

NO: 236, SEQ ID NO: 265, SEQ ID NO: 270, SEQ ID NO: 275, SEQ ID NO: 306, SEQ ID NO: 296, SEQ ID NO: 241, SEQ ID NO: 314, and SEQ ID NO: 223; wherein the antibody or antigen-binding fragment thereof binds to CLEC2D.

[012] The disclosure provides isolated antibodies or antigen-binding fragments thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a sequence selected from any one of SEQ ID NOs: 1-108.

[013] The disclosure provides isolated antibodies or antigen-binding fragments thereof comprising a heavy chain and a light chain, wherein the light chain comprises a sequence selected from any one of SEQ ID NOs: 217-324.

[014] The disclosure provides isolated antibodies or antigen-binding fragments thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a sequence selected from any one of SEQ ID NOs: 1-108, and the light chain comprises a sequence selected from any one of SEQ ID NOs: 217-324.

[015] The disclosure provides isolated antibodies or antigen-binding fragments thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises: (i) a heavy chain (HC) CDR1 comprising a sequence selected from SEQ ID NOs: 433-485; (ii) an HC CDR2 comprising a sequence selected from SEQ ID NOs: 486-546; and (iii) an HC CDR3 comprising a sequence selected from SEQ ID NOs: 547-653, wherein the antibody or antigen-binding fragment thereof binds to CLEC2D.

[016] The disclosure provides isolated antibodies or antigen-binding fragments thereof comprising a heavy chain and a light chain, wherein the light chain comprises: (i) a light chain (LC) CDR1 comprising a sequence selected from SEQ ID NOs: 654-726; (ii) an LC CDR2 comprising a sequence selected from SEQ ID NOs: 727-783; and (iii) an LC CDR3 comprising a sequence selected from SEQ ID NOs: 784-885; wherein the antibody or antigen-binding fragment thereof binds to CLEC2D.

[017] The disclosure provides isolated antibodies or antigen-binding fragments thereof, comprising: a heavy chain comprising an HC CDR1 sequence selected from SEQ ID NOs: 433-485, an HC CDR2 sequence selected from SEQ ID NOs: 486-546, and an HC CDR3 sequence selected from SEQ ID NOs: 547-653; a light chain comprising a LC CDR1 sequence selected from SEQ ID NOs: 654-726, a LC CDR2 sequence selected from SEQ ID NOs: 727-783, and a LC CDR3 sequence selected from SEQ ID NOs: 784-885; or a combination thereof.

[017a] In one aspect, the present disclosure refers to an isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a sequence selected from the group consisting of:

- a. a sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 46, SEQ ID NO: 65, SEQ ID NO: 59, and SEQ ID NO: 99;
- b. a sequence that is at least 80%, at least 81%, at least 82%, at least 83% , at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 57, SEQ ID NO: 91, SEQ ID NO: 98, SEQ ID NO: 84, SEQ ID NO: 58, SEQ ID NO: 88, SEQ ID NO: 96, SEQ ID NO: 47, SEQ ID NO: 17, and SEQ ID NO: 8;
- c. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 93, SEQ ID NO: 53, SEQ ID NO: 95, SEQ ID NO: 23, SEQ ID NO: 103, and SEQ ID NO: 7;
- d. a sequence that is at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 45, SEQ ID NO: 15, SEQ ID NO: 51, SEQ ID NO: 44, SEQ ID NO: 73, SEQ ID NO: 36, SEQ ID NO: 77, SEQ ID NO: 50, and SEQ ID NO: 6;
- e. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 97, SEQ ID NO: 16, SEQ ID NO: 76, SEQ ID NO: 9, SEQ ID NO: 89, SEQ ID NO: 107, SEQ ID NO: 68, SEQ ID NO: 29, SEQ ID NO: 67, SEQ ID NO: 74, SEQ ID NO: 32, SEQ ID NO: 81, SEQ ID NO: 106, SEQ ID NO: 31, SEQ ID NO: 62, SEQ ID NO: 48, SEQ ID NO: 75, SEQ ID NO: 12, SEQ ID

NO: 102, SEQ ID NO: 54, SEQ ID NO: 80, SEQ ID NO: 26, SEQ ID NO: 30, SEQ ID NO: 92, SEQ ID NO: 108, and SEQ ID NO: 79;

- f. a sequence that is at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 105, SEQ ID NO: 101, SEQ ID NO: 4, SEQ ID NO: 72, SEQ ID NO: 28, SEQ ID NO: 64, SEQ ID NO: 25, SEQ ID NO: 60, SEQ ID NO: 55, SEQ ID NO: 52, SEQ ID NO: 27, SEQ ID NO: 43, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 14, SEQ ID NO: 85, SEQ ID NO: 13, SEQ ID NO: 61, SEQ ID NO: 42, SEQ ID NO: 39, SEQ ID NO: 10, SEQ ID NO: 49, SEQ ID NO: 24, SEQ ID NO: 40, SEQ ID NO: 63, SEQ ID NO: 78, SEQ ID NO: 2, SEQ ID NO: 94, and SEQ ID NO: 5;
 - g. a sequence that is at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 11, SEQ ID NO: 35, SEQ ID NO: 86, SEQ ID NO: 22, SEQ ID NO: 69, SEQ ID NO: 41, SEQ ID NO: 3, SEQ ID NO: 66, SEQ ID NO: 37, SEQ ID NO: 56, SEQ ID NO: 21, SEQ ID NO: 38, SEQ ID NO: 90, SEQ ID NO: 100, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 83, SEQ ID NO: 1, and SEQ ID NO: 19; and
 - h. a sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 87, SEQ ID NO: 82, and SEQ ID NO: 104, or
- wherein the light chain comprises a sequence selected from the group consisting of:
- a. a sequence that is at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at

- least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 218, SEQ ID NO: 249, SEQ ID NO: 230, SEQ ID NO: 279, SEQ ID NO: 316, SEQ ID NO: 237, SEQ ID NO: 322, SEQ ID NO: 225, SEQ ID NO: 318, SEQ ID NO: 233, SEQ ID NO: 305, SEQ ID NO: 280, SEQ ID NO: 283, SEQ ID NO: 242, SEQ ID NO: 286, SEQ ID NO: 297, SEQ ID NO: 309, and SEQ ID NO: 246;
- b. a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 222, SEQ ID NO: 258, SEQ ID NO: 219, SEQ ID NO: 313, SEQ ID NO: 294, SEQ ID NO: 303, SEQ ID NO: 317, SEQ ID NO: 273, SEQ ID NO: 266, SEQ ID NO: 315, SEQ ID NO: 257, SEQ ID NO: 288, SEQ ID NO: 301, SEQ ID NO: 221, SEQ ID NO: 240, SEQ ID NO: 299, SEQ ID NO: 247, SEQ ID NO: 263, and SEQ ID NO: 274;
- c. a sequence that is at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 231, SEQ ID NO: 250, SEQ ID NO: 260, SEQ ID NO: 226, SEQ ID NO: 271, SEQ ID NO: 256, SEQ ID NO: 272, SEQ ID NO: 278, SEQ ID NO: 302, SEQ ID NO: 320, SEQ ID NO: 295, SEQ ID NO: 292, SEQ ID NO: 229, SEQ ID NO: 264, SEQ ID NO: 252, SEQ ID NO: 267, SEQ ID NO: 304, SEQ ID NO: 300, SEQ ID NO: 311, and SEQ ID NO: 324;
- d. a sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 259, SEQ ID NO: 239, SEQ ID NO: 281, SEQ ID NO: 228, SEQ ID NO: 217, SEQ ID NO: 227, and SEQ ID NO: 251;
- e. a sequence that is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 307, SEQ ID NO: 262, SEQ

- ID NO: 253, SEQ ID NO: 276, SEQ ID NO: 323, SEQ ID NO: 234, SEQ ID NO: 261, SEQ ID NO: 312, and SEQ ID NO: 290;
- f. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 254, SEQ ID NO: 289, SEQ ID NO: 238, SEQ ID NO: 268, SEQ ID NO: 248, SEQ ID NO: 284, SEQ ID NO: 244, SEQ ID NO: 310, SEQ ID NO: 243, SEQ ID NO: 285, SEQ ID NO: 220, SEQ ID NO: 255, SEQ ID NO: 293, SEQ ID NO: 298, SEQ ID NO: 235, SEQ ID NO: 319, SEQ ID NO: 245, SEQ ID NO: 224, SEQ ID NO: 291, SEQ ID NO: 277, and SEQ ID NO: 232; and
 - g. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 282, SEQ ID NO: 308, SEQ ID NO: 287, SEQ ID NO: 321, SEQ ID NO: 236, SEQ ID NO: 265, SEQ ID NO: 270, SEQ ID NO: 275, SEQ ID NO: 306, SEQ ID NO: 296, SEQ ID NO: 241, SEQ ID NO: 314, and SEQ ID NO: 223; or
- wherein
- (1) the heavy chain comprises a sequence selected from:
- i. a sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 46, SEQ ID NO: 65, SEQ ID NO: 59, and SEQ ID NO: 99;
 - ii. a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 57, SEQ ID NO: 91, SEQ ID NO: 98, SEQ ID NO: 84, SEQ ID NO: 58, SEQ ID NO: 88, SEQ ID NO: 96, SEQ ID NO: 47, SEQ ID NO: 17, and SEQ ID NO: 8;

- iii. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 93, SEQ ID NO: 53, SEQ ID NO: 95, SEQ ID NO: 23, SEQ ID NO: 103, and SEQ ID NO: 7;
- iv. a sequence that is at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 45, SEQ ID NO: 15, SEQ ID NO: 51, SEQ ID NO: 44, SEQ ID NO: 73, SEQ ID NO: 36, SEQ ID NO: 77, SEQ ID NO: 50, and SEQ ID NO: 6;
- v. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 97, SEQ ID NO: 16, SEQ ID NO: 76, SEQ ID NO: 9, SEQ ID NO: 89, SEQ ID NO: 107, SEQ ID NO: 68, SEQ ID NO: 29, SEQ ID NO: 67, SEQ ID NO: 74, SEQ ID NO: 32, SEQ ID NO: 81, SEQ ID NO: 106, SEQ ID NO: 31, SEQ ID NO: 62, SEQ ID NO: 48, SEQ ID NO: 75, SEQ ID NO: 12, SEQ ID NO: 102, SEQ ID NO: 54, SEQ ID NO: 80, SEQ ID NO: 26, SEQ ID NO: 30, SEQ ID NO: 92, SEQ ID NO: 108, and SEQ ID NO: 79;
- vi. a sequence that is at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 105, SEQ ID NO: 101, SEQ ID NO: 4, SEQ ID NO: 72, SEQ ID NO: 28, SEQ ID NO: 64, SEQ ID NO: 25, SEQ ID NO: 60, SEQ ID NO: 55, SEQ ID NO: 52, SEQ ID NO:

27, SEQ ID NO: 43, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 14, SEQ ID NO: 85, SEQ ID NO: 13, SEQ ID NO: 61, SEQ ID NO: 42, SEQ ID NO: 39, SEQ ID NO: 10, SEQ ID NO: 49, SEQ ID NO: 24, SEQ ID NO: 40, SEQ ID NO: 63, SEQ ID NO: 78, SEQ ID NO: 2, SEQ ID NO: 94, and SEQ ID NO: 5;

vii. a sequence that is at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 11, SEQ ID NO: 35, SEQ ID NO: 86, SEQ ID NO: 22, SEQ ID NO: 69, SEQ ID NO: 41, SEQ ID NO: 3, SEQ ID NO: 66, SEQ ID NO: 37, SEQ ID NO: 56, SEQ ID NO: 21, SEQ ID NO: 38, SEQ ID NO: 90, SEQ ID NO: 100, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 83, SEQ ID NO: 1, and SEQ ID NO: 19; and

viii. a sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 87, SEQ ID NO: 82, and SEQ ID NO: 104; and

(2) the light chain comprises a sequence selected from:

ix. a sequence that is at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 218, SEQ ID NO: 249, SEQ ID NO: 230, SEQ ID NO: 279, SEQ ID NO: 316, SEQ ID NO: 237, SEQ ID NO: 322, SEQ ID NO: 225, SEQ ID NO: 318, SEQ ID NO: 233, SEQ ID NO: 305, SEQ ID NO: 280, SEQ ID NO: 283, SEQ ID NO: 242, SEQ ID NO: 286, SEQ ID NO: 297, SEQ ID NO: 309, and SEQ ID NO: 246;

- x. a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 222, SEQ ID NO: 258, SEQ ID NO: 219, SEQ ID NO: 313, SEQ ID NO: 294, SEQ ID NO: 303, SEQ ID NO: 317, SEQ ID NO: 273, SEQ ID NO: 266, SEQ ID NO: 315, SEQ ID NO: 257, SEQ ID NO: 288, SEQ ID NO: 301, SEQ ID NO: 221, SEQ ID NO: 240, SEQ ID NO: 299, SEQ ID NO: 247, SEQ ID NO: 263, and SEQ ID NO: 274;
- xi. a sequence that is at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 231, SEQ ID NO: 250, SEQ ID NO: 260, SEQ ID NO: 226, SEQ ID NO: 271, SEQ ID NO: 256, SEQ ID NO: 272, SEQ ID NO: 278, SEQ ID NO: 302, SEQ ID NO: 320, SEQ ID NO: 295, SEQ ID NO: 292, SEQ ID NO: 229, SEQ ID NO: 264, SEQ ID NO: 252, SEQ ID NO: 267, SEQ ID NO: 304, SEQ ID NO: 300, SEQ ID NO: 311, and SEQ ID NO: 324;
- xii. a sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 259, SEQ ID NO: 239, SEQ ID NO: 281, SEQ ID NO: 228, SEQ ID NO: 217, SEQ ID NO: 227, and SEQ ID NO: 251;
- xiii. a sequence that is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 307, SEQ ID NO: 262, SEQ ID NO: 253, SEQ ID NO: 276, SEQ ID NO: 323, SEQ ID NO: 234, SEQ ID NO: 261, SEQ ID NO: 312, and SEQ ID NO: 290;

- xiv. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 254, SEQ ID NO: 289, SEQ ID NO: 238, SEQ ID NO: 268, SEQ ID NO: 248, SEQ ID NO: 284, SEQ ID NO: 244, SEQ ID NO: 310, SEQ ID NO: 243, SEQ ID NO: 285, SEQ ID NO: 220, SEQ ID NO: 255, SEQ ID NO: 293, SEQ ID NO: 298, SEQ ID NO: 235, SEQ ID NO: 319, SEQ ID NO: 245, SEQ ID NO: 224, SEQ ID NO: 291, SEQ ID NO: 277, and SEQ ID NO: 232; and
- xv. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 282, SEQ ID NO: 308, SEQ ID NO: 287, SEQ ID NO: 321, SEQ ID NO: 236, SEQ ID NO: 265, SEQ ID NO: 270, SEQ ID NO: 275, SEQ ID NO: 306, SEQ ID NO: 296, SEQ ID NO: 241, SEQ ID NO: 314, and SEQ ID NO: 223; or

wherein the heavy chain comprises a sequence selected from any one of SEQ ID NOs: 1-108; or

wherein the light chain comprises a sequence selected from any one of SEQ ID NOs: 217-324; or

wherein the heavy chain comprises a sequence selected from any one of SEQ ID NOs: 1-108, and the light chain comprises a sequence selected from any one of SEQ ID NOs: 217-324; or

wherein the heavy chain comprises:

(i) a heavy chain (HC) CDR1 comprising a sequence selected from SEQ ID NOs: 433-485;

(ii) an HC CDR2 comprising a sequence selected from SEQ ID NOs: 486-546; and

(iii) an HC CDR3 comprising a sequence selected from SEQ ID NOs: 547-653; or

wherein the light chain comprises:

(i) a light chain (LC) CDR1 comprising a sequence selected from SEQ ID NOs: 654-726;

(ii) an LC CDR2 comprising a sequence selected from SEQ ID NOs: 727-783; and

(iii) an LC CDR3 comprising a sequence selected from SEQ ID NOs: 784-885; or

wherein the isolated antibody or antigen-binding fragment thereof comprises a heavy chain comprising an HC CDR1 sequence selected from SEQ ID NOs: 433-485, an HC CDR2 sequence selected from SEQ ID NOs: 486-546, and an HC CDR3 sequence selected from SEQ ID NOs: 547-653; a light chain comprising a LC CDR1 sequence selected from SEQ ID NOs: 654-726, a LC CDR2 sequence selected from SEQ ID NOs: 727-783, and a LC CDR3 sequence selected from SEQ ID NOs: 784-885; or a combination thereof,

wherein the antibody or antigen-binding fragment thereof binds to C-Type Lectin Domain Family 2 Member D (CLEC2D).

[018] In some examples of the antibodies or antigen binding fragments thereof of the disclosure, the antibody or antigen-binding fragment thereof binds to: a human CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 886-909; a human CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 930-1003; a cynomolgus CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 918-920; a mouse CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 911-915; a rat CLEC2D polypeptide comprising a sequence of SEQ ID NO: 910; and/or a dog CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 916-917.

[019] The disclosure provides an isolated antibody or antigen-binding fragment thereof, comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain complementarity determining region (CDRH) 1, CDRH2 and CDRH3 amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, as disclosed in Table 9A, and wherein the light chain comprises a light chain complementarity determining region (CDRL)1, CDRL2 and CDRL3 amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, as disclosed in Table 9A.

[020] The disclosure provides an isolated antibody or antigen-binding fragment thereof, comprising a heavy chain and a light chain, wherein the heavy chain comprises a variable heavy chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, as disclosed in Table 9A, and wherein the light chain comprises a variable light chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, as disclosed in Table 9A.

[020a] In one aspect, the present disclosure refers to an isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain complementarity determining region (CDRH) 1, CDRH2 and CDRH3 amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-N2 in Table 9A, and wherein the light chain comprises a light chain complementarity determining region (CDRL)1, CDRL2 and CDRL3 amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-N2 in Table 9A, or wherein the heavy chain comprises a heavy chain amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-N2 in Table 9A, and wherein the light chain comprises a light chain amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-N2 in Table 9A.

[020b] In one aspect, the present disclosure refers to an isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain complementarity determining region (CDRH) 1, CDRH2 and CDRH3 amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A, and wherein the light chain comprises a light chain complementarity determining region (CDRL)1, CDRL2 and CDRL3 amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A, or wherein the heavy chain comprises a variable heavy chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A, and wherein the light chain comprises a variable light chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A.

[020c] In one aspect, the present disclosure refers to an isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain frame work region sequence of a Germline family of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9B, and wherein the light chain comprises a frame work region sequence of a light chain Germline family of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9B.

[021] The disclosure provides an isolated antibody or antigen-binding fragment thereof, comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain frame work region sequence of a Germline family of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9B, as disclosed herein, and wherein the light chain comprises a frame work region sequence of a light chain Germline family of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9B, as disclosed herein.

[022] In some examples of the antibodies or antigen binding fragments thereof of the disclosure, the antibody or antigen-binding fragment thereof is a monoclonal antibody.

[023] In some examples of the antibodies or antigen binding fragments thereof of the disclosure, the antibody or antigen-binding fragment thereof blocks binding of CLEC2D to a receptor. In some examples, the receptor comprises a CD161 receptor, and the CD161 receptor comprises a sequence selected from SEQ ID NOs: 921-929.

[024] In some examples of the antibodies or antigen binding fragments thereof of the disclosure, the antibody or antigen-binding fragment thereof is human, murine or chimeric. In some examples, the antigen-binding fragment is selected from the group consisting of Fv, Fav, F(ab')₂, Fab', dsFv, scFv, sc(Fv)₂, scFv-CH₃, scFv-Fc, and diabody fragments. In some examples, the antibody or antigen-binding fragment thereof binds to human CLEC2D with an affinity (K_D) of less than 100 nM.

[025] The disclosure provides pharmaceutical compositions comprising peptides (e.g., antibodies or antigen-binding fragments thereof) or nucleic acids described in the disclosure.

[026] The disclosure provides pharmaceutical compositions comprising antibodies or antigen-binding fragments thereof of the disclosure. In one aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody or antigen-binding fragment thereof as disclosed herein.

[027] The disclosure provides pharmaceutical compositions comprising nucleic acids encoding the antibodies or antigen-binding fragments thereof of the disclosure.

[028] In some examples of the pharmaceutical compositions of the disclosure, the pharmaceutical composition further comprises at least one of a buffer, a pharmaceutically acceptable diluent, a carrier, a solubilizer, an emulsifier, and a preservative.

[029] The disclosure provides isolated nucleic acids comprising a polynucleotide sequence that encodes an amino acid heavy chain sequence selected from SEQ ID NOs: 109-216.

[030] The disclosure provides isolated nucleic acids comprising a polynucleotide sequence that encodes an amino acid light chain sequence selected from SEQ ID NOs: 325-432.

[030a] In one aspect, the present disclosure refers to an isolated nucleic acid comprising a polynucleotide sequence that encodes an amino acid heavy chain sequence selected from SEQ ID NOs: 109-216, or a polynucleotide sequence that encodes an amino acid light chain sequence selected from SEQ ID NOs: 325-432, or a plurality of isolated nucleic acids comprising a first nucleic acid that encodes a polypeptide selected from SEQ ID NOs: 109-216 and a second nucleic acid that encodes a polypeptide selected from SEQ ID NOs: 325-432.

[031] The disclosure provides an isolated nucleic acid, comprising a polynucleotide sequence that encodes a heavy chain comprising a CDRH1, CDRH2 and CDRH3 amino acid sequence according to the CDRH1, CDRH2 and CDRH3 amino acid sequence respectively, of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A, as disclosed herein.

[032] The disclosure provides an isolated nucleic acid, comprising a polynucleotide sequence that encodes a light chain comprising a CDRL1, CDRL2 and CDRL3 amino acid sequence according to the CDRL1, CDRL2 and CDRL3 amino acid sequence respectively, of an anti-

CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A, as disclosed herein.

[033] The disclosure provides an isolated nucleic acid, comprising a polynucleotide sequence that encodes a heavy chain amino acid sequence according to variable heavy chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A, as disclosed herein.

[034] The disclosure provides an isolated nucleic acid, comprising a polynucleotide sequence that encodes a light chain amino acid sequence according to variable light chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A, as disclosed herein.

[035] The disclosure provides an isolated nucleic acid, comprising a polynucleotide sequence that encodes a heavy chain comprising a framework region amino acid sequence according to heavy chain framework region amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9B, as disclosed herein.

[036] The disclosure provides an isolated nucleic acid comprising a polynucleotide sequence that encodes a light chain comprising a framework region amino acid sequence according to light chain framework region amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9B, as disclosed herein.

[037] The disclosure provides isolated nucleic acids comprising a polynucleotide sequence that encodes a heavy chain amino acid sequence of an antibody or antigen binding fragment thereof of the disclosure.

[038] The disclosure provides isolated nucleic acids comprising a polynucleotide sequence that encodes a light chain amino acid sequence of an antibody or antigen binding fragment thereof of the disclosure.

[039] The disclosure provides compositions comprising a first nucleic acid that encodes a polypeptide selected from SEQ ID NOs: 109-216 and a second nucleic acid that encodes a polypeptide selected from SEQ ID NOs: 325-432.

[040] The disclosure provides vectors comprising the nucleic acids of the disclosure. In one aspect, the present disclosure refers to a vector comprising the isolated nucleic acid as disclosed herein.

[041] The disclosure provides cells comprising the nucleic acids, nucleic acid compositions or vectors of the disclosure. In some examples, the cell is a eukaryotic cell. In one aspect, the present disclosure refers to a cell comprising the isolated nucleic acid as disclosed herein or the vector as disclosed herein, wherein the cell is a eukaryotic cell. In some examples, the eukaryotic cell is a mammalian cell. In some examples, the mammalian

cell is selected from the group consisting of a CHO cell, a 293 cell, an NSO cell, a PER.C6 cell, and a B cell. In some examples, the mammalian cell is a 293-6E cell or a DG44 cell. In some examples, the cells express the antibodies or antigen binding fragments thereof of the disclosure. In some examples, the cell is a germline cell.

[042] The disclosure provides cells producing the antibodies or antigen-binding fragments thereof of the disclosure

[043] The disclosure provides a method of treating a disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibodies or antigen-binding fragments thereof of the disclosure.

[044] The disclosure provides a composition for use in treating a disease in a subject in need thereof, comprising a therapeutically effective amount of the antibodies or antigen-binding fragments thereof of the disclosure or the nucleic acids encoding the antibodies or antigen-binding fragments thereof of the disclosure.

[044a] In one aspect, the present disclosure refers to use of the isolated antibody or antigen-binding fragment thereof as disclosed herein in the manufacture of a medicament for treating a disease, modulating the activation of an immune response, or increasing the cytotoxicity of a natural killer cell or eliciting anti-tumour response in a subject in need thereof.

[045] The disclosure provides a composition for use in the manufacture of a medicament for the prevention or treatment of a disease in a subject in need thereof, comprising a therapeutically effective amount of the antibodies or antigen-binding fragments thereof of the disclosure or the nucleic acids encoding the antibodies or antigen-binding fragments thereof of the disclosure.

[046] In some examples of the methods or compositions for use of the disclosure, the disease is rheumatoid arthritis. In some examples, the subject exhibits bone loss as a result of having rheumatoid arthritis. In some examples, administration of a therapeutically effective amount of the antibody or antigen-binding fragment thereof slows or reverses the bone loss in the subject.

[047] In some examples of the methods or compositions for use of the disclosure, the disease is a cancer. In some examples, the cancer is selected from the group consisting of breast cancer, prostate cancer, endometrial cancer, uterine cancer, bladder cancer, kidney cancer, esophageal cancer, squamous cell carcinoma, uveal melanoma, glioma, glioblastoma, myeloma, pheochromocytoma, paraganglioma, follicular lymphoma, renal cell carcinoma, cervical cancer, ovarian cancer, cervical cancer, lung cancer, colorectal cancer, brain cancer, pancreatic cancer, gastric cancer, intestinal cancer, testicular cancer, skin cancer, thyroid cancer, thymoma, head and neck cancer, liver cancer, pharynx cancer, adrenocortical cancer, cholangiocarcinoma, mesothelioma, sarcoma, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, melanoma,

astrocytoma, stomach cancer, and pulmonary adenocarcinoma. In some examples, a cell of the cancer expresses CLEC2D on the cell surface. In some examples, administration of a therapeutically effective amount of the antibodies or antigen-binding fragments thereof results in an anti-tumor response in the subject.

[048] In some examples of the methods or compositions for use of the disclosure, the antibodies or antigen-binding fragments thereof are administered as a monotherapy. In some examples, the antibodies or antigen-binding fragments thereof are administered in combination with at least one of a T cell targeted immunomodulatory agent, a second immunomodulatory agent, a cancer vaccine, an adoptive cell therapy, an oncolytic virus, a second antibody therapy, a radiotherapy, an antibody drug conjugate, a small interfering RNA, a chemotherapy, an immunotherapy, an immune checkpoint inhibitor, a mitotic inhibitor, or a combination thereof. In some examples, the adoptive cell therapy comprises a CAR-T therapy. In some examples, administration of a therapeutically effective amount of the antibody or antigen-binding fragment thereof alleviates a sign or a symptom of the disease.

[049] In one aspect, the present disclosure refers to an antibody library comprising at least about 108 unique monoclonal antibody clones, wherein at least about 80% of the antibody clones detectably and specifically bind a CLEC2D antigen.

[050] In some examples of the antibody library of the disclosure, the CLEC2D antigen comprises an amino acid sequence selected from SEQ ID NOs: 886-920 and SEQ ID NOs: 930-1003. In some examples of the antibody library of the disclosure, the CLEC2D antigen comprises an amino acid sequence selected from SEQ ID NOs: 886-909 and SEQ ID NOs: 930-1003. In some examples, the CLEC2D antigen comprises a CLEC2D antigen expressed on a tumor cell surface, a variant of the CLEC2D antigen, or a homolog of the CLEC2D antigen. In some examples, the variant of the CLEC2D antigen comprises a fragment of the CLEC2D protein. In some examples, the homolog of the CLEC2D antigen comprises a human, a mouse, a dog, a rat or a cynomolgus CLEC2D.

[051] The disclosure provides a method of modulating immunity in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibodies or antigen-binding fragments of the disclosure or the nucleic acids encoding the antibodies or antigen-binding fragments thereof of the disclosure.

[052] The disclosure provides a method of modulating (e.g., increasing) innate immunity in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibodies or antigen-binding fragments of the disclosure or the nucleic acids encoding the antibodies or antigen-binding fragments thereof of the disclosure.

[053] The disclosure provides a method of increasing the cytotoxicity of a natural killer cell in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibodies or antigen-binding fragments thereof of the disclosure or the nucleic acids encoding the antibodies or antigen-binding fragments thereof of the disclosure.

[054] The disclosure provides a method of modulating (e.g., increasing) adaptive immunity in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibodies or antigen-binding fragments of the disclosure or the nucleic acids encoding the antibodies or antigen-binding fragments thereof of the disclosure.

[055] The disclosure provides methods of screening a high diversity antibody gene library for antibodies that to a CLEC2D antibody comprising: (a) inserting a library of antibody genes into a phage protein gene and transforming a plurality of phages to produce a phage library, wherein the phages in the phage library display the library of antibody genes on the surface of the phage; (b) panning the phage library with a CLEC2D antigen for individual phages that bind to the CLEC2D antigen, thereby producing an enriched phage library that is enriched for antibody genes that encode antibodies that bind to the CLEC2D antigen; (c) repeating step (b) at least once or at least twice; (d) transferring the antibody genes from the enriched phage library to a yeast surface display library; (e) isolating individual yeast cells that bind to the CLEC2D antigen from the yeast surface display library; (f) culturing the isolated individual yeast cells that bind to the CLEC2D antigen to produce yeast surface display library clones; and (g) sequencing the yeast surface display library clones; thereby isolating antibody genes that bind to the CLEC2D antigen.

[056] In some examples of the methods of screening of the disclosure, the panning step (b) comprises panning the phage library with CLEC2D coated magnetic beads. In some examples, the transferring step (d) comprises cloning the antibody genes into a yeast expression vector and transforming yeast cells. In some examples, the methods further comprise analyzing the surface expression of the antibody genes with a FLAG tag, a c-Myc tag, a polyhistidine tag or a V5 tag. In some examples, the testing step (e) comprises isolating

yeast cells expressing antibody genes that bind to the CLEC2D antigen with flow cytometry. In some examples, the method further comprises repeating the flow cytometry isolation at least 1x, at least 2x, at least 3x, at least 4x or at least 5x. In some examples, the method further comprises cloning the antibody genes that bind to CLEC2D into a mammalian expression vector.

[056a] In one aspect, the present disclosure refers to a method of screening a high diversity antibody gene library for antibodies that bind to a CLEC2D antigen, comprising: a) Inserting a library of antibody genes into a phage protein gene and transforming a plurality of phages to produce a phage library, wherein the phages in the phage library display the library of antibody genes on the surface of the phages; b) Panning the phage library with a CLEC2D antigen for individual phages that bind to the CLEC2D antigen, thereby producing an enriched phage library that is enriched for antibody genes that encode antibodies that bind to the CLEC2D antigen; c) Repeating step (b) at least once or at least twice; d) Transferring the antibody genes from the enriched phage library to a yeast surface display library; e) Isolating individual yeast cells that bind to the CLEC2D antigen from the yeast surface display library; f) Culturing the isolated individual yeast cells that bind to the CLEC2D antigen to produce yeast surface display library clones; and g) Sequencing the yeast surface display library clones; thereby isolating antibody genes that bind to the CLEC2D antigen.

[057] The disclosure provides methods of making a composition comprising anti-CLEC2D antibodies or antigen binding fragments thereof, comprising (a) transforming mammalian cells with a vector comprising a sequence encoding a promoter and a sequence encoding an anti-CLEC2D antibody or antibody fragment, wherein the sequence encoding the promoter and the anti-CLEC2D antibody or antibody fragment are operably linked; (b) culturing the mammalian cells under conditions suitable for the expression of the anti-CLEC2D antibody or antibody fragment; (c) centrifuging the cultured mammalian cells to produce a supernatant; (d) filtering the supernatant; and (e) purifying the filtered supernatant using liquid chromatography.

[057a] In one aspect, the present disclosure refers to a method of making a composition comprising an anti-CLEC2D antibody or antigen-binding fragment thereof, comprising a) Transforming mammalian cells with a vector comprising a sequence encoding a promoter and a sequence encoding an anti-CLEC2D antibody or antigen-binding fragment thereof, wherein the sequence encoding the promoter and the anti-CLEC2D antibody or antigen-binding fragment thereof are operably linked; b) Culturing the mammalian cells under conditions suitable for the expression of the anti-CLEC2D antibody or antigen-binding fragment thereof; and c) Obtaining the anti-CLEC2D antibody or antigen-binding fragment thereof from the cultured mammalian cells to produce a supernatant.

[058] In some examples of the methods of the disclosure, the filtration step (d) comprises a 3 μm - 30 μm filter. In some examples, the filtration step (d) further comprises a 0.22 μm filter. In some examples, the purifying step (e) comprises a Protein A column. In some examples, the protein A column is treated with a high salt wash buffer to remove host cell proteins. In some examples, the anti-CLEC2D antibody or fragment thereof is eluted using 30 mM Phosphate buffer at pH 3.0-4.0. In some examples, the purifying step (e) further comprises an anion exchange chromatography (AEX) step. In some examples, the AEX step comprises a Q Sepharose column. In some examples, the Q Sepharose is pre-equilibrated in a pre-equilibration buffer comprising 10-100 mM Histidine. In some examples, the pre-equilibration buffer further comprises citrate, phosphate 2-(N-morpholino)ethanesulfonic acid (MES), acetate or a combination thereof. In some examples, the pre-equilibration buffer comprises a pH of 4.5-6.5. In some examples, the anti-CLEC2D antibody is eluted at step (e) with an elution buffer comprising 200-1000 mM NaCl, KCl or a combination thereof. In some examples, the elution buffer comprises a pH of 4.5-6.5.

[059] In one example, this disclosure relates to the isolation of novel monoclonal antibodies that bind specifically to a CLEC2D antigen. The novel antibodies modulate (e.g., inhibit) the interaction of CD161 and CLEC2D to modify NK cell/immune cell mediated cytotoxicity and/or cytokine production.

[060] In another example, this disclosure relates to cancer cells expressing CLEC2D are specifically recognized by these novel antibodies which may kill the tumor cells via ADCC (antibody dependent cellular cytotoxicity) and/or CDC (complement dependent cytotoxicity) and/or ADCP (antibody dependent cellular phagocytosis).

[061] In a related example, this disclosure relates to methods of making an anti-CLEC2D antibody, comprising selecting from a high diversity antibody gene library an anti-CLEC2D antibody. In one example, the high diversity antibody gene library is displayed through phage and/or yeast surface display. In one example, the phage- and/or yeast-displayed high diversity antibody gene library is selected using purified CLEC2D antigen as a target. In one example, the selected anti-CLEC2D antibody genes are expressed in a mammalian cell (e.g., Chinese hamster ovary (CHO) cell). In one example, a single cell clone expressing an anti-CLEC2D antibody is expanded into a cell line and verified for anti-CLEC2D antibody expression. In one example, overexpression of selected antibody clones is achieved through defined culture media, supplements, and specific bioreactor processes cumulatively described herein as upstream process development. In one example, the anti-CLEC2D antibodies expressed from the cell line are purified to homogeneity, for example, through various filtration and chromatography, referred to herein as downstream purification processes.

[062] The disclosure provides a method of treating a disease in a subject in need thereof, comprising: determining a level of CLEC2D protein in the subject; and administering a therapeutically effective amount of an anti-CLEC2D antibody to the subject. In one aspect, the present disclosure refers to use of a CLEC2D antibody in the manufacture of a medicament for treating a disease in a subject in need thereof, the use comprising: a. determining the level of CLEC2D protein in the subject; and b. wherein a therapeutically effective amount of the CLEC2D antibody is to be administered to the subject.

[063] In some examples of the methods of the disclosure, the disease is a cancer. In some examples, the cancer comprises breast cancer, prostate cancer, endometrial cancer, uterine cancer, bladder cancer, kidney cancer, esophageal cancer, squamous cell carcinoma, uveal melanoma, glioma, glioblastoma, myeloma, pheochromocytoma, paraganglioma, follicular lymphoma, renal cell carcinoma, cervical cancer, ovarian cancer, cervical cancer, lung cancer, colorectal cancer, brain cancer, pancreatic cancer, gastric cancer, intestinal cancer, testicular cancer, skin cancer, thyroid cancer, thymoma, head and neck cancer, liver cancer, pharynx cancer, adrenocortical cancer, cholangiocarcinoma, mesothelioma, sarcoma, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, melanoma, astrocytoma, stomach cancer, pulmonary adenocarcinoma, adenocarcinoma, acinic cell adenocarcinoma, adrenal cortical carcinomas, alveoli cell carcinoma, anaplastic carcinoma, basaloid carcinoma, basal cell

carcinoma, bronchiolar carcinoma, bronchogenic carcinoma, renal adenocarcinoma, embryonal carcinoma, anaplastic carcinoma, fibrolamellar liver cell carcinoma, follicular carcinomas, giant cell carcinomas, hepatocellular carcinoma, intraepidermal carcinoma, intraepithelial carcinoma, leiomyosarcoma, medullary carcinoma, melanotic carcinoma, meningioma, mesonephric carcinoma, oat cell carcinoma, squamous cell carcinoma, sweat gland carcinoma, transitional cell carcinoma, tubular cell carcinoma, ameloblastic sarcoma, angiolithic sarcoma, botryoid sarcoma, endometrial stroma sarcoma, Ewing sarcoma, fascicular sarcoma, giant cell sarcoma, granulocytic sarcoma, immunoblastic sarcoma, juxtaepithelial osteogenic sarcoma, leiomyosarcoma, leukocytic sarcoma (leukemia), lymphatic sarcoma (lymphoma), medullary sarcoma, myeloid sarcoma (granulocytic sarcoma), osteogenic sarcoma, periosteal sarcoma, reticulum cell sarcoma (histiocytic lymphoma), round cell sarcoma, spindle cell sarcoma, synovial sarcoma, telangiectatic angiosarcoma, Burkitt's lymphoma, NPL, NHL, NML, NH, diffuse lymphomas, Hodgkin's lymphoma, non-Hodgkin's lymphoma, B-cell lymphoma, T-cell lymphoma, diffuse large B-cell lymphoma, acute myeloid leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, mantle cell lymphoma, and follicular lymphoma. In some examples, a cancer cell of the subject has an elevated level of CLEC2D protein when compared to a normal cell that does not have cancer. In some examples, an increased level of CLEC2D is associated with a poor prognostic outcome.

[064] In some examples of the methods of the disclosure, the disease is an autoimmune or inflammatory disorder. In some examples, the autoimmune or inflammatory disorder is type I diabetes, rheumatoid arthritis, lupus, inflammatory bowel diseases, celiac disease, Crohn disease, ulcerative Colitis, psoriasis, or multiple Sclerosis.

[065] In some examples of the methods of the disclosure, the disease is an autoimmune or inflammatory disorder. In some examples, the autoimmune disorder is type I diabetes, rheumatoid arthritis, lupus, inflammatory bowel diseases, celiac disease, Crohn disease, ulcerative Colitis, psoriasis, or multiple Sclerosis.

[066] In some examples of the methods of the disclosure, the disease is infectious disease. In some examples, the disease is HIV infection, human Cytomegalovirus infection, Hepatitis B infection, Hepatitis C infection, Ebola virus infection, Dengue, Yellow fever, Listeriosis, Tuberculosis, Cholera, Malaria, Leishmaniasis, or Trypanosoma infection.

[067] In another example, multiple *in vitro* and *in vivo* assays are used to characterize the novel antibodies produced from CHO cell lines which include, various biophysical parameters, antigen recognition, tumor cell surface binding, tumor cell death, production of cytokines, and analysis of downstream genes to define mode of action. These monoclonal antibodies are also tested for long term stability, various formulations relevant for therapeutic, prognostic and diagnostic uses in cancer, infectious diseases, autoimmune and chronic diseases. In another example, *in vivo* tumor suppression assays are carried out to establish anti-tumor activity of selected antibodies as monotherapy or in combination with other therapeutic products.

[068] In one example, this disclosure further relates to the isolation of novel and unique monoclonal antibodies that bind specifically to CLEC2D antigen. In some example, the novel antibodies influence the interaction of CD161 and CLEC2D to modify immune cell (e.g., NK cell, B-cell, or T-cell) mediated cytotoxicity and/or cytokine production. In some examples, various cancer cells, expressing CLEC2D, are recognized by these novel antibodies and have revealed cytotoxic effects through various means including, ADCC (antibody dependent cellular cytotoxicity) and/or CDC (Complement dependent cytotoxicity and/or ADCP (Antibody dependent cellular phagocytosis). In one example, the disclosure provides emphasis and postulates on the role of CLEC2D in cross-talk between lymphocytes and immune tolerance. In another example, in the realm of approved therapeutics or those in pre-clinical or clinical testing, the methods for identifying novel antibody molecules and related compositions provided herein comprise pharmaceutical features amenable to manufacturability/ developability.

[069] In one example, this disclosure relates to a method of treating a disease or disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or antigen-binding fragment thereof of, wherein the antibody is an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A and B, as disclosed herein.

[070] In one example, this disclosure relates to a method of modulating immunity in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or antigen-binding fragment, wherein the antibody is an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A and B, as disclosed herein.

[071] In one example, this disclosure relates to a method of modulating (e.g., increasing) innate immunity in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or antigen-binding fragment, wherein the antibody is an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A and B, as disclosed herein.

[072] In one example, this disclosure relates to a method of modulating (e.g., increasing) adaptive immunity in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or antigen-binding fragment, wherein the antibody is an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A and B, as disclosed herein.

[073] In one example, this disclosure relates to a method of increasing the cytotoxicity of a natural killer cell in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or antigen-binding fragment, wherein the antibody is an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2, of Table 9A and B, as disclosed herein.

BRIEF DESCRIPTION OF THE FIGURES

[074] The features of the present disclosure will become fully apparent from the following description taken in conjunction with the accompanying figures. The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawings will be provided by the Office upon request and payment of the necessary fee. With the understanding that the figures depict only several embodiments in accordance with the disclosure and are not to be considered limiting its scope, the disclosure will be described further through use of the accompanying figures.

[075] FIGS. 1A-1C illustrate present disclosure in a schematic format in: FIG. 1A, scenario wherein CLEC2D and CD161 interacts resulting in tumor cells escaping immune cells; FIG. 1B, scenario wherein interaction between CLEC2D and CD161 is blocked using an anti-CLEC2D antibody, resulting in lysis signal followed by killing of tumor cells; and FIG. 1C, scenario wherein ligation of CLEC2D antigen with anti-CLEC2D antibody resulting in activation of NK

CLAIMS

1. An isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a sequence selected from the group consisting of:
 - a. a sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 46, SEQ ID NO: 65, SEQ ID NO: 59, and SEQ ID NO: 99;
 - b. a sequence that is at least 80%, at least 81%, at least 82%, at least 83% , at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 57, SEQ ID NO: 91, SEQ ID NO: 98, SEQ ID NO: 84, SEQ ID NO: 58, SEQ ID NO: 88, SEQ ID NO: 96, SEQ ID NO: 47, SEQ ID NO: 17, and SEQ ID NO: 8;
 - c. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 93, SEQ ID NO: 53, SEQ ID NO: 95, SEQ ID NO: 23, SEQ ID NO: 103, and SEQ ID NO: 7;
 - d. a sequence that is at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 45, SEQ ID NO: 15, SEQ ID NO: 51, SEQ ID NO: 44, SEQ ID NO: 73, SEQ ID NO: 36, SEQ ID NO: 77, SEQ ID NO: 50, and SEQ ID NO: 6;
 - e. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 97, SEQ ID NO: 16, SEQ ID NO: 76, SEQ ID NO: 9, SEQ ID NO: 89, SEQ ID NO: 107, SEQ ID NO: 68, SEQ ID NO: 29, SEQ ID NO:

- 67, SEQ ID NO: 74, SEQ ID NO: 32, SEQ ID NO: 81, SEQ ID NO: 106, SEQ ID NO: 31, SEQ ID NO: 62, SEQ ID NO: 48, SEQ ID NO: 75, SEQ ID NO: 12, SEQ ID NO: 102, SEQ ID NO: 54, SEQ ID NO: 80, SEQ ID NO: 26, SEQ ID NO: 30, SEQ ID NO: 92, SEQ ID NO: 108, and SEQ ID NO: 79;
- f. a sequence that is at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 105, SEQ ID NO: 101, SEQ ID NO: 4, SEQ ID NO: 72, SEQ ID NO: 28, SEQ ID NO: 64, SEQ ID NO: 25, SEQ ID NO: 60, SEQ ID NO: 55, SEQ ID NO: 52, SEQ ID NO: 27, SEQ ID NO: 43, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 14, SEQ ID NO: 85, SEQ ID NO: 13, SEQ ID NO: 61, SEQ ID NO: 42, SEQ ID NO: 39, SEQ ID NO: 10, SEQ ID NO: 49, SEQ ID NO: 24, SEQ ID NO: 40, SEQ ID NO: 63, SEQ ID NO: 78, SEQ ID NO: 2, SEQ ID NO: 94, and SEQ ID NO: 5;
- g. a sequence that is at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 11, SEQ ID NO: 35, SEQ ID NO: 86, SEQ ID NO: 22, SEQ ID NO: 69, SEQ ID NO: 41, SEQ ID NO: 3, SEQ ID NO: 66, SEQ ID NO: 37, SEQ ID NO: 56, SEQ ID NO: 21, SEQ ID NO: 38, SEQ ID NO: 90, SEQ ID NO: 100, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 83, SEQ ID NO: 1, and SEQ ID NO: 19; and
- h. a sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical or 100% identical to a sequence selected from SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 87, SEQ ID NO: 82, and SEQ ID NO: 104, or

wherein the light chain comprises a sequence selected from the group consisting of:

- a. a sequence that is at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 218, SEQ ID NO: 249, SEQ ID NO: 230, SEQ ID NO: 279, SEQ ID NO: 316, SEQ ID NO: 237, SEQ ID NO: 322, SEQ ID NO: 225, SEQ ID NO: 318, SEQ ID NO: 233, SEQ ID NO: 305, SEQ ID NO: 280, SEQ ID NO: 283, SEQ ID NO: 242, SEQ ID NO: 286, SEQ ID NO: 297, SEQ ID NO: 309, and SEQ ID NO: 246;
- b. a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 222, SEQ ID NO: 258, SEQ ID NO: 219, SEQ ID NO: 313, SEQ ID NO: 294, SEQ ID NO: 303, SEQ ID NO: 317, SEQ ID NO: 273, SEQ ID NO: 266, SEQ ID NO: 315, SEQ ID NO: 257, SEQ ID NO: 288, SEQ ID NO: 301, SEQ ID NO: 221, SEQ ID NO: 240, SEQ ID NO: 299, SEQ ID NO: 247, SEQ ID NO: 263, and SEQ ID NO: 274;
- c. a sequence that is at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 231, SEQ ID NO: 250, SEQ ID NO: 260, SEQ ID NO: 226, SEQ ID NO: 271, SEQ ID NO: 256, SEQ ID NO: 272, SEQ ID NO: 278, SEQ ID NO: 302, SEQ ID NO: 320, SEQ ID NO: 295, SEQ ID NO: 292, SEQ ID NO: 229, SEQ ID NO: 264, SEQ ID NO: 252, SEQ ID NO: 267, SEQ ID NO: 304, SEQ ID NO: 300, SEQ ID NO: 311, and SEQ ID NO: 324;
- d. a sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 259, SEQ ID NO: 239, SEQ ID NO: 281, SEQ ID NO: 228, SEQ ID NO: 217, SEQ ID NO: 227, and SEQ ID NO: 251;
- e. a sequence that is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or

- 100% identical to a sequence selected from SEQ ID NO: 307, SEQ ID NO: 262, SEQ ID NO: 253, SEQ ID NO: 276, SEQ ID NO: 323, SEQ ID NO: 234, SEQ ID NO: 261, SEQ ID NO: 312, and SEQ ID NO: 290;
- f. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 254, SEQ ID NO: 289, SEQ ID NO: 238, SEQ ID NO: 268, SEQ ID NO: 248, SEQ ID NO: 284, SEQ ID NO: 244, SEQ ID NO: 310, SEQ ID NO: 243, SEQ ID NO: 285, SEQ ID NO: 220, SEQ ID NO: 255, SEQ ID NO: 293, SEQ ID NO: 298, SEQ ID NO: 235, SEQ ID NO: 319, SEQ ID NO: 245, SEQ ID NO: 224, SEQ ID NO: 291, SEQ ID NO: 277, and SEQ ID NO: 232; and
 - g. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 282, SEQ ID NO: 308, SEQ ID NO: 287, SEQ ID NO: 321, SEQ ID NO: 236, SEQ ID NO: 265, SEQ ID NO: 270, SEQ ID NO: 275, SEQ ID NO: 306, SEQ ID NO: 296, SEQ ID NO: 241, SEQ ID NO: 314, and SEQ ID NO: 223; or

wherein

(1) the heavy chain comprises a sequence selected from:

- i. a sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 46, SEQ ID NO: 65, SEQ ID NO: 59, and SEQ ID NO: 99;
- ii. a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 57, SEQ ID NO: 91, SEQ ID NO: 98, SEQ ID NO: 84, SEQ ID NO: 58, SEQ ID NO: 88, SEQ ID NO: 96, SEQ ID NO: 47, SEQ ID NO: 17, and SEQ ID NO: 8;

- iii. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 93, SEQ ID NO: 53, SEQ ID NO: 95, SEQ ID NO: 23, SEQ ID NO: 103, and SEQ ID NO: 7;
- iv. a sequence that is at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 45, SEQ ID NO: 15, SEQ ID NO: 51, SEQ ID NO: 44, SEQ ID NO: 73, SEQ ID NO: 36, SEQ ID NO: 77, SEQ ID NO: 50, and SEQ ID NO: 6;
- v. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 97, SEQ ID NO: 16, SEQ ID NO: 76, SEQ ID NO: 9, SEQ ID NO: 89, SEQ ID NO: 107, SEQ ID NO: 68, SEQ ID NO: 29, SEQ ID NO: 67, SEQ ID NO: 74, SEQ ID NO: 32, SEQ ID NO: 81, SEQ ID NO: 106, SEQ ID NO: 31, SEQ ID NO: 62, SEQ ID NO: 48, SEQ ID NO: 75, SEQ ID NO: 12, SEQ ID NO: 102, SEQ ID NO: 54, SEQ ID NO: 80, SEQ ID NO: 26, SEQ ID NO: 30, SEQ ID NO: 92, SEQ ID NO: 108, and SEQ ID NO: 79;
- vi. a sequence that is at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 105, SEQ ID NO: 101, SEQ ID NO: 4, SEQ ID NO: 72, SEQ ID NO: 28, SEQ ID NO: 64, SEQ ID NO: 25, SEQ ID NO: 60, SEQ ID NO: 55, SEQ ID NO: 52, SEQ ID NO:

27, SEQ ID NO: 43, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 14, SEQ ID NO: 85, SEQ ID NO: 13, SEQ ID NO: 61, SEQ ID NO: 42, SEQ ID NO: 39, SEQ ID NO: 10, SEQ ID NO: 49, SEQ ID NO: 24, SEQ ID NO: 40, SEQ ID NO: 63, SEQ ID NO: 78, SEQ ID NO: 2, SEQ ID NO: 94, and SEQ ID NO: 5;

vii. a sequence that is at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 11, SEQ ID NO: 35, SEQ ID NO: 86, SEQ ID NO: 22, SEQ ID NO: 69, SEQ ID NO: 41, SEQ ID NO: 3, SEQ ID NO: 66, SEQ ID NO: 37, SEQ ID NO: 56, SEQ ID NO: 21, SEQ ID NO: 38, SEQ ID NO: 90, SEQ ID NO: 100, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 83, SEQ ID NO: 1, and SEQ ID NO: 19; and

viii. a sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 87, SEQ ID NO: 82, and SEQ ID NO: 104; and

(2) the light chain comprises a sequence selected from:

ix. a sequence that is at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 218, SEQ ID NO: 249, SEQ ID NO: 230, SEQ ID NO: 279, SEQ ID NO: 316, SEQ ID NO: 237, SEQ ID NO: 322, SEQ ID NO: 225, SEQ ID NO: 318, SEQ ID NO: 233, SEQ ID NO: 305, SEQ ID NO: 280, SEQ ID NO: 283, SEQ ID NO: 242, SEQ ID NO: 286, SEQ ID NO: 297, SEQ ID NO: 309, and SEQ ID NO: 246;

- x. a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 222, SEQ ID NO: 258, SEQ ID NO: 219, SEQ ID NO: 313, SEQ ID NO: 294, SEQ ID NO: 303, SEQ ID NO: 317, SEQ ID NO: 273, SEQ ID NO: 266, SEQ ID NO: 315, SEQ ID NO: 257, SEQ ID NO: 288, SEQ ID NO: 301, SEQ ID NO: 221, SEQ ID NO: 240, SEQ ID NO: 299, SEQ ID NO: 247, SEQ ID NO: 263, and SEQ ID NO: 274;
- xi. a sequence that is at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 231, SEQ ID NO: 250, SEQ ID NO: 260, SEQ ID NO: 226, SEQ ID NO: 271, SEQ ID NO: 256, SEQ ID NO: 272, SEQ ID NO: 278, SEQ ID NO: 302, SEQ ID NO: 320, SEQ ID NO: 295, SEQ ID NO: 292, SEQ ID NO: 229, SEQ ID NO: 264, SEQ ID NO: 252, SEQ ID NO: 267, SEQ ID NO: 304, SEQ ID NO: 300, SEQ ID NO: 311, and SEQ ID NO: 324;
- xii. a sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 259, SEQ ID NO: 239, SEQ ID NO: 281, SEQ ID NO: 228, SEQ ID NO: 217, SEQ ID NO: 227, and SEQ ID NO: 251;
- xiii. a sequence that is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 307, SEQ ID NO: 262, SEQ ID NO: 253, SEQ ID NO: 276, SEQ ID NO: 323, SEQ ID NO: 234, SEQ ID NO: 261, SEQ ID NO: 312, and SEQ ID NO: 290;

- xiv. a sequence that is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 254, SEQ ID NO: 289, SEQ ID NO: 238, SEQ ID NO: 268, SEQ ID NO: 248, SEQ ID NO: 284, SEQ ID NO: 244, SEQ ID NO: 310, SEQ ID NO: 243, SEQ ID NO: 285, SEQ ID NO: 220, SEQ ID NO: 255, SEQ ID NO: 293, SEQ ID NO: 298, SEQ ID NO: 235, SEQ ID NO: 319, SEQ ID NO: 245, SEQ ID NO: 224, SEQ ID NO: 291, SEQ ID NO: 277, and SEQ ID NO: 232; and
 - xv. a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.9% or 100% identical to a sequence selected from SEQ ID NO: 282, SEQ ID NO: 308, SEQ ID NO: 287, SEQ ID NO: 321, SEQ ID NO: 236, SEQ ID NO: 265, SEQ ID NO: 270, SEQ ID NO: 275, SEQ ID NO: 306, SEQ ID NO: 296, SEQ ID NO: 241, SEQ ID NO: 314, and SEQ ID NO: 223; or
- wherein the heavy chain comprises a sequence selected from any one of SEQ ID NOs: 1-108; or
- wherein the light chain comprises a sequence selected from any one of SEQ ID NOs: 217-324; or
- wherein the heavy chain comprises a sequence selected from any one of SEQ ID NOs: 1-108, and the light chain comprises a sequence selected from any one of SEQ ID NOs: 217-324; or
- wherein the heavy chain comprises:
- (i) a heavy chain (HC) CDR1 comprising a sequence selected from SEQ ID NOs: 433-485;
 - (ii) an HC CDR2 comprising a sequence selected from SEQ ID NOs: 486-546; and
 - (iii) an HC CDR3 comprising a sequence selected from SEQ ID NOs: 547-653; or
- wherein the light chain comprises:

(i) a light chain (LC) CDR1 comprising a sequence selected from SEQ ID NOs: 654-726;
(ii) an LC CDR2 comprising a sequence selected from SEQ ID NOs: 727-783; and
(iii) an LC CDR3 comprising a sequence selected from SEQ ID NOs: 784-885; or
wherein the isolated antibody or antigen-binding fragment thereof comprises a heavy chain comprising an HC CDR1 sequence selected from SEQ ID NOs: 433-485, an HC CDR2 sequence selected from SEQ ID NOs: 486-546, and an HC CDR3 sequence selected from SEQ ID NOs: 547-653; a light chain comprising a LC CDR1 sequence selected from SEQ ID NOs: 654-726, a LC CDR2 sequence selected from SEQ ID NOs: 727-783, and a LC CDR3 sequence selected from SEQ ID NOs: 784-885; or a combination thereof,
wherein the antibody or antigen-binding fragment thereof binds to C-Type Lectin Domain Family 2 Member D (CLEC2D).

2. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof binds to:
- a. a human CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 886-909 and 930-1003;
 - b. a cynomolgus CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 918-920;
 - c. a mouse CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 911-915;
 - d. a rat CLEC2D polypeptide comprising a sequence of SEQ ID NO: 910; and/or
 - e. a dog CLEC2D polypeptide comprising a sequence selected from SEQ ID NOs: 916-917.
3. An isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain complementarity determining region (CDRH) 1, CDRH2 and CDRH3 amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-N2 in Table 9A, and wherein the light chain comprises a light chain complementarity determining region (CDRL)1, CDRL2 and CDRL3 amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-N2 in Table 9A, or wherein the heavy chain comprises a heavy chain amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-

N2 in Table 9A, and wherein the light chain comprises a light chain amino acid sequence of any one of the anti-CLEC2D antibody Nos. A1-N2 in Table 9A.

4. An isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain complementarity determining region (CDRH) 1, CDRH2 and CDRH3 amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A, and wherein the light chain comprises a light chain complementarity determining region (CDRL)1, CDRL2 and CDRL3 amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A, or wherein the heavy chain comprises a variable heavy chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A, and wherein the light chain comprises a variable light chain amino acid sequence of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9A.

5. An isolated antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain frame work region sequence of a Germline family of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9B, and wherein the light chain comprises a frame work region sequence of a light chain Germline family of an anti-CLEC2D antibody selected from the group consisting of: A1, B1, E1, P1, U1, Y1, E2, I2 and L2 in Table 9B.

6. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof is afucosylated.

7. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antibody or antigen-binding fragment thereof comprises an IgG1 Fc region, an IgG2 Fc region, an IgG4 Fc region, or an IgG1 N to A Fc region.

8. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen-binding fragment thereof, recognizes and binds to conformational epitope of CLEC2D antigen, comprised of amino acids positions overlapping and/or non-overlapping with CD161 receptor interacting amino acid residues.
9. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof, comprises a variable heavy chain sequence and a variable light chain sequence, that inhibit or abrogate or compete with another antibody that recognizes and binds to conformational epitope of CLEC2D antigen, comprised of amino acids positions either overlapping and/or non-overlapping with CD161 receptor interacting amino acid residues.
10. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody or antigen-binding fragment thereof, comprises a variable heavy chain sequence and a variable light chain sequence that bind to conformational epitope of CLEC2D antigen comprising any of the amino acid positions ARG175; TYR177; GLU179; ARG153; ARG84; HIS190; ARG101; GLU150; GLN154; THR152; GLN141; SER105; ASP107; ASP92; THR93; LYS94; LYS144; GLU138; CYS176; GLN139; ARG180; SER187; LYS181; PHE116; ASN95 or a combination thereof.
11. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody or antigen-binding fragment thereof, comprises a variable heavy chain sequence and a variable light chain sequence that inhibit or abrogate or competes with, the binding of another antibody to conformational epitope of CLEC2D antigen comprising any of the amino acid positions ARG175; TYR177; GLU179; ARG153; ARG84; HIS190; ARG101; GLU150; GLN154; THR152; GLN141; SER105; ASP107; ASP92; THR93; LYS94; LYS144; GLU138; CYS176; GLN139; ARG180; SER187; LYS181; PHE116; ASN95 or a combination thereof.
12. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody or antigen-binding fragment thereof, a variable heavy chain sequence and a

variable light chain sequence that bind to conformational epitope of CLEC2D antigen comprising at least one of the amino acids positions ARG175; TYR177; GLU179; ARG153; ARG84; HIS190; ARG101; GLU150; GLN154; THR152; GLN141; SER105; ASP107; ASP92; THR93; LYS94; LYS144; GLU138; CYS176; GLN139; ARG180; SER187; LYS181; PHE116; ASN95 of SEQ ID No: 886-920 and 930-1003, constituting non-linear scaffolds for CD161 receptor interacting amino acid residues, thereby blocking the interaction between CLEC2D and CD161 receptors.

13. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody or antigen-binding fragment thereof, comprises a variable heavy chain sequence and a variable light chain sequence that bind to conformational epitope of CLEC2D antigen comprising at least one of the amino acids positions ARG175; TYR177; GLU179; ARG153; ARG84; HIS190; ARG101; GLU150; GLN154; THR152; GLN141; SER105; ASP107; ASP92; THR93; LYS94; LYS144; GLU138; CYS176; GLN139; ARG180; SER187; LYS181; PHE116; ASN95 of SEQ ID No: 886-920 and 930-1003, constituting allosteric and non-linear scaffolds for CD161 receptor non-interacting amino acid residues, thereby blocking the interaction between CLEC2D and CD161 receptors.

14. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody or antigen-binding fragment thereof, comprises a variable heavy chain sequence and a variable light chain sequence that when bound to CLEC2D selected from SEQ ID Nos: 886-920 and 930-1003, bind to at least one of the amino acids positions ARG175; TYR177; GLU179; ARG153; ARG84; HIS190; ARG101; GLU150; GLN154; THR152; GLN141; SER105; ASP107; ASP92; THR93; LYS94; LYS144; GLU138; CYS176; GLN139; ARG180 SER187; LYS181; PHE116; ASN95, independently or in combination to induce tumour killing or cytotoxicity.

15. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-14.

16. An isolated nucleic acid comprising a polynucleotide sequence that encodes an amino acid heavy chain sequence selected from SEQ ID NOs: 109-216, or a polynucleotide sequence that encodes an amino acid light chain sequence selected from SEQ ID NOs: 325-432, or a plurality of isolated nucleic acids comprising a first nucleic acid that encodes a polypeptide selected from SEQ ID NOs: 109-216 and a second nucleic acid that encodes a polypeptide selected from SEQ ID NOs: 325-432.
17. A vector comprising the isolated nucleic acid of claim 16.
18. A cell comprising the isolated nucleic acid of claim 16 or the vector of claim 17, wherein the cell is a eukaryotic cell.
19. Use of the isolated antibody or antigen-binding fragment thereof of any one of claims 1-14 in the manufacture of a medicament for treating a disease, modulating the activation of an immune response, or increasing the cytotoxicity of a natural killer cell or eliciting anti-tumour response in a subject in need thereof.
20. An antibody library comprising at least about 108 unique monoclonal antibody clones, wherein at least about 80% of the antibody clones detectably and specifically bind a CLEC2D antigen.
21. A method of screening a high diversity antibody gene library for antibodies that bind to a CLEC2D antigen, comprising:
- a) Inserting a library of antibody genes into a phage protein gene and transforming a plurality of phages to produce a phage library, wherein the phages in the phage library display the library of antibody genes on the surface of the phages;
 - b) Panning the phage library with a CLEC2D antigen for individual phages that bind to the CLEC2D antigen, thereby producing an enriched phage library that is enriched for antibody genes that encode antibodies that bind to the CLEC2D antigen;
 - c) Repeating step (b) at least once or at least twice;

- d) Transferring the antibody genes from the enriched phage library to a yeast surface display library;
- e) Isolating individual yeast cells that bind to the CLEC2D antigen from the yeast surface display library;
- f) Culturing the isolated individual yeast cells that bind to the CLEC2D antigen to produce yeast surface display library clones; and
- g) Sequencing the yeast surface display library clones;
thereby isolating antibody genes that bind to the CLEC2D antigen.

22. A method of making a composition comprising an anti-CLEC2D antibody or antigen-binding fragment thereof, comprising

- a) Transforming mammalian cells with a vector comprising a sequence encoding a promoter and a sequence encoding an anti-CLEC2D antibody or antigen-binding fragment thereof, wherein the sequence encoding the promoter and the anti-CLEC2D antibody or antigen-binding fragment thereof are operably linked;
- b) Culturing the mammalian cells under conditions suitable for the expression of the anti-CLEC2D antibody or antigen-binding fragment thereof; and
- c) Obtaining the anti-CLEC2D antibody or antigen-binding fragment thereof from the cultured mammalian cells to produce a supernatant.

23. Use of a CLEC2D antibody in the manufacture of a medicament for treating a disease in a subject in need thereof, the use comprising:

- a. determining the level of CLEC2D protein in the subject; and
- b. wherein a therapeutically effective amount of the CLEC2D antibody is to be administered to the subject.