WHAT IS CLAIMED:

1. A binding moiety that specifically binds to Claudin18.2, comprising a single domain antibody or an antigen binding fragment thereof comprising:

(i) a CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:1-11 and 113-125;

(ii) a CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:12-23; and

(iii) a CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:24-37 and 126-139.

2. The binding moiety according to claim 1, wherein the single domain antibody or antigen binding fragment thereof comprises:

(1) a CDR1 comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:113; a CDR2 comprising the amino acid sequence of SEQ ID NO:12; and a CDR3 comprising the amino acid sequence of SEQ ID NO:24 or SEQ ID NO:126;

(2) a CDR1 comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:114; a CDR2 comprising the amino acid sequence of SEQ ID NO:13; and a CDR3 comprising the amino acid sequence of SEQ ID NO:25 or SEQ ID NO:127;

(3) a CDR1 comprising the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:115; a CDR2 comprising the amino acid sequence of SEQ ID NO:14; and a CDR3 comprising the amino acid sequence of SEQ ID NO:26 or SEQ ID NO:128;

(4) a CDR1 comprising the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:116; a CDR2 comprising the amino acid sequence of SEQ ID NO:15; and a CDR3 comprising the amino acid sequence of SEQ ID NO:27 or SEQ ID NO:129;

(5) a CDR1 comprising the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:117; a CDR2 comprising the amino acid sequence of SEQ ID NO:16; and a CDR3 comprising the amino acid sequence of SEQ ID NO:28 or SEQ ID NO:130;

(6) a CDR1 comprising the amino acid sequence of SEQ ID NO:6 or SEQ ID NO:118; a CDR2 comprising the amino acid sequence of SEQ ID NO:17; and a CDR3 comprising the amino acid sequence of SEQ ID NO:29 or SEQ ID NO:131;

(7) a CDR1 comprising the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:119; a CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a CDR3 comprising the

amino acid sequence of SEQ ID NO:30 or SEQ ID NO:132;

(8) a CDR1 comprising the amino acid sequence of SEQ ID NO:8 or SEQ ID NO:120; a CDR2 comprising the amino acid sequence of SEQ ID NO:19; and a CDR3 comprising the amino acid sequence of SEQ ID NO:31 or SEQ ID NO:133;

(9) a CDR1 comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:121; a CDR2 comprising the amino acid sequence of SEQ ID NO:20; and a CDR3 comprising the amino acid sequence of SEQ ID NO:32 or SEQ ID NO:134;

(10) a CDR1 comprising the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:122; a CDR2 comprising the amino acid sequence of SEQ ID NO:21; and a CDR3 comprising the amino acid sequence of SEQ ID NO:33 or SEQ ID NO:135;

(11) a CDR1 comprising the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:123; a CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a CDR3 comprising the amino acid sequence of SEQ ID NO:34 or SEQ ID NO:136;

(12) a CDR1 comprising the amino acid sequence of SEQ ID NO:10 or SEQ ID NO:124; a CDR2 comprising the amino acid sequence of SEQ ID NO:23; and a CDR3 comprising the amino acid sequence of SEQ ID NO:35 or SEQ ID NO:137;

(13) a CDR1 comprising the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:122; a CDR2 comprising the amino acid sequence of SEQ ID NO:21; and a CDR3 comprising the amino acid sequence of SEQ ID NO:36 or SEQ ID NO:138; or

(14) a CDR1 comprising the amino acid sequence of SEQ ID NO:11 or SEQ ID NO:125; a CDR2 comprising the amino acid sequence of SEQ ID NO:13 and a CDR3 comprising the amino acid sequence of SEQ ID NO:37 or SEQ ID NO:139.

3. A binding moiety that specifically binds to Claudin18.2, comprising a single domain antibody or an antigen binding fragment thereof comprising:

(i) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:38;

(ii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:39;

(iii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:40;

(iv) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:41;

(v) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1,

CDR2, and CDR3, respectively, as set forth in SEQ ID NO:42;

(vi) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:43;

(vii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:44;

(viii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:45;

(ix) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:46;

(x) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:47;

(xi) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:48;

(xii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:49;

(xiii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:50;

(xiv) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:51;

(xv) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:77;

(xvi) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:78;

(xvii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:79;

(xviii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:80;

(xix) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:81;

(xx) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:82;

(xxi) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:83;

(xxii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1,

CDR2, and CDR3, respectively, as set forth in SEQ ID NO:84 or

(xxiii) a CDR1, a CDR2, and a CDR3 having the amino acid sequences of the CDR1, CDR2, and CDR3, respectively, as set forth in SEQ ID NO:85.

4. The binding moiety of claim 3, wherein the CDR1, CDR2 or CDR3 are determined according to the Kabat numbering scheme, the IMGT numbering scheme, the AbM numbering scheme, the Chothia numbering scheme, the Contact numbering scheme, or a combination thereof.

5. The binding moiety of any one of claims 1 to 4, further comprising one or more FR regions as set forth in SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, and/or SEQ ID NO:85.

6. The binding moiety according to any one of claims 1 to 5, wherein the single domain antibody or antigen binding fragment is camelid, chimeric, human or humanized.

7. The binding moiety according to any one of claims 1 to 6, wherein the single domain antibody or antigen binding fragment comprises a VHH domain.

8. The binding moiety according to any one of claims 1 to 7, wherein the single domain antibody or antigen binding fragment thereof comprises an amino acid sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to any one of SEQ ID NOs: 38-51 and 77-85.

9. The binding moiety according to any one of claims 1 to 8, wherein the single domain antibody or antigen binding fragment thereof comprises an IgG, IgM or IgA heavy chain constant region or a fragment thereof.

10. The binding moiety according to any one of claims 1 to 9, wherein the single domain antibody or antigen binding fragment thereof is genetically fused or chemically conjugated to an agent.

11. A polynucleotide encoding the binding moiety according to any one of claims 1 to 9.

12. A vector comprising the polynucleotide according to claim 11.

13. A host cell comprising the polynucleotide according to claim 11 or the vector according to claim 12.

14. A chimeric antigen receptor (CAR) comprising a polypeptide comprising:

(a) an extracellular antigen binding domain comprising the binding moiety according to any one of claims 1 to 10;

(b) a transmembrane domain; and

(c) an intracellular signaling domain.

15. The CAR of claim 14, wherein the extracellular antigen binding domain further comprises one or more additional antigen binding domain(s).

16. The CAR of claim 14, wherein the extracellular antigen binding domain further comprises one additional antigen binding domain; or wherein the extracellular antigen binding domain further comprises two additional antigen binding domains.

17. The CAR of any one of claims 14 to 16, wherein the transmembrane domain is derived from a molecule selected from a group consisting of CD8α, CD4, CD28, CD137, CD80, CD86, CD152, and PD1.

18. The CAR of claim 17, wherein the transmembrane domain is derived from CD8α.

19. The CAR of any one of claims 14 to 18, wherein the intracellular signaling domain comprises a primary intracellular signaling domain of an immune effector cell.

20. The CAR of claim 19, wherein the primary intracellular signaling domain is derived from CD3-zeta.

21. The CAR of claim 19 or claim 20, wherein the intracellular signaling domain further comprises a co-stimulatory signaling domain.

22. The CAR of claim 21, wherein the co-stimulatory signaling domain is derived from a co-stimulatory molecule selected from the group consisting of CD27, CD28, CD137, OX40, CD30, CD40, CD3, LFA-1, CD2, CD7, LIGHT, NKG2C, B7-H3, ligands of CD83 and combinations thereof.

23. The CAR of claim 22, wherein the co-stimulatory signaling domain is derived from CD137.

24. The CAR of any one of claims 14 to 23, further comprising a hinge domain located between the C-terminus of the extracellular antigen binding domain and the N-terminus of the transmembrane domain.

25. The CAR of claim 24, wherein the hinge domain is derived from CD8α.

26. The CAR of any one of claims 14 to 25, further comprising a signal peptide located at the N-terminus of the polypeptide.

27. The CAR of claim 26, wherein the signal peptide is derived from CD8α.

28. The CAR according to any one of claims 14 to 27, wherein the polypeptide comprises, from N-terminus to C-terminus, a signal peptide, an antigen binding domain comprising a VHH domain, a hinge domain, a transmembrane domain, a primary intracellular signaling domain and a co-stimulatory signaling domain.

29. The CAR according to claim 28, wherein the polypeptide comprises from N-terminus to C-terminus, a signal peptide derived from CD8α, an antigen binding domain comprising a VHH domain, a hinge domain derived from CD8α, a transmembrane domain derived from CD8α, a CD137 cytoplasmic domain , and a CD3-zeta's cytoplasmic domain.

30. The CAR according to claim 29, wherein the polypeptide comprises from N-terminus to C-terminus, a signal peptide of SEQ ID NO:67, an antigen binding domain comprising a VHH domain, a hinge domain of SEQ ID NO:68, a transmembrane domain of SEQ ID NO:69, a CD137 cytoplasmic domain of SEQ ID NO:70, and a CD3-zeta's cytoplasmic domain of SEQ ID NO:72.

31. The CAR according to claim 14, wherein the polypeptide comprises an amino acid sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to SEQ ID NOs:53-66 and 86-93.

32. A polynucleotide encoding the CAR according to any one of claims 14 to 31.

33. A vector comprising the polynucleotide according to claim 32.

34. A host cell comprising the polynucleotide according to claim 32 or the vector according to claim 33.

35. An engineered immune cell that recombinantly expresses the CAR according to any one of claims 14 to 31.

36. The engineered immune cell according to claim 35, wherein the engineered immune cell is a T cell.

37. A pharmaceutical composition comprising a therapeutically effective amount of the binding moiety according to any one of claims 1-10, the chimeric antigen receptor according to any one of claims 14 to 31, the polynucleotide according to claim 11 or 32, the vector according to claim 12 or 33, the host cell according to claim 13 or 34, or the engineered immune cell according to claim 35 or 36, and a pharmaceutically acceptable excipient.

38. Use of the pharmaceutical composition of claim 37 in the manufacture of a medicament for ~~A method for~~ treating a Claudin18.2-expressing tumor or cancer in a subject in need thereof, ~~comprising administering to the subject a therapeutically effective amount of the~~ wherein the pharmaceutical composition ~~of claim 37~~is to be administered to the subject.

39. The ~~method~~use according to claim 38, wherein the Claudin18.2-expressing tumor or cancer is gastric, esophageal, gastroesophageal, pancreatic, ovarian, or lung tumor or cancer.