) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 50 (H chain variable region of J321);

(b6) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 51 (H chain variable region of J326);

(b7) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 52 (H chain variable region of J327);

(b8) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 53 (H chain variable region of J339);

(b9) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 54 (H chain variable region of J344);

(b10) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 55 (H chain variable region of J346); and

(b11) an antigen-binding site comprising an H chain variable region amino acid sequence of SEQ ID NO: 172 (H chain variable region of J142).

6. The multispecific antigen-binding molecule of claim 3, wherein the antigen-binding sites included in the third polypeptide and the fourth polypeptide comprise an antigen-binding site which comprises L chain CDRs consisting of any one of the amino acid sequences selected from the following (c1) to (c10), or an antigen-binding site functionally equivalent thereto:

(c1) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 138, 139, and 140 (L chain CDR of L2), respectively;

(c2) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 141, 142, and 143 (L chain CDR of L45), respectively;

(c3) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 144, 145, and 146 (L chain CDR of L248), respectively;

(c4) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 147, 148, and 149 (L chain CDR of L324), respectively;

(c5) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 150, 151, and 152 (L chain CDR of L334), respectively;

(c6) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences

of SEQ ID NOs: 153, 154, and 155 (L chain CDR of L377), respectively;

(c7) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 156, 157, and 158 (L chain CDR of L404), respectively;

(c8) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 159, 160, and 161 (L chain CDR of L406), respectively;

(c9) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 137, 138, and 139 (L chain CDR of L408), respectively; and

(c10) an antigen-binding site comprising an L chain CDR1, 2, and 3 amino acid sequences of SEQ ID NOs: 177, 178, and 179 (L chain CDR of L180), respectively.

7. The multispecific antigen-binding molecule of claim 3, wherein the antigen-binding sites included in the third polypeptide and the fourth polypeptide comprise an antigen-binding site which comprises an L chain variable region consisting of any one of the amino acid sequences selected from the following (c1) to (c10), or an antigen-binding site functionally equivalent thereto:

(c1) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 56 (L chain variable region of L2);

(c2) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 57 (L chain variable region of L45);

(c3) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 58 (L chain variable region of L248);

(c4) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 59 (L chain variable region of L324);

(c5) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 60 (L chain variable region of L334);

(c6) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 61 (L chain variable region of L377);

(c7) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 62 (L chain variable region of L404);

(c8) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 63 (L chain variable region of L406);

(c9) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 64 (L chain variable region of L408); and

(c10) an antigen-binding site comprising an L chain variable region amino acid sequence of SEQ ID NO: 173 (L chain variable region of L180).

8. The multispecific antigen-binding molecule of claim 3, wherein the first and second polypeptides further comprise an antibody H chain constant region, and the third and fourth polypeptides comprise an antibody L chain constant region.

9. The multispecific antigen-binding molecule of claim 3, wherein the first and second polypeptides comprise an antibody H chain constant region, and the third and fourth polypeptides comprise an antibody L chain constant region, and wherein the third polypeptide and the fourth polypeptide are a commonly shared L chain.

10. The multispecific antigen-binding molecule of claim 8 or 9, wherein the first polypeptide comprises an antibody H chain constant region consisting of any one of the amino acid sequences selected from the group consisting of the following (d1) to (d6) or the group consisting of the following (d7) to (d9), and the second polypeptide comprises an antibody H chain constant region consisting of any one of the amino acid sequences selected from a group different from that of the above-mentioned first polypeptide:

(d1) an H chain constant region of SEQ ID NO: 65 (G4k);
(d2) an H chain constant region of SEQ ID NO: 66 (z7);
(d3) an H chain constant region of SEQ ID NO: 67 (z55);
(d4) an H chain constant region of SEQ ID NO: 68 (z106);
(d5) an H chain constant region of SEQ ID NO: 69 (z118);
(d6) an H chain constant region of SEQ ID NO: 70 (z121);
(d7) an H chain constant region of SEQ ID NO: 71 (G4h);
(d8) an H chain constant region of SEQ ID NO: 72 (z107); and
(d9) an H chain constant region of SEQ ID NO: 73 (z119).

11. The multispecific antigen-binding molecule of claim 8 or 9, wherein the third and fourth polypeptides comprise the antibody L chain constant region consisting of the following amino acid sequence of:
(e) an L chain constant region of SEQ ID NO: 74 (k).

12. The multispecific antigen-binding molecule of claim 8 or 9, wherein the first polypeptide comprises any one antibody H chain selected from the following (a1) to (a14), the second polypeptide comprises any one antibody H chain selected from the following (b1) to (b12), and the third polypeptide and the fourth polypeptide comprise any one antibody L chain selected from the following (c1) to (c10):

(a1) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 1 (Q1-

G4k);

(a2) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 2 (Q31-z7);

(a3) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 3 (Q64-z55);

(a4) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 10 (Q64-z7);

(a5) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 11 (Q85-G4k);

(a6) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 12 (Q153-G4k);

(a7) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 13 (Q354-z106);

(a8) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 14 (Q360-G4k);

(a9) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 15 (Q360-z118);

(a10) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 16 (Q405-G4k);

(a11) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 17 (Q458-z106);

(a12) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 18 (Q460-z121);

(a13) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 19 (Q499-z118);

(a14) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 20 (Q499-z121);

(b1) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 4 (J268-G4h);

(b2) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 5 (J321-G4h);

(b3) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 6 (J326-z107);

(b4) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 7 (J344-z107);

(b5) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 21 (J232-

G4h);

(b6) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 22 (J259-z107);

(b7) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 23 (J300-z107);

(b8) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 24 (J327-z107);

(b9) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 25 (J327-z119);

(b10) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 26 (J339-z119);

(b11) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 27 (J346-z107);

(b12) an antibody H chain consisting of the amino acid sequence of SEQ ID NO: 170 (J142-G4h);

(c1) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 8 (L2-k);

(c2) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 9 (L45-k);

(c3) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 28 (L248-k);

(c4) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 29 (L324-k);

(c5) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 30 (L334-k);

(c6) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 31 (L377-k);

(c7) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 32 (L404-k);

(c8) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 33 (L406-k);

(c9) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 34 (L408-k); and

(c10) an antibody L chain consisting of the amino acid sequence of SEQ ID NO: 171 (L180-k).

13. The multispecific antigen-binding molecule of claim 1, wherein the first polypeptide comprises an antigen-binding site which binds to an epitope overlapping with an epitope that

binds to an antibody consisting of the antibody H chain of any one of (a1) to (a14) and the antibody L chain of any one of (c1) to (c10) of claim 12, and the second polypeptide comprises an antigen-binding site which binds to an epitope overlapping with an epitope that binds to an antibody consisting of the antibody H chain of any one of (b1) to (b12) and the antibody L chain of any one of (c1) to (c10) of claim 12.

14. The multispecific antigen-binding molecule of claim 8 or 9, wherein the first polypeptide comprises any one antibody H chain selected from the following (e1) to (e3), the second polypeptide comprises any one antibody H chain selected from the following (f1) to (f3), and the third polypeptide and the fourth polypeptide comprise any one antibody L chain selected from the following (g1) to (g4):

(e1) an H chain of an antibody which binds to an epitope overlapping with an epitope bound by an antibody consisting of an antibody H chain of any one of (a1) to (a14) and an antibody L chain of any one of (c1) to (c10), of claim 12;

(e2) an antibody H chain, wherein at least one amino acid residue selected from the amino acid residues at positions 34, 35, 49, 61, 62, 96, 98, 100, 100b, and 102 by Kabat numbering in any one antibody H chain selected from (e1) is substituted with another amino acid;

(e3) an antibody H chain, wherein by Kabat numbering, the amino acid residue at position 34 is isoleucine, the amino acid residue at position 35 is asparagine, glutamine, or serine, the amino acid residue at position 49 is serine, the amino acid residue at position 61 is arginine, the amino acid residue at position 62 is glutamic acid, the amino acid residue at position 96 is serine or threonine, the amino acid residue at position 98 is lysine or arginine, the amino acid residue at position 100 is phenylalanine or tyrosine, the amino acid residue at position 100b is glycine, or the amino acid residue at position 102 is tyrosine in any antibody H chain selected from (e1);

(f1) an H chain of an antibody which binds to an epitope overlapping with an epitope bound by an antibody consisting of an antibody H chain of any of (b1) to (b12) of claim 12 and an antibody L chain of any of (c1) to (c10) of claim 12;

(f2) an antibody H chain, wherein at least one amino acid residue selected from the amino acid residues at positions 35, 53, 73, 76, 96, 98, 100, and 100a by Kabat numbering in any antibody H chain of (f1) is substituted with another amino acid;

(f3) an antibody H chain, wherein by Kabat numbering, the amino acid residue at position 35 is aspartic acid, the amino acid residue at position 53 is arginine, the amino acid residue at position 73 is lysine, the amino acid residue at position 76 is glycine, the

amino acid residue at position 96 is lysine or arginine, the amino acid residue at position 98 is tyrosine, the amino acid residue at position 100 is tyrosine, or the amino acid residue at position 100a is histidine in any one antibody H chain selected from (f1);

(g1) an L chain of an antibody which binds to an epitope overlapping with an epitope bound by an antibody which consists of an antibody H chain of any one of (a1) to (a14) and an antibody L chain of any one of (c1) to (c10), of claim 12;

(g2) an L chain of an antibody which binds to an epitope overlapping with an epitope bound by an antibody which consists of an antibody H chain of any one of (b1) to (b12) and an antibody L chain of any one of (c1) to (c10), of claim 12;

(g3) an antibody L chain, wherein at least one amino acid residue selected from the amino acid residues at positions 27, 30, 31, 32, 50, 52, 53, 54, 55, 92, 93, 94, and 95 by Kabat numbering in the antibody L chain of either (g1) or (g2) is substituted with another amino acid; and

(g4) an antibody L chain, wherein by Kabat numbering, the amino acid residue at position 27 is lysine or arginine, the amino acid residue at position 30 is glutamic acid, the amino acid residue at position 31 is arginine, the amino acid residue at position 32 is glutamine, the amino acid residue at position 50 is arginine or glutamine, the amino acid residue at position 52 is serine, the amino acid residue at position 53 is arginine, the amino acid residue at position 54 is lysine, the amino acid residue at position 55 is glutamic acid, the amino acid residue at position 92 is serine, the amino acid residue at position 93 is serine, the amino acid residue at position 94 is proline, or the amino acid residue at position 95 is proline in the antibody L chain of either (g1) or (g2).

15. The multispecific antigen-binding molecule of any one of claims 1 to 14, wherein the multispecific antigen-binding molecule is a multispecific antibody.

16. A bispecific antibody of any one of the following (a) to (u):

(a) a bispecific antibody (Q1-G4k/J268-G4h/L45-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 1, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 4, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 9;

(b) a bispecific antibody (Q1-G4k/J321-G4h/L45-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 1, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 5, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 9;

(c) a bispecific antibody (Q31-z7/J326-z107/L2-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 2, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 6, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 8;

(d) a bispecific antibody (Q64-z55/J344-z107/L45-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 3, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 7, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 9;

(e) a bispecific antibody (Q64-z7/J326-z107/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 10, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 6, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(f) a bispecific antibody (Q64-z7/J344-z107/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 10, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 7, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(g) a bispecific antibody (Q85-G4k/J268-G4h/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 11, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 4, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(h) a bispecific antibody (Q85-G4k/J321-G4h/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 11, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 5, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(i) a bispecific antibody (Q153-G4k/J232-G4h/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 12, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 21, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(j) a bispecific antibody (Q354-z106/J259-z107/L324-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 13, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 22, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 29;

(k) a bispecific antibody (Q360-G4k/J232-G4h/L406-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 14, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 21, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 33;

(l) a bispecific antibody (Q360-z118/J300-z107/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 15, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 23, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(m) a bispecific antibody (Q405-G4k/J232-G4h/L248-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 16, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 21, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 28;

(n) a bispecific antibody (Q458-z106/J346-z107/L408-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 17, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 27, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 34;

(o) a bispecific antibody (Q460-z121/J327-z119/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 18, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 25, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(p) a bispecific antibody (Q499-z118/J327-z107/L334-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 19, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 24, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 30;

(q) a bispecific antibody (Q499-z118/J327-z107/L377-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 19, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 24, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 31;

(r) a bispecific antibody (Q499-z118/J346-z107/L248-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 19, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 27, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 28;

(s) a bispecific antibody (Q499-z121/J327-z119/L404-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 20, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 25, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 32;

(t) a bispecific antibody (Q499-z121/J339-z119/L377-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 20, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 26, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 31;

and

(u) a bispecific antibody (Q153-G4k/J142-G4h/L180-k), wherein the first polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 12, the second polypeptide is an H chain consisting of the amino acid sequence of SEQ ID NO: 170, and the third polypeptide and the fourth polypeptide are a commonly shared L chain of SEQ ID NO: 171.

17. A nucleic acid encoding the multispecific antigen-binding molecule of any one of claims 1 to 15 or the bispecific antibody of claim 16.

18. A vector inserted with the nucleic acid of claim 17.

19. A cell comprising the nucleic acid of claim 17 or the vector of claim 18.

20. A method for producing the multispecific antigen-binding molecule of any one of claims 1 to 15 or the bispecific antibody of claim 16 by culturing the cell of claim 19.

21. A pharmaceutical composition comprising the multispecific antigen-binding molecule of any one of claims 1 to 15 or the bispecific antibody of claim 16, and a pharmaceutically acceptable carrier.

22. The composition of claim 21, which is a pharmaceutical composition used for prevention and/or treatment of bleeding, a disease accompanying bleeding, or a disease caused by bleeding.

23. The composition of claim 22, wherein the bleeding, the disease accompanying bleeding, or the disease caused by bleeding is a disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII.

24. The composition of claim 23, wherein the disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is hemophilia A.

25. The composition of claim 23, wherein the disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is a disease showing emergence of an inhibitor against blood coagulation

factor VIII and/or activated blood coagulation factor VIII.

26. The composition of claim 23, wherein the disease that develops and/or progresses due to a decrease or deficiency in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is acquired hemophilia.

27. The composition of claim 23, wherein the disease that develops and/or progresses due to a decrease in the activity of blood coagulation factor VIII and/or activated blood coagulation factor VIII is von Willebrand disease.

28. A method for preventing and/or treating bleeding, a disease accompanying bleeding, or a disease caused by bleeding, which comprises the step of administering the multispecific antigen-binding molecule of any one of claims 1 to 15 or the bispecific antibody of claim 16, or the composition of any one of claims 21 to 27.

29. A kit for use in the prevention and/or treatment method of claim 28, which comprises at least the multispecific antigen-binding molecule of any one of claims 1 to 15 or the bispecific antibody of claim 16, or the composition of any one of claims 21 to 27.