

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 anti-CLEC2D antibody or antigen-binding fragment thereof comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), comprising:

a) a VH comprising complementarity determining regions (CDR) CDR1, CDR2, and CDR3 of SEQ ID NOs: 433, 486, and 547, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 654, 727, and 784, respectively;

b) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 590, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 688, 755, and 828, respectively;

c) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 589, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 687, 729, and 827, respectively;

d) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 466, 521, and 603, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 662, 732, and 814, respectively; or

e) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 553, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 660, 733, and 790, respectively.

[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 example, the present disclosure refers to an isolated anti-CLEC2D antibody or antigen-binding fragment thereof comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the antibody or antigen-binding fragment thereof comprises:

kk) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:450, 506, and 597, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:667, 734, and 835, respectively;
 ll) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:437, 529, and 616, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:703, 767, and 850, respectively;
 mm) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:473, 495, and 617, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:704, 768, and 851, respectively; or
 nn) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:450, 523, and 607, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs:662, 732, and 834, respectively.

[020b] In one example, the present disclosure refers to an isolated anti-CLEC2D antibody or antigen-binding fragment thereof comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH and VL comprise:

- a) SEQ ID NOs: 1 and 217, respectively;
- b) SEQ ID NOs: 45 and 261, respectively;
- c) SEQ ID NOs: 44 and 260, respectively;
- d) SEQ ID NOs: 58 and 274, respectively;
- e) SEQ ID NOs: 7 and 223, respectively;
- f) SEQ ID NOs: 42 and 258, respectively;
- h) SEQ ID NOs: 73 and 289, respectively;
- i) SEQ ID NOs: 21 and 237, respectively;
- j) SEQ ID NOs: 35 and 251, respectively;
- j) SEQ ID NOs: 75 and 291, respectively;
- k) SEQ ID NOs: 77 and 293, respectively;
- l) SEQ ID NOs: 56 and 272, respectively;
- m) SEQ ID NOs: 64 and 280, respectively;
- n) SEQ ID NOs: 50 and 266, respectively;
- o) SEQ ID NOs: 43 and 259, respectively;
- p) SEQ ID NOs: 80 and 296, respectively;
- q) SEQ ID NOs: 33 and 249, respectively;
- r) SEQ ID NOs: 23 and 239, respectively;
- s) SEQ ID NOs: 24 and 240, respectively;
- t) SEQ ID NOs: 59 and 275, respectively;
- u) SEQ ID NOs: 74 and 290, respectively;

- v) SEQ ID NOs: 25 and 241, respectively;
- w) SEQ ID NOs: 61 and 277, respectively;
- x) SEQ ID NOs: 60 and 276, respectively;
- y) SEQ ID NOs: 28 and 244, respectively;
- z) SEQ ID NOs: 4 and 220, respectively;
- aa) SEQ ID NOs: 6 and 222, respectively;
- bb) SEQ ID NOs: 46 and 262, respectively;
- cc) SEQ ID NOs: 63 and 279, respectively;
- dd) SEQ ID NOs: 57 and 273, respectively;
- ee) SEQ ID NOs: 47 and 263, respectively;
- ff) SEQ ID NOs: 83 and 299, respectively;
- gg) SEQ ID NOs: 87 and 245, respectively;
- hh) SEQ ID NOs: 81 and 297, respectively;
- ii) SEQ ID NOs: 76 and 292, respectively;
- jj) SEQ ID NOs: 36 and 252, respectively;
- kk) SEQ ID NOs: 52 and 268, respectively;
- ll) SEQ ID NOs: 71 and 287, respectively;
- mm) SEQ ID NOs: 72 and 288, respectively; or
- nn) SEQ ID NOs: 62 and 278, respectively.

[020c] In one example, the present disclosure refers to an isolated anti-CLEC2D antibody comprising a heavy chain and a light chain, wherein:

- a) the heavy chain comprises SEQ ID NO: 1481, 1913, 2129, or 2345, and the light chain comprises SEQ ID NO:1589;
- b) the heavy chain comprises SEQ ID NO:1525, 1957, 2713, or 2389, and the light chain comprises SEQ ID NO:1633;
- c) the heavy chain comprises SEQ ID NO: 1524, 1956, 2172, or 2388, and the light chain comprises SEQ ID NO:1632;
- d) the heavy chain comprises SEQ ID NO: 1538, 1970, 2186, or 2402, and the light chain comprises SEQ ID NO:1646;
- e) the heavy chain comprises SEQ ID NO: 1487, 1919, 2135, or 2351, and the light chain comprises SEQ ID NO:1595;
- f) the heavy chain comprises SEQ ID NO: 1552, 1954, 2170, or 2386, and the light chain comprises SEQ ID NO:1630;
- g) the heavy chain comprises SEQ ID NO: 1553, 1985, 2201, or 2417, and the light chain comprises SEQ ID NO:1661;
- h) the heavy chain comprises SEQ ID NO: 1501, 1933, 2149, or 2365, and the light chain comprises SEQ ID NO:1609; or
- i) the heavy chain comprises SEQ ID NO: 1515, 1947, 2163, or 2379, and the light chain comprises SEQ ID NO:1623.

[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 framework 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 framework 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.

CLAIMS

1. An isolated anti-CLEC2D antibody or antigen-binding fragment thereof comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), comprising:
 - a) a VH comprising complementarity determining regions (CDR) CDR1, CDR2, and CDR3 of SEQ ID NOs: 433, 486, and 547, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 654, 727, and 784, respectively;
 - b) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 590, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 688, 755, and 828, respectively;
 - c) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 589, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 687, 729, and 827, respectively;
 - d) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 466, 521, and 603, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 662, 732, and 814, respectively; or
 - e) a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 553, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 660, 733, and 790, respectively.

2. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 433, 486, and 547, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 654, 727, and 784, respectively, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence at least 90% identical to SEQ ID NO: 1, and a VL amino acid sequence at least 90% identical to SEQ ID NO:217, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence of SEQ ID NO: 1, and a VL amino acid sequence of SEQ ID NO:217, and optionally wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 1481, 1913, 2129, or 2345, and the light chain comprises an amino acid sequence of SEQ ID NO:1589.

3. The isolated antibody of antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 590, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 688, 755, and 828, respectively, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence at least 90% identical to SEQ ID NO: 45, and a VL amino acid sequence at least 90% identical to SEQ ID NO:261, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence of SEQ ID NO: 45, and a VL amino acid sequence of SEQ ID NO:261, and optionally wherein the heavy chain comprises an amino acid sequence of SEQ ID NO:1525, 1957, 2173, or 2389, and the light chain comprises an amino acid sequence of SEQ ID NO:1633.

4. The isolated antibody of antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 589, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 687, 729, and 827, respectively, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence at least 90% identical to SEQ ID NO: 44, and a VL amino acid sequence at least 90% identical to SEQ ID NO:260, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence of SEQ ID NO: 44, and a VL amino acid sequence of SEQ ID NO:260, and optionally wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 1524, 1956, 2172, or 2388, and the light chain comprises an amino acid sequence of SEQ ID NO:1632.

5. The isolated antibody of antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 466, 521, and 603, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 662, 732, and 814, respectively, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence at least 90% identical to SEQ ID NO: 58, and a VL amino acid sequence at least 90% identical to SEQ ID NO:274, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence of SEQ ID NO: 58, and a VL amino acid sequence of SEQ ID NO:274, and optionally

wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 1538, 1970, 2186, or 2402, and the light chain comprises an amino acid sequence of SEQ ID NO:1646.

6. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 439, 492, and 553, respectively, and a VL comprising CDR1, CDR2, and CDR3 of SEQ ID NOs: 660, 733, and 790, respectively, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence at least 90% identical to SEQ ID NO: 7, and a VL amino acid sequence at least 90% identical to SEQ ID NO:223, optionally wherein the antibody or antigen-binding fragment thereof comprises a VH amino acid sequence of SEQ ID NO: 7, and a VL amino acid sequence of SEQ ID NO:223, and optionally wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 1487, 1919, 2135, or 2351, and the light chain comprises an amino acid sequence of SEQ ID NO:1595.

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

8. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the antibody comprises an IgG1 Fc region, an IgG2 Fc region, an IgG4 Fc region, or an IgG1 Fc region comprising an N297A substitution.

9. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein:

a) the antibody or antigen-binding fragment thereof comprises a VH and a VL that bind to a 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 of SEQ ID NOs: 886-920 and 930-1003;

b) the antibody or antigen-binding fragment thereof comprises a VH and a VL that inhibit or abrogate or competes with the binding of another antibody to a 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 of SEQ ID NOs: 886-920 and 930-1003;

c) the antibody or antigen-binding fragment thereof comprises a VH and a VL that bind to a 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 NOs: 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;

d) the antibody or antigen-binding fragment thereof comprises a VH and a VL that bind to a 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 NOs: 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; and/or

e) the antibody or antigen-binding fragment thereof comprises a VH and a VL 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.

10. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-9 and a pharmaceutically acceptable excipient.

11. An isolated nucleic acid comprising a polynucleotide sequence that encodes the isolated antibody or antigen-binding fragment thereof of any one of claims 1-9.

12. An expression vector comprising the isolated nucleic acid of claim 11.
13. A host cell comprising the isolated nucleic acid of claim 11 or the expression vector of claim 12, wherein the cell is a eukaryotic cell.
14. Use of the isolated antibody or antigen-binding fragment thereof of any one of claims 1-9 or the pharmaceutical composition of claim 10 in the manufacture of a medicament for treating a cancer, modulating the activation of an immune response, increasing the cytotoxicity of a natural killer cell, or eliciting anti-tumour response in a subject in need thereof.
15. An antibody library comprising at least about 108 unique monoclonal antibody clones, wherein the antibody library comprises an isolated antibody or antigen-binding fragment thereof of any one of claims 1-9, and wherein at least about 80% of the antibody clones detectably and specifically bind a CLEC2D antigen.
16. 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,
wherein the antibody genes comprise the amino acid sequence of an isolated antibody or antigen-binding fragment thereof of any one of claims 1-9.

17. 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,
wherein the anti-CLEC2D antibody or antigen-binding fragment thereof comprises the isolated antibody or antigen-binding fragment thereof of any one of claims 1-9.

18. Use of the isolated antibody or antigen-binding fragment thereof of any one of claims 1-9 or the pharmaceutical composition of claim 10 in the manufacture of a medicament for treating a cancer in a subject in need thereof, wherein the subject in need thereof has an aberrant or differential cellular expression of CLEC2D.

19. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-9 or the pharmaceutical composition of claim 10 for use in combination with an immune checkpoint inhibitor for treating cancer, an autoimmune disorder, or an inflammatory disorder in a subject in need thereof.

20. The antibody or pharmaceutical composition for use of claim 19, wherein the immune checkpoint inhibitor is selected from the group consisting of a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a TIM-3 inhibitor, and a LAG-3 inhibitor.

21. The antibody or pharmaceutical composition for use of claim 20, wherein:

- a) the PD-1 inhibitor is selected from the group consisting of Pembrolizumab, Nivolumab, and Cemiplimab;
- b) the PD-L1 inhibitor is selected from the group consisting of Atezolizumab, Avelumab, and Durvalumab; or
- c) the CTLA-4 inhibitor is Ipilimumab.

22. The antibody or pharmaceutical composition for use of claim 21, wherein the antibody is a bispecific antibody comprising a first specificity for CLEC2D and a second specificity for an immune checkpoint protein, for use in treating cancer.

23. The antibody or pharmaceutical composition for use of claim 22, wherein the immune checkpoint protein is selected from PD-1, PD-L1, CTLA-4, TIM-3, LAG-3, TIGIT, OX40, CD137, or GITR.

24. The antibody or pharmaceutical composition for use of claim 22 or 23, further in combination with an adoptive cell therapy comprising a CAR-T cell or CAR-NK cell directed against the second antigen.

25. The antibody or pharmaceutical composition for use of any one of claims 14 or 18-24, wherein the cancer is selected from non-small cell lung cancer, melanoma, breast cancer, gastric cancer, prostate cancer, renal cell carcinoma, colorectal cancer, pancreatic cancer, lymphoma, urothelial cancer, or head and neck squamous cell carcinoma.

26. The antibody or pharmaceutical composition for use of any one of claims 14 or 18-25, further in combination with at least one additional anti-cancer therapy selected from the group consisting of chemotherapeutics, targeted small molecules, cancer vaccines, adoptive cell therapies, and oncolytic viruses.

27. The antibody or pharmaceutical composition for use of claim 26, wherein the chemotherapeutic is selected from the group consisting of taxanes, platinum-based drugs, antimetabolites, and alkylating agents.

28. The antibody or pharmaceutical composition for use of any one of claims 19-27, wherein the

autoimmune or inflammatory disorder is selected from rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, psoriasis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, ankylosing spondylitis, Sjögren's syndrome, type 1 diabetes, autoimmune uveitis, and autoimmune thyroiditis.