

Citation or discussion of a reference herein shall not be construed as an admission that such is prior art to the present disclosure.

SUMMARY

In one aspect, the present invention refers to an isolated antibody, or antigen-binding
5 fragment thereof, that binds to a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC4 (SEQ ID NO: 1245), CC5 (SEQ ID NO: 1246), CC8 (SEQ ID NO: 1249), and CC10 (SEQ ID NO: 1251), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated CC2 (SEQ ID NO: 1243), CC3 (SEQ ID NO: 1244), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), and CC9 (SEQ ID NO: 1250). In another aspect, the present invention refers to an antibody-drug conjugate comprising the antibody as disclosed herein
10 conjugated to a cytotoxic agent. In yet another aspect, the present invention refers to a polynucleotide comprising a nucleotide sequence encoding the antibody as disclosed herein. In a further aspect, the present invention refers to an expression vector comprising the polynucleotide as disclosed herein. In another aspect, the present invention refers to a host cell comprising the expression vector as disclosed herein. In yet another aspect, the present invention refers to a method of producing the antibody or antigen-binding fragment thereof, as disclosed herein, said method comprising a step of culturing the host cell as disclosed herein under conditions that
15 promotes the production of the antibody. In a further aspect, the present invention refers to a pharmaceutical composition comprising the antibody as disclosed herein or the antibody-drug conjugate as disclosed herein, and a pharmaceutically acceptable diluent, carrier or excipient. In another aspect, the present invention refers to use of the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating, preventing or alleviating one or more symptoms of a cancer. In yet another aspect, the present invention refers to use of the pharmaceutical composition as disclosed herein in the manufacture of a medicament for inhibiting the growth of a tumor with inflammation in a subject. In a further aspect, the present invention refers to use of an antibody as disclosed herein or an antibody-drug
20 conjugate of as disclosed herein in the manufacture of a medicament for treating cancer. In another aspect, the present invention refers to a method for detecting C10orf54 in a sample comprising contacting the sample with the antibody as

disclosed herein. In yet another aspect, the present invention refers to a kit comprising the antibody as disclosed herein.

The present disclosure describes antibodies that bind C10orf54, including humanized antibodies and antibody-drug conjugates comprising the humanized antibodies, and methods of use of the antibodies and the antibody-drug conjugates, including for the diagnosis and treatment of cancers. The present disclosure further describes proteins that bind to C10orf54, including binding proteins, such as antibodies, that bind to one or more C10orf54 proteins or chimeric proteins. Such binding proteins, including antibodies, may be antagonists (*e.g.*, inhibit one or more of the biological activities of C10orf54).

In one example, disclosed herein are antibodies that bind to C10orf54, including a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope, collectively referred to herein as anti-C10orf54 antibodies. Also disclosed herein are anti-C10orf54 antibodies that are conjugated to drugs as antibody-drug conjugates (ADCs), including ADCs of the formula A-L-CTX, wherein A is an antibody, L is a linker, and CTX is cytotoxin. In some examples the anti-C10orf54 antibodies are humanized antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In certain examples, the anti-C10orf54 antibody comprises a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of monoclonal antibody 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33), or a humanized variant thereof. In certain examples, the anti-C10orf54 antibody can further comprise a VH FR1, VH FR2, VH FR3, VH FR4, VL FR1, VL FR2, VL FR3, and/or VL FR4 of a human germline immunoglobulin amino acid sequence or a variant thereof.

In certain examples, the antibody comprises less than six CDRs. In some examples, the antibody comprises or consists of one, two, three, four, or five CDRs selected from the group consisting of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3. In specific examples, the antibody comprises or consists of one, two, three, four, or five CDRs selected from the group consisting of

VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of the monoclonal antibody 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33), or a humanized variant thereof. In specific examples, the antibody
 5 further comprises a VH FR1, VH FR2, VH FR3, VH FR4, VL FR1, VL FR2, VL FR3, and/or VL FR4 of a human germline immunoglobulin amino acid sequence or a variant thereof.

In specific examples, the antibody is a humanized antibody, a monoclonal antibody, a recombinant antibody, an antigen binding fragment or any combination thereof. In
 10 particular examples, the antibody is a humanized monoclonal antibody as described herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3), or antigen binding fragment thereof, that binds to a
 15 C10orf54 polypeptide (e.g., a cell surface-expressed or soluble C10orf54), a C10orf54 fragment, or a C10orf54 epitope.

In another example, disclosed herein are antibodies, including humanized antibodies, (i) that competitively block (e.g., in a dose-dependent manner) an anti-C10orf54 antibody disclosed herein from binding to a C10orf54 polypeptide (e.g., a cell surface-expressed or
 20 soluble C10orf54), a C10orf54 fragment, or a C10orf54 epitope and/or (ii) that bind to a C10orf54 epitope that is bound by an anti-C10orf54 antibody (e.g., humanized anti-C10orf54 antibodies) disclosed herein. In other examples, the antibody competitively blocks (e.g., in a dose-dependent manner) monoclonal antibody 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D,
 25 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) or a humanized variant thereof from binding to a C10orf54 polypeptide (e.g., a cell surface-expressed or soluble C10orf54), a C10orf54 fragment, or a C10orf54 epitope. In other examples, the antibody binds to a C10orf54 epitope that is bound (e.g., recognized) by monoclonal antibody 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A,
 30 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) or a humanized variant thereof (e.g. humanized anti-C10orf54 antibodies).

In certain examples, the anti-C10orf54 antibodies (e.g., humanized anti-C10orf54 antibodies) disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A,

230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) are conjugated or recombinantly fused to a diagnostic agent, detectable agent or therapeutic agent. In some examples, the therapeutic agent is a chemotherapeutic agent (*e.g.*, a cytotoxic agent such as cytotoxin). In some examples, the detectable agent is a radioisotope, an enzyme, a fluorescent compound, a bioluminescent compound or a chemiluminescent compound. In certain examples, the anti-C10orf54 antibodies disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) are conjugated to drugs as antibody-drug conjugates (ADCs). In some examples, the antibody-drug conjugate (ADC) is of the formula A-L-CTX, wherein A is an antibody, L is a linker, and CTX is a cytotoxin.

In certain examples, disclosed are compositions comprising an anti-C10orf54 antibody (*e.g.*, humanized anti-C10orf54 antibodies) described herein. In some examples, the compositions comprise an antibody-drug conjugate wherein the antibody is an anti-C10orf54 antibody disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3). Also disclosed herein are pharmaceutical compositions comprising an anti-C10orf54 antibody, including a humanized anti-C10orf54 antibody, disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3).

In certain examples, the antibody disclosed herein binds to a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC4 (SEQ ID NO: 1245), CC5 (SEQ ID NO: 1246), CC8 (SEQ ID NO: 1249), and CC10 (SEQ ID NO: 1251), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated CC2 (SEQ ID NO: 1243), CC3 (SEQ ID NO: 1244), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), and CC9 (SEQ ID NO: 1250).

In certain examples, the antibody disclosed herein binds a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC4 (SEQ ID NO: 1245), CC5 (SEQ ID NO: 1246), and CC8 (SEQ ID NO: 1249), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated CC2 (SEQ ID NO: 1243), CC3 (SEQ ID NO: 1244), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), CC9 (SEQ ID NO: 1250), and CC10 (SEQ ID NO: 1251). In some examples, such an antibody does not comprise one or more CDR sequences selected from the group consisting of 30, 1099, 1104, 1105, 1110, 31, 1100, 1106, 1111, 1116, 32, 1101, 1107, 1112, 45, 1102, 1108, 1113, 40, 1103, 1114, 41, 1109, and 1115.

In certain examples, the antibody disclosed herein binds to a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC4 (SEQ ID NO: 1245), and CC5 (SEQ ID NO: 1246), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated (SEQ ID NO: 1243), CC3 (SEQ ID NO: 1244), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), CC8 (SEQ ID NO: 1249), CC9 (SEQ ID NO: 1250), and CC10 (SEQ ID NO: 1251). In some examples, such an antibody does not comprise one or more CDR sequences selected from the group consisting of 36, 1081, 1086, 1087, 1092, 37, 1082, 1088, 1093, 1098, 38, 1083, 1089, 1094, 45, 1084, 1090, 1095, 46, 1085, 1096, 47, 1091, and 1097.

In certain examples, the antibody disclosed herein binds to a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC4 (SEQ ID NO: 1245), CC5 (SEQ ID NO: 1246), CC8 (SEQ ID NO: 1249), and CC9 (SEQ ID NO: 1250), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated CC2 (SEQ ID NO: 1243), CC3 (SEQ ID NO: 1244), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), CC9 (SEQ ID NO: 1250), and CC10 (SEQ ID NO: 1251). In some examples, such an antibody does not comprise one or more CDR sequences selected from the group consisting of 33, 1117, 1122, 1123, 1128, 34, 1118, 1124, 1129, 1134, 35, 1119, 1125, 1130, 42, 1120, 1126, 1131, 43, 1121, 1132, 44, 1127, and 1133.

In certain examples, the antibody disclosed herein binds to a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC3 (SEQ ID NO: 1244), CC4 (SEQ ID NO: 1245), CC5 (SEQ ID NO: 1246), CC8 (SEQ ID NO: 1249), and CC9 (SEQ ID NO: 1250), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated CC2 (SEQ ID NO: 1243), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), and CC10 (SEQ ID NO: 1251).

In certain examples, the antibody disclosed herein binds to a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC4 (SEQ ID NO: 1245), CC5 (SEQ ID NO: 1246), CC8 (SEQ ID NO: 1249), and CC10 (SEQ ID NO: 1251), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated CC2 (SEQ ID NO: 1243), CC3 (SEQ ID NO: 1244), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), CC9 (SEQ ID NO: 1250), and CC10 (SEQ ID NO: 1251).

In another example, disclosed are isolated nucleic acid molecules encoding a VH chain, VL chain, VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of anti-C10orf54 antibodies as described herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3), including humanized anti-C10orf54 antibodies, that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope. In certain examples, the nucleic acid molecule encodes a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of monoclonal antibody 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33), or a humanized variant thereof. In certain examples, the nucleic acid molecule further encodes a VH FR1, VH FR2, VH FR3, VH FR4, VL FR1, VL FR2, VL FR3, and/or VL FR4 of a human germline immunoglobulin amino acid sequence or a variant thereof. Also disclosed herein are vectors and host cells comprising the nucleic acid molecules encoding an anti-C10orf54 antibody (*e.g.*, humanized anti-C10orf54 antibodies), as well as methods of producing an anti-C10orf54 antibody by culturing the host cells disclosed herein under conditions that promote the production of the anti-C10orf54 antibody.

In another examples, disclosed herein are methods of treating, preventing or alleviating a disease, disorder or condition, including one or more symptoms of a disease, disorder or condition, comprising administering a therapeutically effective amount of an anti-C10orf54 antibody as described herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3), including an antibody-drug conjugate (ADC) comprising an anti-C10orf54 antibody, disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A,

175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) to a subject, thereby treating, preventing or alleviating the disease, disorder or condition, including one or more symptoms of the disease, disorder or condition. In some

5 examplesthe anti-C10orf54 antibodies are humanized antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In one examples, the disease, disorder or condition is caused by or otherwise associated with C10orf54, including by or associated with C10orf54-expressing cells (e.g., tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or

10 regulatory T cells (T regs)). In certain examples, the disease is a cancer, such as a leukemia, a bladder cancer, a skin cancer, a colon cancer, a breast cancer, a liver cancer, a kidney cancer, a lung cancer, a stomach cancer, a pancreas cancer, an esophagus cancer or a fibrosarcoma. In one examples, the leukemia is an acute myeloid leukemia (AML). In other examples, the disease is graft-versus-host disease (GVHD).

15 Additional methods disclosed include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells, disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3), for

20 example, as an unconjugated antibody or conjugated antibody (ADC), including to inhibit and/or kill the C10orf54-expressing cells (e.g., with anti-tumor activity to mediate an anti-tumor effect). In certain examples, the anti-C10orf54 antibodies, including ADCs comprising the anti-C10orf54 antibodies, disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D,

25 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) inhibit C10orf54-mediated suppressor activity on T cells (e.g., to allow an effective anti-tumor immune response). In certain examples, the anti-C10orf54 antibodies disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A,

30 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) directly kill C10orf54-expressing cells (e.g., C10orf54-bearing tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or regulatory T cells (T regs)), for example, via antibody-dependent cellular

35 cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC) In certain

examples, antibody drug conjugates (ADCs) comprising anti-C10orf54 antibodies disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) directly kill C10orf54-expressing cells including by binding to cells expressing C10orf54 (*e.g.*, tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and/or regulatory T cells (T regs)), for example, by allowing internalization of the cytotoxic drug. In certain examples, the anti-C10orf54 antibodies disclosed herein or antibody drug conjugates (ADCs) comprising anti-C10orf54 antibodies disclosed herein are used in methods for treating cancers (*e.g.*, bladder, breast, colon, connective tissue, rectal, gastric, esophageal, lung, larynx, kidney, oral, ovarian, or prostate cancer, or a sarcoma, melanoma, glioma, lymphoma or leukemia) or tumors associated with myeloid-derived suppressor cells (MDSC) (*e.g.*, colon carcinoma, mammary carcinoma, fibrosarcoma, thymoma, lung carcinoma, renal cell carcinoma, mesothelioma, glioma, lymphoma, sarcoma, prostate carcinoma, sarcoma, or head and neck carcinoma). In any of the above examples, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In yet another example, disclosed herein are methods of inhibiting the growth of cells and/or killing cells having cell surface expression of C10orf54 comprising contacting the cells with an effective amount of an anti-C10orf54 antibody or antibody-drug conjugates comprising the anti-C10orf54 antibody disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3). In one example, the cell is a regulatory T cell (*e.g.*, a CD4⁺ Foxp3⁺ regulatory T cell). In certain examples, disclosed herein is a method of inhibiting the growth of a tumor with inflammation in a subject comprising administering an effective amount of the anti-C10orf54 antibodies, including ADCs comprising the anti-C10orf54 antibodies, disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A,

259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3). In other examples, the cell is a myeloid-derived suppressor cell (e.g., a CD11b⁺ or CD11b^{high} myeloid-derived suppressor cell) or a suppressive dendritic cell (e.g., a CD11b⁺ or CD11b^{high} dendritic cell). In other examples, the cell is a cancerous or pre-cancerous cell. Additional methods disclosed include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3), for example, as an unconjugated antibody or conjugated antibody (ADC) including to inhibit and/or kill C10orf54-expressing cells (e.g., with anti-tumor activity to mediate an anti-tumor effect). In certain examples, the anti-C10orf54 antibodies, including ADCs comprising the anti-C10orf54 antibodies, disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) inhibit C10orf54-mediated suppressor activity on T cells (e.g., to allow an effective anti-tumor immune response). In certain examples, the anti-C10orf54 antibodies disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) directly kill C10orf54-expressing cells (e.g., C10orf54-bearing tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or regulatory T cells (T regs)), for example, via antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC). In certain examples, antibody drug conjugates (ADCs) comprising anti-C10orf54 antibodies disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) directly kill C10orf54-expressing cells including by binding to cells expressing C10orf54 (e.g., tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and/or regulatory T cells (T regs)), for example, by allowing internalization of the cytotoxic drug. In any of the above examples, the anti-

C10orf54 antibody can be a humanized anti-C10orf54 antibody disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In one example, disclosed herein are methods of modulating an immune response in a subject comprising administering an effective amount of an anti-C10orf54 antibody (*e.g.*, a humanized anti-C10orf54 antibody) disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) to a subject. In one example, the modulating comprises increasing T cell activation. In other example, the modulating comprises increasing T cell proliferation. In another example, the modulating comprises increasing cytokine production.

In an example, disclosed herein are methods for detecting C10orf54 in a sample comprising contacting the sample with an anti-C10orf54 antibody (*e.g.*, a humanized anti-C10orf54 antibody) disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3), such as an antibody that comprises a detectable agent. In certain examples, the sample comprises a cell expressing C10orf54 on its surface.

In yet another example, disclosed herein are methods of treating cancers comprising administering to a subject an anti-C10orf54 antibody (*e.g.*, a humanized anti-C10orf54 antibody) or an antibody-drug conjugate (ADC) comprising the anti-C10orf54 antibody (*e.g.*, an ADC of the formula A-L-CTX, wherein A is the antibody, L is a linker, and CTX is a cytotoxic agent) disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) in a therapeutically effective amount, including in an amount effective to kill a C10orf54-expressing cell (*e.g.*, tumor cell, myeloid-derived suppressor cell (MDSC), suppressive dendritic cell (suppressive

DC), and /or regulatory T cell (T reg)). In some examples the cancer is acute myeloid leukemia (AML). In any of the above examples, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In one example, disclosed herein are methods of killing C10orf54-expressing cells (e.g., tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or regulatory T cells (T reg)) comprising contacting a C10orf54-expressing cell (e.g., tumor cell, myeloid-derived suppressor cell (MDSC), suppressive dendritic cell (suppressive DC), and /or regulatory T cell (T reg)) with an amount of an anti-C10orf54 antibody or an antibody-drug conjugate (ADC) comprising an anti-C10orf54 antibody (e.g., an ADC of the formula A-L-CTX, wherein A is the antibody, L is a linker, and CTX is a cytotoxic agent) disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) effective to kill the cell (e.g., tumor cell, myeloid-derived suppressor cell (MDSC), suppressive dendritic cell (suppressive DC), and /or regulatory T cell (T reg)). In some examples, the tumor cell is an AML cell. In any of the above examples, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3) that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a further example, disclosed herein is a kit comprising an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody) that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope disclosed herein (e.g., 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (e.g., Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3). In some examples, the kits comprise an antibody-drug conjugate (ADC) wherein the antibody is an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody)

disclosed herein (*e.g.*, 5B, 46A, 97A, 128A, 146C, 208A, 215A, 26A, 164A, 230A, 76E1, 53A, 259A, 33A, 39A, 124A, 175A, 321D, 141A, 51A, 353A, or 305A described herein (*e.g.*, Tables 12-33) with a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3).

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TERMINOLOGY

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art. All patents, applications, published applications and other publications are incorporated

WHAT IS CLAIMED:

1. An isolated antibody, or antigen-binding fragment thereof, that binds to a first group of C10orf54 proteins or chimeric proteins designated CC1 (SEQ ID NO: 1079), CC4 (SEQ ID NO: 1245), CC5 (SEQ ID NO: 1246), CC8 (SEQ ID NO: 1249), and CC10 (SEQ ID NO: 1251), and does not bind to a second group of C10orf54 proteins or chimeric proteins designated CC2 (SEQ ID NO: 1243), CC3 (SEQ ID NO: 1244), CC6 (SEQ ID NO: 1247), CC7 (SEQ ID NO: 1248), and CC9 (SEQ ID NO: 1250).
5
2. The antibody of claim 1, or antigen-binding fragment thereof, wherein said antibody is a monoclonal antibody.
10
3. The antibody of any one of claims 1 or 2, or antigen-binding fragment thereof, wherein said antibody is the antibody 26A, comprising:
 - a heavy chain comprising the following three CDRs, respectively CDR-H1 having the sequence SEQ ID NO: 1296, CDR-H2 having a sequence selected from SEQ ID NO: 1358, SEQ ID NO. 1556, SEQ ID NO. 1557, SEQ ID NO. 1558, and SEQ ID NO. 1559, and CDR-H3 having the sequence SEQ ID No. 1393; and
15
 - a light chain comprising the following three CDRs, respectively CDR-L1 having the sequence SEQ ID No. 1435, CDR-L2 having a sequence selected from SEQ ID NO: 1476, SEQ ID NO. 1630, SEQ ID NO. 1631, SEQ ID NO. 1632, and SEQ ID NO. 1633, and CDR-L3 having the sequence SEQ ID No.1499.
20
4. The antibody of any one of claims 1 to 3, or antigen-binding fragment thereof, wherein said antibody is humanized.
- 25 5. An antibody according to claim 4, or antigen-binding fragment thereof, said antibody comprising a heavy chain variable domain of sequence selected between amino acid sequences SEQ ID NO. 1529, SEQ ID NO. 1530, and SEQ ID NO. 1531, and a light chain variable domain of sequence selected between amino acid sequences SEQ ID NO. 1532, SEQ ID NO. 1533, and
30 SEQ ID NO. 1534.

6. The antibody of any one of claims 1 to 5, wherein the antibody is a Fab Fragment, F(ab')₂ fragment, single chain Fv (sFv), diabody, triabody, or minibody.
- 5 7. An antibody-drug conjugate comprising the antibody of any one of claims 1 to 6 conjugated to a cytotoxic agent.
8. A polynucleotide comprising a nucleotide sequence encoding the antibody of any one of claims 1 to 6.
9. An expression vector comprising the polynucleotide of claim 8.
10. A host cell comprising the expression vector of claim 9.
- 10 11. A method of producing the antibody or antigen-binding fragment thereof, of any of claims 1 to 6, said method comprising a step of culturing the host cell of claim 10 under conditions that promotes the production of the antibody.
12. A pharmaceutical composition comprising the antibody of any one of claims 1 to 6 or the antibody-drug conjugate of claim 7, and a pharmaceutically acceptable diluent, carrier or excipient.
- 15 13. Use of the pharmaceutical composition of claim 12 in the manufacture of a medicament for treating, preventing or alleviating one or more symptoms of a cancer.
14. The use of claim 13, wherein the cancer is a leukemia, preferably acute myeloid leukemia (AML), a bladder cancer, a skin cancer, a colon cancer, a breast cancer, a liver cancer, a kidney cancer, a lung cancer, a stomach cancer, a pancreas cancer, an esophagus cancer or a fibrosarcoma.
- 20 15. Use of the pharmaceutical composition of claim 12 in the manufacture of a medicament for inhibiting the growth of a tumor with inflammation in a subject.
- 25 16. The use of any one of claims 13 to 15, said use comprising inhibiting the growth of a cell having cell surface expression of C10orf54.
17. The use of claim 16, wherein the cell is a regulatory T cell.

18. The use of any one of claims 16 or 17, wherein the cell is a cancerous or pre-cancerous cell.
19. The use of any one of claims 13 to 15, said use comprising modulating an immune response.
- 5 20. The use of claim 19, wherein the modulating comprises:
- (a) increasing T cell activation;
 - (b) increasing T cell proliferation; or
 - (c) increasing cytokine production.
- 10 21. Use of an antibody of any one of claims 1 to 6 or an antibody-drug conjugate of claim 7 in the manufacture of a medicament for treating cancer.
22. The use of claim 21, said use comprising killing a tumor cell.
23. A method for detecting C10orf54 in a sample comprising contacting the sample with the antibody of any one claims 1 to 6.
24. A kit comprising the antibody of any one of claims 1 to 6.
- 15 25. The kit of claim 24, wherein said antibody is conjugated to a detectable substrate.