

cell surface and the reduced performance of ADCs against targets with low expression. Furthermore, ADC molecules often demonstrate toxicity related to free warhead, likely a result of linker degradation, resulting in maximum tolerated dose limitations and potential impacts on efficacy unrelated to the target chosen for the antibody. This is less likely to be an issue for a T cell-engaging bispecific molecule, engineered to engage DLL3 and CD3 simultaneously, given the required sensitivity of T cells for their targets, and highly potent in vitro cytotoxicity has been demonstrated on cell lines expressing several hundred target proteins per cell. Additionally, the usually smaller size of a bispecific T cell engaging antibody construct relative to a normal antibody (full-length IgG) may improve tissue penetration and increase potency due to more efficient engagement of the DLL3 and CD3 targets, resulting in improved synapse formation between the T cell and target tumor cell.

SCLC remains a significant unmet medical need, and new therapeutic options are required to improve the outlook for this sizable patient population. The above discussed bispecific antibody modality is clinically validated, and as such an antibody construct targeting DLL3 and CD3 represents a promising new possibility for the treatment of SCLC and an opportunity to improve the survival of patients suffering with this indication. As there is still a need for having available further options for the treatment of tumor or cancer diseases related to the overexpression of DLL3, there are provided herewith means and methods for the solution of this problem in the form of a bispecific antibody construct with one binding domain directed to DLL3 and a second binding domain directed to CD3 on T cells.

Summary

Thus, in a first example, the present disclosure provides a bispecific antibody construct comprising a first binding domain which binds to human DLL3 on the surface of a target cell and a second binding domain which binds to human CD3 on the surface of a T cell, wherein the first binding domain binds to an epitope of DLL3 which is comprised within the region as depicted in SEQ ID NO: 260.

In one aspect, the present disclosure provides for a polypeptide comprising a first binding domain which binds to human delta-like 3 (DLL3) on the surface of a target cell and a second binding domain which binds to human CD3 on the surface of a T cell, wherein the first binding domain binds to an epitope of DLL3 within the amino acid sequence of SEQ ID NO: 269, wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from the group

consisting of: a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 171, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 172, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 173, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 174, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 175 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 176; b) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 181, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 182, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 183, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 184, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 185 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 186; c) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 191, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 192, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 193, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 194, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 195 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 196; and d) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 201, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 202, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 203, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 204, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 205 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 206, and wherein the second binding domain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 and a VH region comprising CDR-H1, CDR-H2 and CDR-H3 selected from the group consisting of: a) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 342, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 343, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 344; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 345, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 346, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 347; b) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 351, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 352, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 353; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 354, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 355, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 356; c) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 360, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 361, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 362; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 363, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 364, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 365; d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 369, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 370, CDR-L3 comprising the amino acid sequence of SEQ

ID NO: 371; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 372, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 373, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 374; e) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 378, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 379, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 380; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 381, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 382, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 383; f) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 387, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 388, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 389; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 392; g) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 397, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 398; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 399, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 400, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 401; h) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 405, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 406, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 407; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 408, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 409, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 410; i) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 414, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 415, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 416; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 417, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 418, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 419; and j) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 423, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 424, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 425; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 426, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 427, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 428.

In another aspect, the present disclosure provides for a pharmaceutical composition comprising the polypeptide as disclosed herein and a pharmaceutical acceptable carrier.

In yet another aspect, the present disclosure provides for the polypeptide or the pharmaceutical composition as disclosed herein for use in therapy. In a further aspect, the present disclosure

provides for a use of the polypeptide as disclosed herein in the manufacture of a medicament for treating a tumor or cancer disease or a metastatic cancer disease.

In yet another aspect, the present disclosure provides for a kit comprising a polypeptide as disclosed herein and a pharmaceutically acceptable excipient.

In yet another aspect, the present disclosure provides for an antibody construct which binds to human delta-like 3 (DLL3) on the surface of a target cell and comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3, wherein the CDR-H1, CDR-H2 and CDR-H3 and CDR-L1, CDR-L2 and CDR-L3 are selected from the group consisting of: a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 171, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 172, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 173, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 174, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 175 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 176; b) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 181, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 182, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 183, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 184, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 185 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 186; c) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 191, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 192, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 193, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 194, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 195 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 196; and d) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 201, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 202, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 203, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 204, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 205 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 206.

It must be noted that as used herein, the singular forms “a”, “an”, and “the” include plural references unless the context clearly indicates otherwise. Thus, for example, reference to “a reagent” includes one or more of such different reagents and reference to “the method” includes reference to equivalent steps and methods known to those of ordinary skill in the art that could be modified or substituted for the methods described herein.

Claims

1. A polypeptide comprising a first binding domain which binds to human delta-like 3 (DLL3) on the surface of a target cell and a second binding domain which binds to human CD3 on the surface of a T cell, wherein the first binding domain binds to an epitope of DLL3 within the amino acid sequence of SEQ ID NO: 269, wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from the group consisting of:
 - a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 171, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 172, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 173, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 174, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 175 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 176;
 - b) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 181, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 182, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 183, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 184, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 185 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 186;
 - c) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 191, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 192, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 193, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 194, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 195 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 196; and
 - d) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 201, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 202, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 203, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 204, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 205 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 206,

and wherein the second binding domain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 and a VH region comprising CDR-H1, CDR-H2 and CDR-H3 selected from the group consisting of:

- a) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 342, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 343, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 344; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 345, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 346, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 347;
- b) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 351, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 352, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 353; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 354, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 355, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 356;
- c) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 360, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 361, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 362; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 363, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 364, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 365;
- d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 369, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 370, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 371; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 372, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 373, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 374;
- e) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 378, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 379, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 380; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 381, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 382, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 383;
- f) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 387, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 388, CDR-L3 comprising the

- amino acid sequence of SEQ ID NO: 389; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 392;
- g) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 397, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 398; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 399, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 400, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 401;
 - h) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 405, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 406, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 407; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 408, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 409, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 410;
 - i) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 414, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 415, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 416; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 417, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 418, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 419; and
 - j) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 423, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 424, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 425; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 426, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 427, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 428.
2. The polypeptide according to claim 1, wherein the first binding domain further binds to macaque DLL3.
 3. The polypeptide according to claim 2, wherein the first binding domain further binds to *Macaca fascicularis* DLL3.

4. The polypeptide according to any one of claims 1-3, wherein the second binding domain binds to human CD3 and macaque CD3.
5. The polypeptide according to claim 4, wherein the second binding domain binds to human CD3 epsilon and macaque CD3 epsilon.
6. The polypeptide according to any one of claims 1-5, wherein the second binding domain binds to human CD3 epsilon and to *Callithrix jacchus*, *Saguinus Oedipus* or *Saimiri sciureus* CD3 epsilon.
7. The polypeptide according to any one of claims 1-6, wherein the first binding domain comprises a VH region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 177, SEQ ID NO: 187, SEQ ID NO: 197, and SEQ ID NO: 207.
8. The polypeptide according to any one of claims 1-7, wherein the first binding domain comprises a VL region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 178, SEQ ID NO: 188, SEQ ID NO: 198, and SEQ ID NO: 208.
9. The polypeptide according to any one of claims 1-8, wherein the first binding domain comprises a VH region and a VL region comprising the pair of amino acid sequences selected from the group consisting of: SEQ ID NOs: 177 and 178, SEQ ID NOs: 187 and 188, SEQ ID NOs: 197 and 198, and SEQ ID NOs: 207 and 208.
10. The polypeptide according to any one of claims 1-9, wherein the first binding domain comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209.
11. The polypeptide according to any one of claims 1-10, wherein the second binding domain binds to one or more residues comprised within amino acid residues 1-27 of the human CD3 epsilon extracellular domain.
12. The polypeptide according to any one of claims 1-11, wherein the second binding domain comprises a VL region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 349, SEQ ID NO: 358, SEQ ID NO: 367, SEQ ID NO:

376, SEQ ID NO: 385, SEQ ID NO: 394, SEQ ID NO: 403, SEQ ID NO: 412, SEQ ID NO: 421, and SEQ ID NO: 430.

13. The polypeptide according to any one of claims 1-12, wherein the second binding domain comprises a VH region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 348, SEQ ID NO: 357, SEQ ID NO: 366, SEQ ID NO: 375, SEQ ID NO: 384, SEQ ID NO: 393, SEQ ID NO: 402, SEQ ID NO: 411, SEQ ID NO: 420, and SEQ ID NO: 429.
14. The polypeptide according to any one of claims 1-13, wherein the second binding domain comprises a VH region and a VL region comprising the pair of amino acid sequences selected from the group consisting of: SEQ ID NOs: 348 and 349; SEQ ID NOs: 357 and 358; SEQ ID NOs: 366 and 367; SEQ ID NOs: 375 and 376; SEQ ID NOs: 384 and 385; SEQ ID NOs: 393 and 394; SEQ ID NOs: 402 and 403; SEQ ID NOs: 411 and 412; SEQ ID NOs: 420 and 421; and SEQ ID NOs: 429 and 430.
15. The polypeptide according to any one of claims 1-14, wherein the second binding domain comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 350, SEQ ID NO: 359, SEQ ID NO: 368, SEQ ID NO: 377, SEQ ID NO: 386, SEQ ID NO: 395, SEQ ID NO: 404, SEQ ID NO: 413, SEQ ID NO: 422, and SEQ ID NO: 431.
16. The polypeptide according to any one of claims 1-15, wherein the polypeptide comprises a polypeptide selected from the group consisting of: SEQ ID NO: 180, SEQ ID NO: 190, SEQ ID NO: 200, and SEQ ID NO: 210.
17. The polypeptide according to any one of claims 1-16, wherein the polypeptide is in a format of two single-chain variable fragments ((scFv)₂), a scFv-single domain monoclonal antibody (Mab), or a diabody or an oligomer of any of the foregoing formats.
18. The polypeptide according to any one of claims 1-17, wherein the polypeptide comprises two single-chain variable fragments ((scFv)₂).
19. The polypeptide according to any one of claims 1-18, wherein the polypeptide further comprises a third domain that extends the serum half-life of the antibody construct.

20. The polypeptide according to claim 19, wherein the third domain comprises an Fc region.
21. A pharmaceutical composition comprising the polypeptide according to any one of claims 1-20 and a pharmaceutical acceptable carrier.
22. The polypeptide of any one of claims 1-20, or the pharmaceutical composition of claim 21 for use in therapy.
23. Use of the polypeptide according to any one of claims 1 to 20 in the manufacture of a medicament for treating a tumor or cancer disease or a metastatic cancer disease.
24. The use of claim 23, wherein the tumor or cancer disease is small cell lung cancer (SCLC), melanoma or neuroendocrine prostate cancer.
25. A kit comprising a polypeptide according to any one of claims 1-20 and a pharmaceutically acceptable excipient.
26. The kit according to claim 25, further comprising directions for use.
27. An antibody construct which binds to human delta-like 3 (DLL3) on the surface of a target cell and comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3, wherein the CDR-H1, CDR-H2 and CDR-H3 and CDR-L1, CDR-L2 and CDR-L3 are selected from the group consisting of:
 - a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 171, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 172, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 173, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 174, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 175 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 176;
 - b) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 181, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 182, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 183, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 184, CDR-L2 comprising the amino acid sequence of

- SEQ ID NO: 185 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 186;
- c) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 191, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 192, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 193, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 194, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 195 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 196; and
- d) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 201, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 202, CDR-H3 comprising the amino acid sequence of SEQ ID NO: 203, CDR-L1 comprising the amino acid sequence of SEQ ID NO: 204, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 205 and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 206.
28. The antibody construct of claim 27, comprising a pair of amino acid sequences selected from the group consisting of: SEQ ID NOs: 177 and 178, SEQ ID NOs: 187 and 188, SEQ ID NOs: 197 and 198, and SEQ ID NOs: 207 and 208.
29. The antibody construct of claim 27 or 28, wherein the antibody construct is in a format of a single-chain variable fragment (scFv) or Fab.
30. The antibody construct of any one of claims 27 to 29, wherein the antibody construct is a monoclonal antibody.