CLAIMS

1. An isolated polynucleotide comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises:

(1) an extracellular domain comprising at least one antigen binding domain that specifically binds DLL3;

(2) a hinge region;

(3) a transmembrane region; and

(4) an intracellular signaling domain.

2. The isolated polynucleotide of claim 1, wherein the antigen binding domain comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, HCDR3, a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the polypeptide sequences of:

(1) SEQ ID NOs: 25, 26, 27, 61, 62 and 63, respectively, or SEQ ID NOs: 97, 98, 99, 133, 134 and 135, respectively;

(2) SEQ ID NOs: 28, 29, 30, 64, 65 and 66, respectively, or SEQ ID NOs: 100, 101, 102, 136, 137 and 138, respectively;

(3) SEQ ID NOs: 31, 32, 33, 67, 68 and 69, respectively, or SEQ ID NOs: 103, 104, 105, 139, 140 and 141, respectively;

(4) SEQ ID NOs: 34, 35, 36, 70, 71 and 72, respectively, or SEQ ID NOs: 106, 107, 108, 142, 143 and 144, respectively;

(5) SEQ ID NOs: 37, 38, 39, 73, 74 and 75, respectively, or SEQ ID NOs: 109, 110, 111, 145, 146 and 147, respectively;

(6) SEQ ID NOs: 40, 41, 42, 76, 77 and 78, respectively, or SEQ ID NOs: 112, 113, 114, 148, 149 and 150, respectively;

(7) SEQ ID NOs: 43, 44, 45, 79, 80 and 81, respectively, or SEQ ID NOs: 115, 116, 117, 151, 152 and 153, respectively;

(8) SEQ ID NOs: 46, 47, 48, 82, 83 and 84, respectively, or SEQ ID NOs: 118, 119, 120, 154, 155 and 156, respectively;

(9) SEQ ID NOs: 49, 50, 51, 85, 86 and 87, respectively, or SEQ ID NOs: 121, 122, 123, 157, 158 and 159, respectively;

(10) SEQ ID NOs: 52, 53, 54, 88, 89 and 90, respectively, or SEQ ID NOs: 124, 125, 126, 160, 161 and 162, respectively;

(11) SEQ ID NOs: 55, 56, 57, 91, 92 and 93, respectively, or SEQ ID NOs: 127, 128, 129, 163, 164 and 165, respectively; or

(12) SEQ ID NOs: 58, 59, 60, 94, 95 and 96, respectively, or SEQ ID NOs: 130, 131, 132, 166, 167 and 168, respectively;

wherein the antigen binding domain specifically binds DLL3, preferably human DLL3.

3. The isolated polynucleotide of claim 1 or 2, wherein the antigen binding domain comprises a heavy chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 170, 175-209, or 248-255, or a light chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 171-174, 210-240, or 256-264.

4. The isolated polynucleotide of any one of claims 1-3, wherein the antigen binding domain comprises:

(1) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:1, and a light chain variable region having the polypeptide sequence of SEQ ID NO:2;

(2) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:3, and a light chain variable region having the polypeptide sequence of SEQ ID NO:4;

(3) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:5, and a light chain variable region having the polypeptide sequence of SEQ ID NO:6;

(4) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:7, and a light chain variable region having the polypeptide sequence of SEQ ID NO:8;

(5) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:9, and a light chain variable region having the polypeptide sequence of SEQ ID NO:10;

(6) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:11, and a light chain variable region having the polypeptide sequence of SEQ ID NO:12;

(7) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:13, and a light chain variable region having the polypeptide sequence of SEQ ID NO:14;

(8) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:15, and a light chain variable region having the polypeptide sequence of SEQ ID NO:16;

(9) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:17, and a light chain variable region having the polypeptide sequence of SEQ ID NO:18;

(10) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:19, and a light chain variable region having the polypeptide sequence of SEQ ID NO:20;

(11) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:21, and a light chain variable region having the polypeptide sequence of SEQ ID NO:22;

(12) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:23, and a light chain variable region having the polypeptide sequence of SEQ ID NO:24;

(13) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:170, and a light chain variable region having the polypeptide sequence of SEQ ID NO:171;

(14) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:170, and a light chain variable region having the polypeptide sequence of SEQ ID NO:172;

(15) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:170, and a light chain variable region having the polypeptide sequence of SEQ ID NO:173.

(16) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:217;

(17) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:218;

(18) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:217;

(19) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:218;

(20) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:198, and a light chain variable region having the polypeptide sequence of SEQ ID NO:229;

(21) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:200, and a light chain variable region having the polypeptide sequence of SEQ ID NO:229;

(22) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:198, and a light chain variable region having the polypeptide sequence of SEQ ID NO:231;

(23) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:200, and a light chain variable region having the polypeptide sequence of SEQ ID NO:231;

(24) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:201, and a light chain variable region having the polypeptide sequence of SEQ ID NO:229;

(25) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:201, and a light chain variable region having the polypeptide sequence of SEQ ID NO:230;

(26) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:201, and a light chain variable region having the polypeptide sequence of SEQ ID NO:231;

(27) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:175, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(28) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:175, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(29) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:175, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(30) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:176, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(31) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:176, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(32) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:176, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(33) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(34) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(35) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:178, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(36) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:178, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(37) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(38) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(39) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:178, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(40) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:179, and a light chain variable region having the polypeptide sequence of SEQ ID NO:213;

(41) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:179, and a light chain variable region having the polypeptide sequence of SEQ ID NO:214;

(42) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:179, and a light chain variable region having the polypeptide sequence of SEQ ID NO:215;

(43) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:180, and a light chain variable region having the polypeptide sequence of SEQ ID NO:213;

(44) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:180, and a light chain variable region having the polypeptide sequence of SEQ ID NO:214;

(45) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:180, and a light chain variable region having the polypeptide sequence of SEQ ID NO:215;

(46) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:181, and a light chain variable region having the polypeptide sequence of SEQ ID NO:213;

(47) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:181, and a light chain variable region having the polypeptide sequence of SEQ ID NO:214;

(48) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:182, and a light chain variable region having the polypeptide sequence of SEQ ID NO:215;

(49) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:202, and a light chain variable region having the polypeptide sequence of SEQ ID NO:232;

(50) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:202, and a light chain variable region having the polypeptide sequence of SEQ ID NO:233;

(51) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:202, and a light chain variable region having the polypeptide sequence of SEQ ID NO:234;

(52) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:203, and a light chain variable region having the polypeptide sequence of SEQ ID NO:232;

(53) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:203, and a light chain variable region having the polypeptide sequence of SEQ ID NO:233;

(54) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:203, and a light chain variable region having the polypeptide sequence of SEQ ID NO:234;

(55) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:204, and a light chain variable region having the polypeptide sequence of SEQ ID NO:234;

(56) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:208, and a light chain variable region having the polypeptide sequence of SEQ ID NO:239;

(57) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:208, and a light chain variable region having the polypeptide sequence of SEQ ID NO:240;

(58) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:253, and a light chain variable region having the polypeptide sequence of SEQ ID NO:261; or

(59) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:255, and a light chain variable region having the polypeptide sequence of SEQ ID NO:263.

5. The isolated polynucleotide of any one of claims 1-4, wherein the antigen binding domain is a single chain variable fragment (scFv) that specifically binds DLL3, preferably human DLL3, optionally wherein the single chain variable fragment (scFv) is humanized.

6. The isolated polynucleotide of claim 5, wherein the single chain variable fragment (scFv) comprises a polypeptide sequence at least 95% identical to any one of SEQ ID NOs: 241-247 or 265-286.

7. The isolated polynucleotide of any one of claims 1-6, wherein the chimeric antigen receptor (CAR) comprises one or more antigen binding domains, and/or wherein the intracellular signaling domain comprises one or more costimulatory domains and one or more activating domains.

8. A chimeric antigen receptor (CAR) encoded by the isolated polynucleotide of any one of claims 1-7.

9. A vector comprising the isolated polynucleotide of any one of claims 1-7.

10. A host cell comprising the vector of claim 9, optionally, wherein the host cell is a T cell or NK cell, preferably a human T cell or human NK cell.

11. A method of making a host cell expressing a chimeric antigen receptor (CAR), the method comprising transducing a T cell or NK cell with the vector of claim 9.

12. A method of producing a chimeric antigen receptor (CAR)-T cell or chimeric antigen receptor (CAR)-NK cell, the method comprising culturing T cells or NK cells comprising the isolated polynucleotide comprising a nucleic acid encoding a chimeric antigen receptor (CAR) of any one of claims 1-7 under conditions to produce the CAR-T cell or CAR-NK cell and recovering the CAR-T cell or CAR-NK cell.

13. A method of generating a cell comprising a chimeric antigen receptor (CAR), the method comprising contacting a cell with the isolated polynucleotide comprising a nucleic acid encoding a chimeric antigen receptor (CAR) of any one of claims 1-7, wherein the isolated polynucleotide is an *in vitro* transcribed RNA or synthetic RNA.

14. The host cell of claim 10 for use in a method of treating cancer in a subject in need thereof, wherein the host cell is to be administered to the subject.

15. Use of the host cell of claim 10 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to the subject.

16. The host cell for use of claim 14, or the use of claim 15, wherein the cancer is selected from a lung cancer such as small cell lung cancer (SCLC), large cell neuroendocrine carcinoma (LCNEC), a gastric cancer, a colon cancer, a hepatocellular carcinoma, a renal cell carcinoma, a bladder urothelial carcinoma, a metastatic melanoma, a breast cancer, an ovarian cancer, a

cervical cancer, a head and neck cancer, a pancreatic cancer, a glioma, a glioblastoma, and other solid tumors, and a non-Hodgkin's lymphoma (NHL), an acute lymphocytic leukemia (ALL), a chronic lymphocytic leukemia (CLL), a chronic myelogenous leukemia (CML), a multiple myeloma (MM), an acute myeloid leukemia (AML), and other liquid tumors.

17. The host cell for use of claim 14 or 16, or the use of claim 15 or 16, further comprising an agent that increases the efficacy of a cell expressing a CAR, an agent that ameliorates one or more side effects associated with administration of a cell expressing a CAR molecule, or an agent that treats the disease associated with DLL3, to be administered to the subject in need thereof.

18. A humanized anti-DLL3 monoclonal antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region having a polypeptide sequence at least 95% identical to any one of SEQ ID NOs: 170, 175-209 or 248-255, or a light chain variable region having a polypeptide sequence at least 95% identical to any one of SEQ ID NOs: 171-174, 210-240 or 256-264.

19. The humanized anti-DLL3 monoclonal antibody or antigen-binding fragment thereof of claim 18, wherein the antibody or antigen-binding fragment thereof comprises:

(1) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:170, and a light chain variable region having the polypeptide sequence of SEQ ID NO:171;

(2) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:170, and a light chain variable region having the polypeptide sequence of SEQ ID NO:172;

(3) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:170, and a light chain variable region having the polypeptide sequence of SEQ ID NO:173.

(4) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:217;

(5) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:183, and a light chain variable region having the polypeptide sequence of SEQ ID NO:218;

(6) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:217;

(7) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:184, and a light chain variable region having the polypeptide sequence of SEQ ID NO:218;

(8) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:198, and a light chain variable region having the polypeptide sequence of SEQ ID NO:229;

(9) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:200, and a light chain variable region having the polypeptide sequence of SEQ ID NO:229;

(10) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:198, and a light chain variable region having the polypeptide sequence of SEQ ID NO:231;

(11) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:200, and a light chain variable region having the polypeptide sequence of SEQ ID NO:231;

(12) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:201, and a light chain variable region having the polypeptide sequence of SEQ ID NO:229;

(13) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:201, and a light chain variable region having the polypeptide sequence of SEQ ID NO:230;

(14) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:201, and a light chain variable region having the polypeptide sequence of SEQ ID NO:231;

(15) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:175, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(16) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:175, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(17) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:175, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(18) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:176, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(19) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:176, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(20) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:176, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(21) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(22) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(23) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:178, and a light chain variable region having the polypeptide sequence of SEQ ID NO:210;

(24) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:178, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(25) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:211;

(26) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:177, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(27) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:178, and a light chain variable region having the polypeptide sequence of SEQ ID NO:212;

(28) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:179, and a light chain variable region having the polypeptide sequence of SEQ ID NO:213;

(29) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:179, and a light chain variable region having the polypeptide sequence of SEQ ID NO:214;

(30) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:179, and a light chain variable region having the polypeptide sequence of SEQ ID NO:215;

(31) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:180, and a light chain variable region having the polypeptide sequence of SEQ ID NO:213;

(32) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:180, and a light chain variable region having the polypeptide sequence of SEQ ID NO:214;

(33) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:180, and a light chain variable region having the polypeptide sequence of SEQ ID NO:215;

(34) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:181, and a light chain variable region having the polypeptide sequence of SEQ ID NO:213;

(35) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:181, and a light chain variable region having the polypeptide sequence of SEQ ID NO:214;

(36) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:182, and a light chain variable region having the polypeptide sequence of SEQ ID NO:215;

(37) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:202, and a light chain variable region having the polypeptide sequence of SEQ ID NO:232;

(38) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:202, and a light chain variable region having the polypeptide sequence of SEQ ID NO:233;

(39) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:202, and a light chain variable region having the polypeptide sequence of SEQ ID NO:234;

(40) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:203, and a light chain variable region having the polypeptide sequence of SEQ ID NO:232;

(41) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:203, and a light chain variable region having the polypeptide sequence of SEQ ID NO:233;

(42) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:203, and a light chain variable region having the polypeptide sequence of SEQ ID NO:234;

(43) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:204, and a light chain variable region having the polypeptide sequence of SEQ ID NO:234;

(44) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:208, and a light chain variable region having the polypeptide sequence of SEQ ID NO:239;

(45) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:208, and a light chain variable region having the polypeptide sequence of SEQ ID NO:240;

(46) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:253, and a light chain variable region having the polypeptide sequence of SEQ ID NO:261; or

(47) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:255, and a light chain variable region having the polypeptide sequence of SEQ ID NO:263.

20. The humanized anti-DLL3 monoclonal antibody or antigen-binding fragment thereof of claim 18 or 19, wherein the monoclonal antibody or antigen-binding fragment thereof is capable of inducing effector-mediated tumor cell lysis, mediating the recruitment of conjugated drugs, and/or forms a bispecific antibody with another monoclonal antibody or antigen-binding fragment with a cancer-killing effect.

21. An isolated nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof of any one of claims 18-20.

22. A vector comprising the isolated nucleic acid of claim 21.

23. A host cell comprising the vector of claim 22.

24. A pharmaceutical composition comprising the isolated monoclonal antibody or antigen-binding fragment thereof of any one of claims 18-20 and a pharmaceutically acceptable carrier.

25. The pharmaceutical composition of claim 24 for use in a method of targeting DLL3 on a cancer cell surface or treating cancer in a subject in need thereof, wherein the composition is to be administered to the subject in need thereof.

26. Use of the pharmaceutical composition of claim 24 in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein the medicament is to be administered to the subject in need thereof.

27. The pharmaceutical composition for use of claim 24, or the use of claim 26, wherein the cancer is selected from a lung cancer such as small cell lung cancer (SCLC), large cell neuroendocrine carcinoma (LCNEC), a gastric cancer, a colon cancer, a hepatocellular carcinoma, a renal cell carcinoma, a bladder urothelial carcinoma, a metastatic melanoma, a breast cancer, an ovarian cancer, a cervical cancer, a head and neck cancer, a pancreatic cancer, a glioma, a glioblastoma, and other solid tumors, and a non-Hodgkin's lymphoma (NHL), an acute lymphocytic leukemia (ALL), a chronic lymphocytic leukemia (CLL), a chronic myelogenous

leukemia (CML), a multiple myeloma (MM), an acute myeloid leukemia (AML), and other liquid tumors.

28. A method of producing the monoclonal antibody or antigen-binding fragment thereof of any one of claims 18-20, comprising culturing a cell comprising a nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof under conditions to produce the monoclonal antibody or antigen-binding fragment thereof, and recovering the antibody or antigen-binding fragment thereof from the cell or culture.

29. A method of producing a pharmaceutical composition comprising the monoclonal antibody or antigen-binding fragment thereof of any one of claims 18-20, comprising combining the monoclonal antibody or antigen-binding fragment thereof with a pharmaceutically acceptable carrier to obtain the pharmaceutical composition.