ANTI-C10ORF54 ANTIBODIES AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of priority of United States Provisional Application Serial No. 61/934,615, filed January 31, 2014, and United States Provisional Application Serial No. 61/832,135, filed June 6, 2013, the entire contents of which are earch incorporated herein by reference.

FIELD

The present disclosure relates generally to anti-C10orf54 antibodies, including antibody-drug conjugates comprising the antibodies, and methods of their use.

BACKGROUND

C10orft54 is a single-pass type I transmembrane protein that is 311 amino acids in length and includes a signal sequence and one IgV-like domain in its intracellular region. It is potentially a member of the B7 family of proteins and it has approximately 24% sequence identity to B7-H1/PD-L1 (Flajnik et al., *Immunogenetic* 64:571-590 (2012)). The mouse ortholog to C10orf54 is known as V-region Immunoglobulin-containing Suppressor of T Cell Activation (VISTA; also known as PD-L3). VISTA was cloned from a library of CD4 positive regulatory T cells (T_{reg}) (Wang et al., *JEM* 208(3):577-592 (2011)). VISTA is primarily expressed on hematopoietic cells, and VISTA expression is highly regulated on myeloid antigen-presenting cells (APCs) and T cells (Wang et al., *supra*).

VISTA appears to have functional activities that are nonredundant with other Ig superfamily members and may play a role in the development of autoimmunity and immune surveillance in cancer. For example, expression of a VISTA-Ig fusion protein has been shown to inhibit T cell proliferation and cytokine production *in vitro* and overexpression of VISTA on MCA105 tumor cells interferes with a host's protective antitumor immunity (Wang et al., *supra*). Moreover, administration of a VISTA-specific monoclonal antibody enhanced CD4 positive T cell response *in vivo* and the development of autoimmunity (Wang et al., *supra*). Monoclonal antibodies against

C10orf54 have also been shown to prevent acute graft-versus-host disease in mice (Flies et al., *J. Immunology* 187(4):1537-1541 (2011)).

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

SUMMARY

In one aspect, the present disclosure refers to an isolated antibody that binds to C10orf54, said antibody being selected from:

a. an antibody comprising:
   i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 36, SEQ ID NO. 37, and SEQ ID NO. 38, and
   ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 46, and SEQ ID NO. 47;

b. an antibody comprising:
   i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 30, SEQ ID NO. 31, and SEQ ID NO. 32, and
   ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 40, and SEQ ID NO. 41; and

c. an antibody comprising:
   i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 33, SEQ ID NO. 34, and SEQ ID NO. 35, and
   ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 42, SEQ ID NO. 43, and SEQ ID NO. 44.

In another aspect, the present disclosure refers to an isolated nucleic acid molecule encoding an antibody as disclosed herein, said nucleic acid molecule comprising or consisting of a nucleic acid sequence that encodes the V_H region and/or V_L region of said antibody. In yet another aspect, the present disclosure refers to a vector comprising the nucleic acid molecule as disclosed herein. In another aspect, the present disclosure refers to a host cell comprising the vector as disclosed herein. In

yet a further aspect, the present disclosure refers to a method of producing an antibody comprising culturing the host cell as disclosed herein under conditions that promotes the production of the antibody. In a further aspect, disclosed herein is a pharmaceutical composition comprising the antibody as disclosed herein and a pharmaceutically-acceptable excipient. In still another aspect, the present disclosure refers to the antibody or the composition as disclosed herein for use as a medicament. In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating or alleviating one or more symptoms of a disease, wherein the disease is a cancer or graft-versus-host disease. In a further aspect, the present disclosure refers to the antibody or the composition as disclosed herein for use in treating or alleviating one or more symptoms of a cancer by stimulating an immune response in a subject. In another aspect, the present disclosure refers to the use of the anti-C10orf54 antibody as disclosed herein or an antibody-drug conjugate as disclosed herein, in the manufacture of a medicament for treating cancer. In another aspect, the present disclosure refers to the use of the anti-C10orf54 antibody as disclosed herein or an antibody-drug conjugate as disclosed herein, in the manufacture of a medicament for killing a tumor cell.

In a first example, provided 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 provided 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 175A, 76E1 or 141A described herein, 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 175A, 76E1 or 141A described herein, or a humanized variant thereof. In specific examples, the antibody 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 particular examples, the antibody is a humanized monoclonal antibody, or antigen binding fragment thereof, that binds to a C10orf54 polypeptide (*e.g.,* a cell surface-expressed or soluble C10orf54), a C10orf54 fragment, or a C10orf54 epitope.

In a second example, provided herein are antibodies, including humanized antibodies, (i) that competitively block (*e.g.,* in a dose-dependent manner) an anti-C10orf54 antibody provided herein from binding to a C10orf54 polypeptide (*e.g.,* a cell surface-expressed or 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) provided herein. In other examples, the antibody competitively blocks (*e.g.,* in a dose-dependent manner) monoclonal antibody 175A, 76E1 or 141A described herein 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 175A, 76E1, or 141A described herein or a humanized variant thereof (e.g. humanized anti-C10orf54 antibodies).

In certain examples, the anti-C10orf54 antibodies (*e.g.*, humanized anti-C10orf54 antibodies) provided herein 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 cystotoxic 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 provided herein 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, provided 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. Also provided herein are pharmaceutical compositions comprising an anti-C10orf54 antibody, including a humanized anti-C10orf54 antibody, provided herein.

In a third example, provided 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, 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 175A, 76E1 or 141A described herein, 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 provided 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 provided herein under conditions that promote the production of the anti-C10orf54 antibody.

In a fourth example, provided 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, including an antibody-drug conjugate (ADC) comprising an anti-C10orf54 antibody, provided herein 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 examples the anti-C10orf54 antibodies are humanized antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In one example, 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 regulatory T cells (T regs)). In certain examples, the disease is a cancer, such as a leukemia, a bladder cancer or a fibrosarcoma. In one example, the leukemia is an acute myeloid leukemia (AML). In other examples, the disease is graft-versus-host disease (GVHD). Additional methods provided include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells, provided herein, for 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, provided herein 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 provided herein 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 provided herein 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 provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a fifth example, provided 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

provided herein. In one example, the cell is a regulatory T cell (*e.g.*, a $CD4^+$ $Foxp3^+$ regulatory T cell). 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 provided include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells provided herein, 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, provided herein 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 provided herein 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 provided herein 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 provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a sixth example, provided 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) provided herein 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 a seventh example, provided 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) provided herein, such as an antibody that comprises a detectible agent. In certain examples, the sample comprises a cell expressing C10orf54 on its surface.

In an eighth example, provided herein are methods of treating cancers comprising administering to a subject an anti-C10orf54 antibody or an antibody-drug conjugate (ADC) comprising an anti-C10orf54 (*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) 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 provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a ninth example, provided 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 regs)) 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) 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 provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a tenth example, provided 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 provided herein. 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).

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 by reference in their entirety. In the event that there are a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

The term “about” or “approximately” means within 20%, such as within 10%, or within 5% (or 1% or less) of a given value or range.

As used herein, "administer" or "administration" refers to the act of injecting or otherwise physically delivering a substance as it exists outside the body (*e.g.*, an anti-C10orf54 antibody provided herein) into a patient, such as by mucosal, intradermal, intravenous, intramuscular delivery and/or any other method of physical delivery described herein or known in the art. When a disease, or a symptom thereof, is being treated, administration of the substance typically occurs after the onset of the disease or symptoms thereof. When a disease, or symptoms thereof, are being prevented, administration of the substance typically occurs before the onset of the disease or symptoms thereof.

As used herein, an "agonist" of C10orf54 refers to a molecule that is capable of activating or otherwise increasing one or more of the biological activities of C10orf54, such as in a cell expressing C10orf54 or in a cell expressing a C10orf54 ligand, such as a C10orf54 receptor. In some embodiments, an agonist of C10orf54 (*e.g.*, an agonistic antibody provided herein) may, for example, act by activating or otherwise increasing the activation and/or cell signaling pathways of the cell expressing a C10orf54 or a C10orf54 receptor, thereby increasing a C10orf54-mediated biological activity of the cell the relative to the C10orf54-mediated biological activity in the absence of agonist. In certain embodiments the antibodies provided herein are agonistic anti-C10orf54 antibodies.

The term "alkyl," as used herein, means a straight, branched chain, or cyclic (in this case, it would also be known as "cycloalkyl") hydrocarbon containing from 1-10 carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylhexyl, n-heptyl, n-octyl, n-nonyl, and n-decyl. In certain embodiments, alkyl groups are optionally substituted.

The term "C_{1-6}alkyl," as used herein, means a straight, branched chain, or cyclic (in this case, it would also be known as "cycloalkyl") hydrocarbon containing from 1-6 carbon atoms.

The term "C_{1-3}alkyl," as used herein, means a straight or branched chain hydrocarbon containing from 1-3 carbon atoms.

The term "alkenyl," as used herein, means a straight, branched chain, or cyclic (in which case, it would also be known as a "cycloalkenyl") hydrocarbon containing from 2-10 carbons and containing at least one carbon-carbon double bond formed by the removal of two hydrogens. In some embodiments, depending on the structure, an alkenyl group is a monoradical or a diradical (*e.g.*, an alkenylene group). In some embodiments, alkenyl groups are optionally substituted. Examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, and 2-methyl-1-heptenyl. In certain embodiments, alkenyl groups are optionally substituted.

The term "C_{2-6} alkenyl," as used herein, means a straight, branched chain, or cyclic (in this case, it would also be known as "cycloalkyl") hydrocarbon containing from 2-6 carbon atoms and at least one carbon-carbon double bond formed by the removal of two hydrogens.

The term "alkoxy," as used herein, means an alkyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, tert-butoxy, pentyloxy, and hexyloxy.

An "amino acid" (or AA) or amino acid residue include but are not limited to the 20 naturally occurring amino acids acids commonly designated by three letter symbols and also includes 4-hydroxyproline, hydroxyysine, demosine, isodemosine, 3-methylhistidine, norvalin, beta-alanine, gamma-aminobutyric acid, homocysteine, homoserine, ornithine and methionine sulfone. The amino acid residue of the present application also include the corresponding N-methyl amino acids, such as $-N(CH_3)CH_2C(O)O-$, $-NHC(O)CH_2CH_2CH(NHCH_3)C(O)O-$, etc. The amino acids, dipeptides, tripeptides, oligomers and polypeptides designated as $-(AA)_r-$ of the present application may include the corresponding non-N-alkylated amino acids and peptides (such as non-N-methylated amino acids in the peptides), as well as a mixture of the non-N-alkylated amino acids and the N-alkylated amino acids of the peptides.

An "antibody-drug conjugate" or "ADC" is an antibody that is conjugated to one or more cytotoxins, through one or more linkers. An antibody-drug conjugate (ADC)

may be of the formula A-L-CTX, wherein A is an antibody, L is a linker, and CTX is a cytotoxin.

In the context of a polypeptide, the term "analog" as used herein refers to a polypeptide that possesses a similar or identical function as a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an anti-C10orf54 antibody but does not necessarily comprise a similar or identical amino acid sequence of a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an anti-C10orf54 antibody, or possess a similar or identical structure of a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an anti-C10orf54 antibody. A polypeptide that has a similar amino acid sequence refers to a polypeptide that satisfies at least one of the following: (a) a polypeptide having an amino acid sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to the amino acid sequence of a C10orf54 polypeptide (*e.g.,* SEQ ID NO:1079), a fragment of a C10orf54 polypeptide, or an anti-C10orf54 antibody described herein; (b) a polypeptide encoded by a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence encoding a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an anti-C10orf54 antibody (or VH or VL region thereof) described herein of at least 5 amino acid residues, at least 10 amino acid residues, at least 15 amino acid residues, at least 20 amino acid residues, at least 25 amino acid residues, at least 40 amino acid residues, at least 50 amino acid residues, at least 60 amino residues, at least 70 amino acid residues, at least 80 amino acid residues, at least 90 amino acid residues, at least 100 amino acid residues, at least 125 amino acid residues, or at least 150 amino acid residues (see, *e.g.,* Sambrook *et al.* (2001) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY; Maniatis *et al.* (1982) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, NY); and (c) a polypeptide encoded by a nucleotide sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to the nucleotide sequence encoding a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an anti-C10orf54 antibody (or VH or VL region thereof) described herein. A

polypeptide with similar structure to a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an anti-C10orf54 antibody described herein refers to a polypeptide that has a similar secondary, tertiary or quaternary structure of a C10orf54 polypeptide, a fragment of a C10orf54, or a C10orf54 antibody described herein. The structure of a polypeptide can determined by methods known to those skilled in the art, including but not limited to, X-ray crystallography, nuclear magnetic resonance, and crystallographic electron microscopy.

As used herein, an "antagonist" or "inhibitor" of C10orf54 refers to a molecule that is capable of inhibiting or otherwise decreasing one or more of the biological activities of C10orf54, such as in a cell expressing C10orf54 or in a cell expressing a C10orf54 ligand, such as a C10orf54 receptor. In some embodiments, an antagonist of C10orf54 (*e.g.*, an antagonistic antibody provided herein) may, for example, act by inhibiting or otherwise decreasing the activation and/or cell signaling pathways of the cell expressing a C10orf54 or a C10orf54 receptor, thereby inhibiting a C10orf54-mediated biological activity of the cell the relative to the C10orf54-mediated biological activity in the absence of antagonist. In certain embodiments the antibodies provided herein are antagonistic anti-C10orf54 antibodies.

The terms "antibody" and "immunoglobulin" or "Ig" are used interchangeably herein, and are intended to include a polypeptide product of B cells within the immunoglobulin class of polypeptides that is able to bind to a specific molecular antigen and is composed of two identical pairs of polypeptide chains, wherein each pair has one heavy chain (about 50-70 kDa) and one light chain (about 25 kDa) and each amino-terminal portion of each chain includes a variable region of about 100 to about 130 or more amino acids and each carboxy-terminal portion of each chain includes a constant region (*See*, Borrebaeck (ed.) (1995) Antibody Engineering, Second Ed., Oxford University Press.; Kuby (1997) Immunology, Third Ed., W.H. Freeman and Company, New York). In specific embodiments, the specific molecular antigen can be bound by an antibody provided herein includes the target C10orf54 polypeptide, fragment or epitope.

Antibodies also include, but are not limited to, synthetic antibodies, monoclonal antibodies, recombinantly produced antibodies, multispecific antibodies (including bi-specific antibodies), human antibodies, humanized antibodies, camelized antibodies,

chimeric antibodies, intrabodies, anti-idiotypic (anti-Id) antibodies, and functional fragments of any of the above, which refers a portion of an antibody heavy or light chain polypeptide that retains some or all of the binding activity of the antibody from which the fragment was derived. Non-limiting examples of functional fragments include single-chain Fvs (scFv) (*e.g.*, including monospecific, bispecific, *etc.*), Fab fragments, F(ab') fragments, $F(ab)_2$ fragments, $F(ab')_2$ fragments, disulfide-linked Fvs (sdFv), Fd fragments, Fv fragments, diabody, triabody, tetrabody and minibody. In particular, antibodies provided herein include immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, *e.g.*, antigen binding domains or molecules that contain an antigen-binding site that binds to a C10orf54 antigen (*e.g.*, one or more complementarity determining regions (CDRs) of an anti-C10orf54 antibody). Such antibody fragments can be found described in, for example, Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, New York (1989); Myers (ed.), Molec. Biology and Biotechnology: A Comprehensive Desk Reference, New York: VCH Publisher, Inc.; Huston et al., *Cell Biophysics*, 22:189-224 (1993); Plückthun and Skerra, *Meth. Enzymol.*, 178:497-515 (1989) and in Day, E.D., Advanced Immunochemistry, Second Ed., Wiley-Liss, Inc., New York, NY (1990). The antibodies provided herein can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA and IgY), any class (*e.g.*, IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2), or any subclass (*e.g.*, IgG2a and IgG2b) of immunoglobulin molecule. An anti-C10orf54 antibodies provided herein can be agonistic antibodies or antagonistic antibodies.

The terms "antibodies that specifically bind to C10orf54," "antibodies that specifically bind to a C10orf54 epitope," "anti-C10orf54 antibodies" and analogous terms are also used interchangeably herein and refer to antibodies that specifically bind to a C10orf54 polypeptide, such as a C10orf54 antigen or epitope. Such antibodies include humanized antibodies. An antibody that specifically binds to a C10orf54 antigen may be cross-reactive with related antigens. In certain embodiments, an antibody that specifically binds to a C10orf54 antigen does not cross-react with other antigens. An antibody that specifically binds to a C10orf54 antigen can be identified, for example, by immunoassays, BIAcore, or other techniques known to those of skill in the art. An antibody binds specifically to a C10orf54 antigen when it binds to a C10orf54 antigen with higher affinity than to any cross-reactive antigen as determined

using experimental techniques, such as radioimmunoassays (RIA) and enzyme-linked immunosorbent assays (ELISAs). Typically a specific or selective reaction will be at least twice background signal or noise and more typically more than 10 times background. See, *e.g.*, Paul, ed., 1989, Fundamental Immunology Second Edition, Raven Press, New York at pages 332-336 for a discussion regarding antibody specificity. In certain embodiments, an antibody "which binds" an antigen of interest is one that binds the antigen with sufficient affinity such that the antibody is useful as a diagnostic and/or therapeutic agent in targeting a cell or tissue expressing the antigen, and does not significantly cross-react with other proteins. In such embodiments, the extent of binding of the antibody to a "non-target" protein will be less than about 10% of the binding of the antibody to its particular target protein as determined by fluorescence activated cell sorting (FACS) analysis or radioimmunoprecipitation (RIA). With regard to the binding of an antibody to a target molecule, the term "specific binding" or "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a particular polypeptide target means binding that is measurably different from a non-specific interaction. Specific binding can be measured, for example, by determining binding of a molecule compared to binding of a control molecule, which generally is a molecule of similar structure that does not have binding activity. For example, specific binding can be determined by competition with a control molecule that is similar to the target, for example, an excess of non-labeled target. In this case, specific binding is indicated if the binding of the labeled target to a probe is competitively inhibited by excess unlabeled target. The term "specific binding" or "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a particular polypeptide target as used herein can be exhibited, for example, by a molecule having a Kd for the target of at least about 10^{-4} M, alternatively at least about 10^{-5} M, alternatively at least about 10^{-6} M, alternatively at least about 10^{-7} M, alternatively at least about 10^{-8} M, alternatively at least about 10^{-9} M, alternatively at least about 10^{-10} M, alternatively at least about 10^{-11} M, alternatively at least about 10^{-12} M, or greater. In one embodiment, the term "specific binding" refers to binding where a molecule binds to a particular polypeptide or epitope on a particular polypeptide without substantially binding to any other polypeptide or polypeptide epitope. In certain embodiments, an antibody that binds to C10orf54 has a dissociation constant (Kd) of ≤ 1μM, ≤ 100 nM, ≤ 10 nM, ≤ 1nM, or ≤

0.1nM. In certain embodiments, anti- C10orf54 antibody binds to an epitope of C10orf54 that is conserved among C10orf54 from different species.

An "anti-c10orf54 antibody" or "an antibody that binds to C10orf54 " refers to an antibody that is capable of binding C10orf54, including, for example, an antibody, with sufficient affinity such that the antibody is useful as a diagnostic and/or therapeutic agent in targeting C10orf54. Such antibodies include humanized antibodies. Preferably, the extent of binding of an anti-C10orf54 antibody to an unrelated, non-C10orf54 protein is less than about 10% of the binding of the antibody to C10orf54 as measured, *e.g.,* by fluorescence activated cell sorting (FACS) analysis or a radioimmunoassay (RIA). An antibody that "specifically binds to" or is "specific for" C10orf54 is defined as above. In certain embodiments, an antibody that binds to C10orf54 has a dissociation constant (Kd) of < 1 μM, < 100 nM, < 10 nM, < 1 nM, or < 0.1 nM. In certain embodiments, anti-C10orf54 antibody binds to an epitope of C10orf54 that is conserved among C10orf54 from different species.

An "antigen" is a predetermined antigen to which an antibody can selectively bind. The target antigen may be a polypeptide, carbohydrate, nucleic acid, lipid, hapten or other naturally occurring or synthetic compound. In specific embodiments, the target antigen is a polypeptide.

The term "antigen binding fragment," "antigen binding domain," "antigen binding region," and similar terms refer to that portion of an antibody which comprises the amino acid residues that interact with an antigen and confer on the binding agent its specificity and affinity for the antigen (*e.g.,* the complementarity determining regions (CDRs)).

The terms "binds" or "binding" as used herein refer to an interaction between molecules to form a complex. Interactions can be, for example, non-covalent interactions including hydrogen bonds, ionic bonds, hydrophobic interactions, and/or van der Waals interactions. A complex can also include the binding of two or more molecules held together by covalent or non-covalent bonds, interactions or forces. The strength of the total non-covalent interactions between a single antigen-binding site on an antibody and a single epitope of a target molecule, such as C10orf54, is the affinity of the antibody or functional fragment for that epitope. The ratio of

association (k_1) to dissociation (k_{-1}) of an antibody to a monovalent antigen (k_1/ k_{-1}) is the association constant *K*, which is a measure of affinity. The value of *K* varies for different complexes of antibody and antigen and depends on both k_1 and k_{-1}. The association constant *K* for an antibody provided herein can be determined using any method provided herein or any other method well known to those skilled in the art. The affinity at one binding site does not always reflect the true strength of the interaction between an antibody and an antigen. When complex antigens containing multiple, repeating antigenic determinants, such as a polyvalent C10orf54, come in contact with antibodies containing multiple binding sites, the interaction of antibody with antigen at one site will increase the probability of a reaction at a second site. The strength of such multiple interactions between a multivalent antibody and antigen is called the avidity. The avidity of an antibody can be a better measure of its binding capacity than is the affinity of its individual binding sites. For example, high avidity can compensate for low affinity as is sometimes found for pentameric IgM antibodies, which can have a lower affinity than IgG, but the high avidity of IgM, resulting from its multivalence, enables it to bind antigen effectively.

The term "C10orf54" or "C10orf54 polypeptide" and similar terms refers to the polypeptide ("polypeptide," "peptide" and "protein" are used interchangeably herein) encoded by the human Chromosome 10 Open Reading Frame 54 (C10orf54) gene, which is also known in the art as B7-H5, platelet receptor Gi24, GI24, Stress Induced Secreted Protein1, SISP1, and PP2135, comprising the amino acid sequence of:

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  1 mgvptaleag swrwgsllfa lflaaslgpv aafkvatpys lyvcpegqnv tltcrllgpv
 61 dkghdvtfyk twyrssrgev qtcserrpir nltfqdlhlh hgghqaants hdlaqrhgle
121 sasdhhgnfs itmrnltlld sglycclvve irhhhsehrv hgamelqvqt gkdapsncvv
181 ypsssqdsen itaaalatga civgilclpl illlvykqrq aasnrraqel vrmdsniqgi
241 enpgfeaspp aqgipeakvr hplsyvaqrq psesgrhlls epstplsppg pgdvffpsld
301 pvpdspnfev I (SEQ ID NO:1079)
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and related polypeptides, including SNP variants thereof. The C10orf54 polypeptide has been shown to or is predicted to comprise several distinct regions within the amino acid sequence including: a signal sequence (residues 1-32; *see* Zhang et al., *Protein Sci.* 13:2819-2824 (2004)); an immunoglobulin domain - IgV-like (residues 33-162); and a transmembrane region (residues 195-215). The mature C10orf54 protein includes amino acid residues 33-311 of SEQ ID NO: 1079. The extracellular domain

of the C10orf54 protein includes amino acid residues 33-194 of SEQ ID NO: 1079. Related polypeptides include allelic variants (*e.g.*, SNP variants); splice variants; fragments; derivatives; substitution, deletion, and insertion variants; fusion polypeptides; and interspecies homologs, preferably, which retain C10orf54 activity and/or are sufficient to generate an anti-C10orf54 immune response. As those skilled in the art will appreciate, an anti-C10orf54 antibody provided herein can bind to a C10orf54 polypeptide, polypeptide fragment, antigen, and/or epitope, as an epitope is part of the larger antigen, which is part of the larger polypeptide fragment, which, in turn, is part of the larger polypeptide. C10orf54 can exist in a native or denatured form. The C10ORF54 polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods. A "native sequence C10ORF54 polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding C10ORF54 polypeptide derived from nature. Such native sequence C10ORF54 polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence C10ORF54 polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific C10ORF54 polypeptide *(e.g.,* an extracellular domain sequence), naturally-occurring variant forms *(e.g.,* alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide.

A cDNA nucleic acid sequence encoding the C10orf54 polypeptide comprises:

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1   atgggcgtcc ccacggccct ggaggccggc agctggcgct ggggatccct gctcttcgct
61  ctcttcctgg ctgcgtccct aggtccggtg gcagccttca aggtcgccac gccgtattcc
121 ctgtatgtct gtcccgaggg gcagaacgtc accctcacct gcaggctctt gggccctgtg
181 gacaaagggc acgatgtgac cttctacaag acgtggtacc gcagctcgag gggcgaggtg
241 cagacctgct cagagcgccg gcccatccgc aacctcacgt tccaggacct tcacctgcac
301 catggaggcc accaggctgc caacaccagc cacgacctgg ctcagcgcca cgggctggag
361 tcggcctccg accaccatgg caacttctcc atcaccatgc gcaacctgac cctgctggat
421 agcggcctct actgctgcct ggtggtggag atcaggcacc accactcgga gcacagggtc
481 catggtgcca tggagctgca ggtgcagaca ggcaaagatg caccatccaa ctgtgtggtg
541 tacccatcct cctcccagga tagtgaaaac atcacggctg cagccctggc tacgggtgcc
601 tgcatcgtag gaatcctctg cctccccctc atcctgctcc tggtctacaa gcaaaggcag
661 gcagcctcca accgccgtgc ccaggagctg gtgcggatgg acagcaacat tcaagggatt
721 gaaaaccccg gctttgaagc ctcaccacct gcccagggga tacccgaggc caaagtcagg
781 caccccctgt cctatgtggc ccagcggcag ccttctgagt ctgggcggca tctgctttcg
841 gagcccagca cccccctgtc tcctccaggc cccggagacg tcttcttccc atccctggac
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901 cctgtccctg actctccaaa ctttgaggtc atctag (SEQ ID NO:1080)

Orthologs to the C10orf54 polypeptide are also well known in the art. For example, the mouse ortholog to the C10orf54 polypeptide is V-region Immunoglobulin-containing Suppressor of T cell Activation (VISTA) (also known as PD-L3, PD-1H, PD-XL, Pro1412 and UNQ730), which shares approximately 70% sequence identity to the human polypeptide. Orthologs of C10orf54 can also be found in additional organisms including chimpanzee, cow, rat and zebrafish.

A "C10orf54-expressing cell," "a cell having expression of C10orf54" or a grammatical equivalent thereof refers to a cell that expresses endogenous or transfected C10orf54 on the cell surface. C10orf54 expressing cells include a C10orf54-berring tumor cells, regulatory tumor cells (*e.g.*, $CD4^+$ $Foxp3^+$ regulatory T cells), myeloid-derived suppressor cells (*e.g.*, $CD11b^+$ or $CD11b^{high}$ myeloid-derived suppressor cells) and/or suppressive dendritic cells (e.g., $CD11b^+$ or $CD11b^{high}$ dendritic cells). A cell expressing C10orf54 produces sufficient levels of C10orf54 on its surface, such that an anti-C10orf54 antibody can bind thereto. In some aspect, such binding may have a therapeutic effect with respect to the cancer. A cell that "overexpresses" C10orf54 is one that has significantly higher levels of C10orf54 at the cell surface thereof, compared to a cell of the same tissue type that is known to express C10orf54. Such overexpression may be caused by gene amplification or by increased transcription or translation. C10orf54 overexpression may be determined in a diagnostic or prognostic assay by evaluating increased levels of the C10orf54 protein present on the surface of a cell (*e.g.* via an immunohistochemistry assay; FACS analysis). Alternatively, or additionally, one may measure levels of C10orf54-encoding nucleic acid or mRNA in the cell, *e.g.* via fluorescent in situ hybridization; (FISH; see W098/45479 published October, 1998), Southern blotting, Northern blotting, or polymerase chain reaction (PCR) techniques, such as real time quantitative PCR (RT-PCR). Aside from the above assays, various *in vivo* assays are available to the skilled practitioner. For example, one may expose cells within the body of the patient to an antibody which is optionally labeled with a detectable agent, and binding of the antibody to cells in the patient can be evaluated, *e.g.* by external scanning for radioactivity or by analyzing a biopsy taken from a patient previously exposed to the

antibody. A C10orf54-expressing tumor cell includes, but is not limited to, acute myeloid leukemia (AML) tumor cells.

A "C10orf54-mediated disease," "C10orf54-mediated disorder" and "C10orf54-mediated condition" are used interchangeably and refer to any disease, disorder or condition that is completely or partially caused by or is the result of C10orf54. Such diseases, disorders or conditions include those 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 regulatory T cells (T regs)). In certain embodiments, C10orf54 is aberrantly (*e.g.*, highly) expressed on the surface of a cell. In some embodiments, C10orf54 may be aberrantly upregulated on a particular cell type. In other embodiments, normal, aberrant or excessive cell signaling is caused by binding of C10orf54 to a C10orf54 ligand, which can bind or otherwise interact with C10orf54.

The terms "cell proliferative disorder" and "proliferative disorder" refer to disorders that are associated with some degree of abnormal cell proliferation. In one embodiment, the cell proliferative disorder is a tumor or cancer. "Tumor," as used herein, refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues. The terms "cancer," "cancerous," "cell proliferative disorder," "proliferative disorder" and "tumor" are not mutually exclusive as referred to herein. The terms "cancer" and "cancerous" refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth. Examples of cancer include, but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia or lymphoid malignancies. More particular examples of such cancers include squamous cell cancer (*e.g.* epithelial squamous cell cancer), lung cancer including small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung and squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer including gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, oral cancer, liver cancer, bladder cancer, cancer of the urinary tract, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile

carcinoma, melanoma, multiple myeloma and B-cell lymphoma, brain cancer, as well as head and neck cancer, and associated metastases.

The term "carrier" refers to a diluent, adjuvant (*e.g.,* Freund's adjuvant (complete and incomplete)), excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a exemplary carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, *etc.* Examples of suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA. Such compositions will contain a prophylactically or therapeutically effective amount of the antibody, *e.g.,* in isolated or purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

The term "chemical group," as used herein, refers to two or more atoms bound together as a single unit and forming part of a molecule.

A "chemotherapeutic agent" is a chemical agent (*e.g.,* compound or drug) useful in the treatment of cancer, regardless of mechanism of action. Chemotherapeutic agents include compounds used in targeted therapy and conventional chemotherapy. Examples of chemotherapeutic agents include, but are not limited to, alkylating agents such as thiotepa and CYTOXAN® cyclosphosphamide; alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone,

meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, trietylenephosphoramide, triethiylenethiophosphoramide and trimethylolomelamine; acetogenins (especially bullatacin and bullatacinone); delta-9-tetrahydrocannabinol (dronabinol, AR1NOL®); beta-lapachone; lapachol; colchicines; betulinic acid; a camptothecin (including the synthetic analogue topotecan (HYCAMTIN®), CPT-11 (irinotecan, CAMPTOSAR®), acetylcamptothecin, scopolectin, and 9-aminocamptothecin); bryostatin; callystatin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogues); podophyllotoxin; podophyllinic acid; teniposide; cryptophycins (particularly cryptophycin 1 and cryptophycin 8); dolastatin; duocarmycin (including the synthetic analogues, KW-2189 and CB1 -TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimnustine; antibiotics such as the enediyne antibiotics (*e.g.*, calicheamicin, especially calicheamicin gammal I and calicheamicin omega II (see, *e.g.*, Agnew, *Chem Intl. Ed. Engl.* 33:183-186 (1994)); dynemicin, including dynemicin A; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antiobiotic chromophores), aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, ADRIAMYCIN®, doxorubicin (including morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane,

trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfornithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidanmol; nitraerine; pentostatin; phenamet; pirarubicin; losoxantrone; 2-ethylhydrazide; procarbazine; PSK® polysaccharide complex (JHS Natural Products, Eugene, Oreg.); razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2"-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine (ELDISINE®, FILDESIN®); dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); thiotepa; taxoids, *e.g.*, TAXOL® paclitaxel (Bristol-Myers Squibb Oncology, Princeton, N.J.), ABRAXANE™ Cremophor-free, albumin-engineered nanoparticle formulation of paclitaxel (American Pharmaceutical Partners, Schaumberg, IL.), and TAXOTERE® doxetaxel (Rhone-Poulenc Rorer, Antony, France); chloranbucil; gemcitabine (GEMZAR®); 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine (VELBAN®); platinum; etoposide (VP- 16); ifosfamide; mitoxantrone; vincristine (ONCOVIN®); oxaliplatin; leucovovin; vinorelbine (NAVELBINE®); novantrone; edatrexate; daunomycin; aminopterin; ibandronate; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoids such as retinoic acid; capecitabine (XELODA®); pharmaceutically acceptable salts, acids or derivatives of any of the above; as well as combinations of two or more of the above such as CHOP, an abbreviation for a combined therapy of cyclophosphamide, doxorubicin, vincristine, and prednisolone, and FOLFOX, an abbreviation for a treatment regimen with oxaliplatin (ELOXATIN™) combined with 5-FU and leucovovin. Additional chemotherapeutic agents include cytotoxic agents useful as antibody drug conjugates, such as maytansinoids (DM1 and DM4, for example) and auristatins (MMAE and MMAF, for example).

Also included in the definition of chemotherapeutic agent are: (i) anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens and selective estrogen receptor modulators (SERMs), including, for example, tamoxifen (including NOLVADEX®; tamoxifen citrate), raloxifene, droloxifene, 4-

hydroxytamoxifen, trioxifene, keoxifene, LY 117018, onapristone, and FARESTON® (toremifine citrate); (ii) aromatase inhibitors that inhibit the enzyme aromatase, which regulates estrogen production in the adrenal glands, such as, for example, 4(5)-imidazoles, aminoglutethimide, MEGASE® (megestrol acetate), AROMASIN® (exemestane; Pfizer), formestanie, fadrozole, RI VISor® (vorozole), FEMARA® (letrozole; Novartis), and ARIMIDEX® (anastrozole; AstraZeneca); (iii) anti-androgens such as flutamide, nilutamide, bicalutamide, leuprolide, and goserelin; as well as troxacitabine (a 1,3-dioxolane nucleoside cytosine analog); (iv) protein kinase inhibitors such as ME inhibitors (WO 2007/044515); (v) lipid kinase inhibitors; (vi) antisense oligonucleotides, particularly those which inhibit expression of genes in signaling pathways implicated in aberrant cell proliferation, for example, PKC-alpha, Raf and H-Ras, such as oblimersen (GENASENSE®, Genta Inc.); (vii) ribozymes such as VEGF expression inhibitors (*e.g.*, ANGIOZYME®) and HER2 expression inhibitors; (viii) vaccines such as gene therapy vaccines, for example, ALLOVECTIN®, LEUVECTIN®, and VAX1D®; PROLEUKIN® rIL-2; topoisomerase 1 inhibitors such as LURTOTECAN®; ABARELIX® rmRH; (ix) anti-angiogenic agents such as bevacizumab (AVASTIN®, Genentech); and pharmaceutically acceptable salts, acids and derivatives of any of the above.

The antibodies provided herein can include "chimeric" antibodies in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (see U.S. Patent No. 4,816,567; and Morrison et al., Proc. Natl. Acad. Sci. USA, 81:6851-6855 (1984)).

As used herein, the term "composition" is intended to encompass a product containing the specified ingredients (*e.g.*, an antibody provided herein) in, optionally, the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in, optionally, the specified amounts.

A "CDR" refers to one of three hypervariable regions (H1, H2 or H3) within the non-framework region of the immunoglobulin (Ig or antibody) VH β-sheet framework, or

one of three hypervariable regions (L1, L2 or L3) within the non-framework region of the antibody VL β-sheet framework. Accordingly, CDRs are variable region sequences interspersed within the framework region sequences. CDR regions are well known to those skilled in the art and have been defined by, for example, Kabat as the regions of most hypervariability within the antibody variable (V) domains (Kabat et al., *J. Biol. Chem.* 252:6609-6616 (1977); Kabat, *Adv. Prot. Chem.* 32:1-75 (1978)). CDR region sequences also have been defined structurally by Chothia as those residues that are not part of the conserved β-sheet framework, and thus are able to adapt different conformations (Chothia and Lesk, *J. Mol. Biol.* 196:901-917 (1987)). Both terminologies are well recognized in the art. CDR region sequences have also been defined by AbM, Contact and IMGT. CDR region sequences are illustrated in **FIG. 16A** and **16B**. The positions of CDRs within a canonical antibody variable domain have been determined by comparison of numerous structures (Al-Lazikani et al., *J. Mol. Biol.* 273:927-948 (1997); Morea et al., *Methods* 20:267-279 (2000)). Because the number of residues within a hypervariable region varies in different antibodies, additional residues relative to the canonical positions are conventionally numbered with a, b, c and so forth next to the residue number in the canonical variable domain numbering scheme (Al-Lazikani et al., *supra* (1997)). Such nomenclature is similarly well known to those skilled in the art.

The term "hypervariable region", "HVR", or "HV", when used herein refers to the regions of an antibody variable domain that are hypervariable in sequence and/or form structurally defined loops. Generally, antibodies comprise six hypervariable regions; three in the VH (H 1, H2, H3), and three in the VL (LI, L2, L3). A number of hypervariable region delineations are in use and are encompassed herein. The Kabat CDRs are based on sequence variability and are the most commonly used (Kabat *eta/., Sequences of Proteins of Immunological Interest,* 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD. (1991)). Chothia refers instead to the location of the structural loops (Chothia and Lesk *J Mol. Bioi.* 196:901-917 (1987)). The end of the Chothia CDR-HI loop when numbered using the Kabat numbering convention varies between H32 and H34 depending on the length of the loop (this is because the Kabat numbering scheme places the insertions at H35A and H35B; if neither 35A nor 35B is present, the loop ends at 32; if only 35A is present, the loop ends at 33; if both 35A and 35B are present, the loop ends at 34). The AbM

hypervariable regions represent a compromise between the Kabat CDRs and Chothia structural loops, and are used by Oxford Molecular's AbM antibody modeling software. The "contact" hypervariable regions are based on an analysis of the available complex crystal structures. The residues from each of these hypervariable regions are noted below.

Recently, a universal numbering system has been developed and widely adopted, ImMunoGeneTics (IMGT) Information System® (Lafranc et al., *Dev. Comp. Immunol.* 27(1):55-77 (2003)). IMGT is an integrated information system specializing in immunoglobulins (IG), T cell receptors (TR) and major histocompatibility complex (MHC) of human and other vertebrates. Herein, the CDRs are referred to in terms of both the amino acid sequence and the location within the light or heavy chain. As the "location" of the CDRs within the structure of the immunoglobulin variable domain is conserved between species and present in structures called loops, by using numbering systems that align variable domain sequences according to structural features, CDR and framework residues and are readily identified. This information can be used in grafting and replacement of CDR residues from immunoglobulins of one species into an acceptor framework from, typically, a human antibody. Correspondence between the Kabat numbering and the IMGT unique numbering system is also well known to one skilled in the art (*e.g.* Lefranc et al., *supra*) and is also illustrated in **FIG. 16A** and **16B**. An Exemplary system, shown herein, combines Kabat and Chothia.

Table 1: CDR Definitions

	Exemplary (Kabat + Chothia)	IMGT	Kabat	AbM	Chothia	Contact
V_H CDR1	26-35	27-38	31-35	26-35	26-32	30-35
V_H CDR2	50-65	56-65	50-65	50-58	53-55	47-58
V_H CDR3	95-102	105-117	95-102	95-102	96-101	93-101
V_L CDR1	24-34	27-38	24-34	24-34	26-32	30-36
V_L CDR2	50-56	56-65	50-56	50-56	50-52	46-55
V_L CDR3	89-97	105-117	89-97	89-97	91-96	89-96

Hypervariable regions may comprise "extended hypervariable regions" as follows: 24-36 or 24-34 (LI), 46-56 or 50-56 (L2) and 89-97 or 89-96 (L3) in the VL and 26-35 or 26-35A (H1), 50-65 or 49-65 (H2) and 93-102, 94-1 02, or 95-102 (H3) in the VH. The

variable domain residues are 25 numbered according to Kabat et al., *supra*, for each of these definitions. As used herein, the terms "HVR" and "CDR" are used interchangeably.

The term "constant region" or "constant domain" refers to a carboxy terminal portion of the light and heavy chain which is not directly involved in binding of the antibody to antigen but exhibits various effector function, such as interaction with the Fc receptor. The terms refer to the portion of an immunoglobulin molecule having a more conserved amino acid sequence relative to the other portion of the immunoglobulin, the variable domain, which contains the antigen binding site. The constant domain contains the CH1, CH2 and CH3 domains of the heavy chain and the CL domain of the light chain.

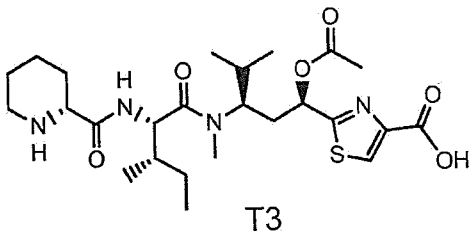
The term "cycloalkyl," as used herein, means a monocyclic or polycyclic radical that contains only carbon and hydrogen, and includes those that are saturated, partially unsaturated, or fully unsaturated. Cycloalkyl groups include groups having from 3 to 10 ring atoms.

In the context of a polypeptide, the term "derivative" as used herein refers to a polypeptide that comprises an amino acid sequence of a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an antibody that binds to a C10orf54 polypeptide which has been altered by the introduction of amino acid residue substitutions, deletions or additions. The term "derivative" as used herein also refers to a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or an antibody that binds to a C10orf54 polypeptide which has been chemically modified, *e.g.*, by the covalent attachment of any type of molecule to the polypeptide. For example, but not by way of limitation, a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or a C10orf54 antibody may be chemically modified, *e.g.*, by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, *etc.* The derivatives are modified in a manner that is different from naturally occurring or starting peptide or polypeptides, either in the type or location of the molecules attached. Derivatives further include deletion of one or more chemical groups which are naturally present on the peptide or polypeptide. A derivative of a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or a C10orf54 antibody may be

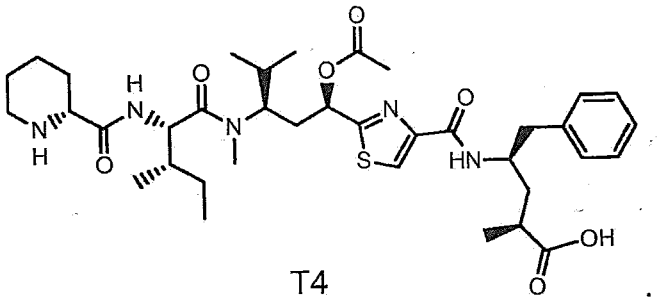
chemically modified by chemical modifications using techniques known to those of skill in the art, including, but not limited to specific chemical cleavage, acetylation, formulation, metabolic synthesis of tunicamycin, *etc.* Further, a derivative of a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or a C10orf54 antibody may contain one or more non-classical amino acids. A polypeptide derivative possesses a similar or identical function as a C10orf54 polypeptide, a fragment of a C10orf54 polypeptide, or a C10orf54 antibody described herein.

The term "cytotoxic agent" or "cytotoxin" or "CTX" as used herein refers to a substance that inhibits or prevents the function of cells and/or has a cytotoxic effect on cells (*e.g.,* causes destruction of cells). The term is intended to include alkylating agents, an anthracyclines, a cytoskeletal disruptors (taxanes), an epothilones, an histone deacetylase Inhibitor (HDAC), an inhibitor of Topoisomerase I, an Inhibitor of Topoisomerase II, a kinase inhibitor, a monoclonal antibodies, a nucleotide analog, a peptide antibiotic, a platinum-based agent, a retinoids, a Vinca alkaloid or a derivative thereof, and radioisotope. The term is also intended to include Actinomycin, all-trans retinoic acid, Azacitidine, Azathioprine, Bleomycin, Bortezomib, Carboplatin, Capecitabine, Cisplatin, Chlorambucil, Cyclophosphamide, Cytarabine, Daunorubicin, Docetaxel, Doxifluridine, Doxorubicin, Epirubicin, Epothilone, Etoposide, Fluorouracil, Gemcitabine, Hydroxyurea, Idarubicin, Imatinib, Irinotecan, Mechlorethamine, Mercaptopurine, Methotrexate, Mitoxantrone, Oxaliplatin, Paclitaxel, Pemetrexed, Teniposide, Tioguanine, Topotecan, Valrubicin, Vinblastine, Vincristine, Vindesine, and Vinorelbine. The term is also intended to include a tubulin stabilizer, a tubulin destabilizer, a DNA alkylator, a DNA minor groove binder, a DNA intercalator, a topoisomerase I inhibitor, a topoisomerase II inhibitor, a gyrase inhibitor, a protein synthesis inhibitor, a proteosome inhibitor, and an anti-metabolite. The term is also intended to include Actinomycin D, Amonafide, an auristatin, benzophenone, benzothiazole, a calicheamicin, Camptothecin, CC-1065 (NSC 298223), Cemadotin, Colchicine, Combretastatin A4, Dolastatin, Doxorubicin, Elinafide, Emtansine (DM1), Etoposide, KF-12347 (Leinamycin), a maytansinoid, Methotrexate, Mitoxantrone, Nocodazole, Proteosome Inhibitor 1 (PSI 1), Roridin A, T-2 Toxin (trichothecene analog), Taxol, a tubulysin, Velcade®, and Vincristine. Preferred cytotoxins include an auristatin, a calicheamicin, a maytansinoid, and a tubulysin. Other preferred cytotoxins include monomethylauristatin E, monomethylauristatin F, calicheamicin γ,

mertansine, tubulysin T3, and tubulysin T4, the structures for which are provided below:



T3



T4

Other cytotoxic agents including various antitumor or anticancer agents are known in the art.

The term "detectable probe," as used herein, refers to a composition that provides a detectable signal. The term includes, without limitation, any fluorophore, chromophore, radiolabel, enzyme, antibody or antibody fragment, and the like, that provide a detectable signal via its activity.

The term "diagnostic agent" refers to a substance administered to a subject that aids in the diagnosis of a disease. Such substances can be used to reveal, pinpoint, and/or define the localization of a disease causing process. In certain embodiments, a diagnostic agent includes a substance that is conjugated to an antibody provided herein, that when administered to a subject or contacted to a sample from a subject aids in the diagnosis of cancer, tumor formation, or any other C10orf54-mediated disease.

The term "detectable agent" refers to a substance that can be used to ascertain the existence or presence of a desired molecule, such as an antibody provided herein, in a sample or subject. A detectable agent can be a substance that is capable of being visualized or a substance that is otherwise able to be determined and/or measured (*e.g.*, by quantitation).

An "effective amount" is an amount sufficient to effect beneficial or desired results. An effective amount can be administered in one or more administrations, applications or dosages. Such delivery is dependent on a number of variables including the time period for which the individual dosage unit is to be used, the bioavailability of the

agent, the route of administration, *etc.* In some embodiments, effective amount also refers to the amount of an antibody provided herein to achieve a specified result (*e.g.*, inhibition of a C10orf54 biological activity of a cell, such as modulating T cell activation and/or proliferation). In some embodiments, this term refers to the amount of a therapy (*e.g.*, an antibody or pharmaceutical composition provided herein) which is sufficient to reduce and/or ameliorate the severity and/or duration of a given disease and/or a symptom related thereto. This term also encompasses an amount necessary for the reduction or amelioration of the advancement or progression of a given disease, reduction or amelioration of the recurrence, development or onset of a given disease, and/or to improve or enhance the prophylactic or therapeutic effect(s) of another therapy (*e.g.*, a therapy other than anti-C10orf54 antibody provided herein). In some embodiments, the effective amount of an antibody is from about 0.1 mg/kg (mg of antibody per kg weight of the subject) to about 100 mg/kg. In certain embodiments, an effective amount of an antibody provided therein is about 0.1 mg/kg, about 0.5 mg/kg, about 1 mg/kg, 3 mg/kg, 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 60 mg/kg, about 70 mg/kg, about 80 mg/kg about 90 mg/kg or about 100 mg/kg (or a range therein).

The term "electrophilic leaving group," as used herein, refers to a leaving group that accepts an electron pair to make a covalent bond. In general, electrophiles are susceptible to attack by complementary nucleophiles, including the reduced thiols from the disulfide bond of an antibody.

The term "electrophilic leaving group that reacts selectively with thiols," as used herein, refers to electrophilic leaving group that reacts selectively with thiols, over other nucleophiles. In certain embodiments, an electrophilic leaving group that reacts selectively with thiols reacts selectively with the reduced thiols from the disulfide bond of an antibody.

The term "encode" or grammatical equivalents thereof as it is used in reference to nucleic acid molecule refers to a nucleic acid molecule in its native state or when manipulated by methods well known to those skilled in the art that can be transcribed to produce mRNA, which is then translated into a polypeptide and/or a fragment

thereof. The antisense strand is the complement of such a nucleic acid molecule, and the encoding sequence can be deduced therefrom.

The term "epitope" as used herein refers to a localized region on the surface of an antigen, such as C10orf54 polypeptide or C10orf54 polypeptide fragment, that is capable of being bound to one or more antigen binding regions of an antibody, and that has antigenic or immunogenic activity in an animal, such as a mammal (*e.g.*, a human), that is capable of eliciting an immune response. An epitope having immunogenic activity is a portion of a polypeptide that elicits an antibody response in an animal. An epitope having antigenic activity is a portion of a polypeptide to which an antibody binds as determined by any method well known in the art, for example, by an immunoassay. Antigenic epitopes need not necessarily be immunogenic. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and have specific three dimensional structural characteristics as well as specific charge characteristics. A region of a polypeptide contributing to an epitope may be contiguous amino acids of the polypeptide or the epitope may come together from two or more non-contiguous regions of the polypeptide. The epitope may or may not be a three-dimensional surface feature of the antigen. In certain embodiments, a C10orf54 epitope is a three-dimensional surface feature of a C10orf54 polypeptide. In other embodiments, a C10orf54 epitope is linear feature of a C10orf54 polypeptide. Generally an antigen has several or many different epitopes and reacts with many different antibodies.

The term "excipient" as used herein refers to an inert substance which is commonly used as a diluent, vehicle, preservative, binder, or stabilizing agent, and includes, but not limited to, proteins (*e.g.*, serum albumin, *etc.*), amino acids (*e.g.*, aspartic acid, glutamic acid, lysine, arginine, glycine, histidine, *etc.*), fatty acids and phospholipids (*e.g.*, alkyl sulfonates, caprylate, *etc.*), surfactants (*e.g.*, SDS, polysorbate, nonionic surfactant, *etc.*), saccharides (*e.g.*, sucrose, maltose, trehalose, *etc.*) and polyols (*e.g.*, mannitol, sorbitol, *etc.*). See, also, Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA, which is hereby incorporated by reference in its entirety.

In the context of a peptide or polypeptide, the term "fragment" as used herein refers to a peptide or polypeptide that comprises less than the full length amino acid sequence.

Such a fragment may arise, for example, from a truncation at the amino terminus, a truncation at the carboxy terminus, and/or an internal deletion of a residue(s) from the amino acid sequence. Fragments may, for example, result from alternative RNA splicing or from *in vivo* protease activity. In certain embodiments, C10orf54 fragments include polypeptides comprising an amino acid sequence of at least 5 contiguous amino acid residues, at least 10 contiguous amino acid residues, at least 15 contiguous amino acid residues, at least 20 contiguous amino acid residues, at least 25 contiguous amino acid residues, at least 40 contiguous amino acid residues, at least 50 contiguous amino acid residues, at least 60 contiguous amino residues, at least 70 contiguous amino acid residues, at least 80 contiguous amino acid residues, at least 90 contiguous amino acid residues, at least contiguous 100 amino acid residues, at least 125 contiguous amino acid residues, at least 150 contiguous amino acid residues, at least 175 contiguous amino acid residues, at least 200 contiguous amino acid residues, or at least 250 contiguous amino acid residues of the amino acid sequence of a C10orf54 polypeptide or an antibody that binds to a C10orf54 polypeptide. In a specific embodiment, a fragment of a C10orf54 polypeptide or an antibody that binds to a C10orf54 antigen retains at least 1, at least 2, or at least 3 functions of the polypeptide or antibody.

The term "framework" or "FR" residues are those variable domain residues flanking the CDRs. FR residues are present, *e.g.*, in chimeric, humanized, human, domain antibodies, diabodies, linear antibodies, and bispecific antibodies. FR residues are those variable domain residues other than the hypervariable region residues herein defined.

A "functional fragment" of an antibody will exhibit at least one if not some or all of the biological functions attributed to the intact antibody, the function comprising at least specific binding to the target antigen.

The term "fusion protein" as used herein refers to a polypeptide that comprises an amino acid sequence of an antibody and an amino acid sequence of a heterologous polypeptide or protein (*e.g.*, a polypeptide or protein not normally a part of the antibody (*e.g.*, a non-anti-C10orf54 antigen antibody)). The term "fusion" when used in relation to C10orf54 or to an anti-C10orf54 antibody refers to the joining of a peptide or polypeptide, or fragment, variant and/or derivative thereof, with a

heterologous peptide or polypeptide. In certain embodiments, the fusion protein retains the biological activity of the C10orf54 or anti-C10orf54 antibody. In certain embodiments, the fusion protein comprises a C10orf54 antibody VH domain, VL domain, VH CDR (one, two or three VH CDRs), and/or VL CDR (one, two or three VL CDRs), wherein the fusion protein binds to a C10orf54 epitope.

The term "heavy chain" when used in reference to an antibody refers to a polypeptide chain of about 50-70 kDa, wherein the amino-terminal portion includes a variable region of about 120 to 130 or more amino acids and a carboxy-terminal portion that includes a constant region. The constant region can be one of five distinct types, referred to as alpha (α), delta (δ), epsilon (ε), gamma (γ) and mu (μ), based on the amino acid sequence of the heavy chain constant region. The distinct heavy chains differ in size: α, δ and γ contain approximately 450 amino acids, while μ and ε contain approximately 550 amino acids. When combined with a light chain, these distinct types of heavy chains give rise to five well known classes of antibodies, IgA, IgD, IgE, IgG and IgM, respectively, including four subclasses of IgG, namely IgG1, IgG2, IgG3 and IgG4. A heavy chain can be a human heavy chain.

The term "host" as used herein refers to an animal, such as a mammal (*e.g.*, a human).

The term "host cell" as used herein refers to the particular subject cell transfected with a nucleic acid molecule and the progeny or potential progeny of such a cell. Progeny of such a cell may not be identical to the parent cell transfected with the nucleic acid molecule due to mutations or environmental influences that may occur in succeeding generations or integration of the nucleic acid molecule into the host cell genome.

"Humanized" forms of nonhuman (*e.g.*, murine) antibodies are chimeric antibodies that include human immunoglobulins (recipient antibody) in which the native CDR residues are replaced by residues from the corresponding CDR of a nonhuman species (donor antibody) such as mouse, rat, rabbit or nonhuman primate having the desired specificity, affinity, and capacity. In some instances, one or more FR region residues of the human immunoglobulin are replaced by corresponding nonhuman residues. Furthermore, humanized antibodies can comprise residues that are not found in the recipient antibody or in the donor antibody. These modifications are

made to further refine antibody performance. A humanized antibody heavy or light chain can comprise substantially all of at least one or more variable domains, in which all or substantially all of the CDRs correspond to those of a nonhuman immunoglobulin and all or substantially all of the FRs are those of a human immunoglobulin sequence. In certain embodiments, the humanized antibody will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. For further details, see, Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992); Carter et al., *Proc. Natl. Acd. Sci. USA* 89:4285-4289 (1992); and U.S. Patent Nos: 6,800,738 (issued Oct. 5, 2004), 6,719,971 (issued Sept. 27, 2005), 6,639,055 (issued Oct. 28, 2003), 6,407,213 (issued June 18, 2002), and 6,054,297 (issued April 25, 2000).

An antibody that "inhibits the growth of and/or kills cells expressing C10orf54" or a "growth inhibitory" or "cytotoxic" antibody is one which results in measurable growth inhibition and/or killing of cells expressing or overexpressing the appropriate C10orf54 polypeptide. In some embodiments, such antibodies can inhibit the growth of and/or kill cells expressing C10orf54. Such cells include regulatory T cells (e.g., a CD4+ Foxp3+ regulatory T cells), a myeloid-derived suppressor cells (e.g.,a CD11b+ or CD11bhigh myeloid-derived suppressor cells) and/or a suppressive dendritic cells (e.g., a CD11b+ or CD11bhigh dendritic cells). In a specific embodiment, antibodies inhibit the growth of and/or kill a cancer cell, a pre-cancerous cell, or a cell comprising a tumor. Certain growth inhibitory anti-C10orf54 antibodies inhibit growth of and/or kill C10orf54-expressing cells by greater than 20%, such as from about 20% to about 50%, or by greater than 50% (*e.g.*, from about 50% to about 100%) as compared to the appropriate control, the control typically being cells not treated with the antibody being tested. In one embodiment, growth inhibition and/or killing can be measured at an antibody concentration of about 0.1 to 30 g/ml or about 0.5 nM to 200 nM in cell culture, where the growth inhibition is determined 1-10 days after exposure of the tumor cells to the antibody. Growth inhibition and/or killing of cells *in vivo* can be determined in various ways such as is described below. In the context of inhibiting a cancer cell or a cell comprising a tumor, the antibody is growth inhibitory or kills *in vivo* if administration of the anti-C10orf54 antibody at about 1 g/kg to about 100 mg/kg body weight results in reduction in tumor size or tumor cell proliferation within about 5

days to 3 months from the first administration of the antibody, such as within about 5 to 30 days.

As used herein, the term "in combination" in the context of the administration of other therapies refers to the use of more than one therapy. The use of the term "in combination" does not restrict the order in which therapies are administered to a subject with an infection. A first therapy can be administered before (*e.g.*, 1 minute, 45 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours, 96 hours, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 8 weeks, or 12 weeks), concurrently, or after (*e.g.*, 1 minute, 45 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours, 96 hours, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 8 weeks, or 12 weeks) the administration of a second therapy to a subject which had, has, or is susceptible to a C10orf54-mediated disease. Any additional therapy can be administered in any order with the other additional therapies. In certain embodiments, the antibodies can be administered in combination with one or more therapies (*e.g.*, therapies that are not the antibodies that are currently administered to prevent, treat, manage, and/or ameliorate a C10orf54-mediated disease. Non-limiting examples of therapies that can be administered in combination with an antibody include analgesic agents, anesthetic agents, antibiotics, or immunomodulatory agents or any other agent listed in the U.S. Pharmacopoeia and/or Physician's Desk Reference.

An antibody that "induces cell death" is one that causes a viable cell to become nonviable. The cell is of a cell type that specifically expresses or overexpresses a C10orf54 polypeptide. The cell may be cancerous or a normal cell of the particular cell type, such as a regulatory T cell. Cell death *in vitro* may be determined in the absence of complement and immune effector cells to distinguish cell death induced by antibody-dependent cell-mediated cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC). Thus, the assay for cell death may be performed using heat inactivated serum (*e.g.*, in the absence of complement) and in the absence of immune effector cells. To determine whether the antibody is able to induce cell death, loss of membrane integrity as evaluated by uptake of propidium iodide (PI), trypan blue (see Moore *et al. Cytotechnology* 17:1-11 (1995)). In some

embodiments, cell death-inducing antibodies are those which induce PI uptake in the PI uptake assay in C10orf54 expressing cells.

An "isolated" antibody is substantially free of cellular material or other contaminating proteins from the cell or tissue source and/or other contaminant components from which the antibody is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of an antibody in which the antibody is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, an antibody that is substantially free of cellular material includes preparations of antibody having less than about 30%, 20%, 10%, or 5% (by dry weight) of heterologous protein (also referred to herein as a "contaminating protein"). In certain embodiments, when the antibody is recombinantly produced, it is substantially free of culture medium, *e.g.*, culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. In certain embodiments, when the antibody is produced by chemical synthesis, it is substantially free of chemical precursors or other chemicals, *e.g.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of the antibody have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the antibody of interest. Contaminant components can also include, but are not limited to, materials that would interfere with therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In certain embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method (Lowry *et al.* J. Bio. Chem. 193: 265-275, 1951), such as 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody *in situ* within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step. In a specific embodiment, antibodies provided herein are isolated

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. In a specific embodiment, a nucleic acid molecule(s) encoding an antibody provided herein is isolated or purified.

The term "leaving group," as used herein, refers to any group that leaves in the course of a chemical reaction involving the group as described herein and includes but is not limited to halogen, sulfonates (brosylate, mesylate, tosylate triflate etc ...), p-nitrobenzoate and phosphonate groups, for example.

The term "light chain" when used in reference to an antibody refers to a polypeptide chain of about 25 kDa, wherein the amino-terminal portion includes a variable region of about 100 to about 110 or more amino acids and a carboxy-terminal portion that includes a constant region. The approximate length of a light chain is 211 to 217 amino acids. There are two distinct types, referred to as kappa (κ) of lambda (λ) based on the amino acid sequence of the constant domains. Light chain amino acid sequences are well known in the art. A light chain can be a human light chain.

A "linker" (noted as L or L^1, L^2 and L^3) is a molecule with two reactive termini, one for conjugation to an antibody or to another linker and the other for conjugation to a cytotoxin. The antibody conjugation reactive terminus of the linker is typically a site that is capable of conjugation to the antibody through a cysteine thiol or lysine amine group on the antibody, and so is typically a thiol-reactive group such as a double bond (as in maleimide) or a leaving group such as a chloro, bromo or iodo or an R-sulfanyl group or sulfonyl group, or an amine-reactive group such as a carboxyl group or as defined herein; while the antibody conjugation reactive terminus of the linker is typically a site that is capable of conjugation to the cytotoxin through formation of an amide bond with a basic amine or carboxyl group on the cytotoxin, and so is typically a carboxyl or basic amine group. In one embodiment, when the term "linker" is used in describing the linker in conjugated form, one or both of the reactive termini will be absent (such as the leaving group of the thiol-reactive group) or incomplete (such as the being only the carbonyl of the carboxylic acid) because of the formation of the

bonds between the linker and/or the cytotoxin. The linkers disclosed herein may be cleavable under normal physiological and/or intracellular conditions, or may remain stable (*e.g.*, uncleaved or non-cleavable) under those same conditions. Examples of cleavable linkers are linkers which contain dipeptide moieties, where the peptide bond connecting the two peptides has the potential to be selectively cleaved by lysosomal proteases (*e.g.*, cathepsin-B). Valine-citruline (Val-Cit) is a dipeptide moiety commonly used in cleavable linkers.

As used herein, the terms "manage," "managing," and "management" refer to the beneficial effects that a subject derives from a therapy (*e.g.*, a prophylactic or therapeutic agent), which does not result in a cure of the disease. In certain embodiments, a subject is administered one or more therapies (*e.g.*, prophylactic or therapeutic agents, such as an antibody provided herein) to "manage" a C10orf54-mediated disease, one or more symptoms thereof, so as to prevent the progression or worsening of the disease.

The term "monoclonal antibody" refers to an antibody obtained from a population of homogenous or substantially homogeneous antibodies, and each monoclonal antibody will typically recognize a single epitope on the antigen. In specific embodiments, a "monoclonal antibody," as used herein, is an antibody produced by a single hybridoma or other cell, wherein the antibody binds to only a C10orf54 epitope as determined, *e.g.*, by ELISA or other antigen-binding or competitive binding assay known in the art. The term "monoclonal" is not limited to any particular method for making the antibody. For example, monoclonal antibodies provided herein may be made by the hybridoma method as described in Kohler *et al.*; Nature, 256:495 (1975) or may be isolated from phage libraries using the techniques. Other methods for the preparation of clonal cell lines and of monoclonal antibodies expressed thereby are well known in the art (see, for example, Chapter 11 in: Short Protocols in Molecular Biology, (2002) 5th Ed., Ausubel *et al.*, eds., John Wiley and Sons, New York). Other exemplary methods of producing other monoclonal antibodies are provided in the Examples herein.

The term "native" when used in connection with biological materials such as nucleic acid molecules, polypeptides, host cells, and the like, refers to those which are found in nature and not manipulated by a human being.

The term "pharmaceutically acceptable" as used herein means being approved by a regulatory agency of the Federal or a state government, or listed in the U.S. Pharmacopeia, European Pharmacopeia or other generally recognized Pharmacopeia for use in animals, and more particularly in humans.

"Polyclonal antibodies" as used herein refers to an antibody population generated in an immunogenic response to a protein having many epitopes and thus includes a variety of different antibodies directed to the same and to different epitopes within the protein. Methods for producing polyclonal antibodies are known in the art (See, *e.g.*, see, for example, Chapter 11 in: Short Protocols in Molecular Biology, (2002) 5th Ed., Ausubel *et al.*, eds., John Wiley and Sons, New York).

As used herein, the term "polynucleotide," "nucleotide," nucleic acid" "nucleic acid molecule" and other similar terms are used interchangeable and include DNA, RNA, mRNA and the like.

A "pre-cancerous cell" refers to a cell that has an abnormal appearance such as a difference in size or shape in comparison to cells of the surrounding tissue or normal cells of its cell type, but are not invasive. The appearance of pre-cancerous cells can be suggestive of an increased cancer risk. Pre-cancerous cells expressing C10orf54 can be identified using methods disclosed herein, which can include analyzing a sample of cells from a patient.

As used herein, the terms "prevent," "preventing," and "prevention" refer to the total or partial inhibition of the development, recurrence, onset or spread of a C10orf54-mediated disease and/or symptom related thereto, resulting from the administration of a therapy or combination of therapies provided herein (*e.g.*, a combination of prophylactic or therapeutic agents, such as an antibody provided herein).

As used herein, the term "prophylactic agent" refers to any agent that can totally or partially inhibit the development, recurrence, onset or spread of a C10orf54-mediated disease and/or symptom related thereto in a subject. In certain embodiments, the term "prophylactic agent" refers to an anti-C10orf54 antibody provided herein. In certain other embodiments, the term "prophylactic agent" refers to an agent other than an anti-C10orf54 antibody provided herein. In certain embodiments, a prophylactic agent is an agent which is known to be useful to or has been or is

currently being used to prevent a C10orf54-mediated disease and/or a symptom related thereto or impede the onset, development, progression and/or severity of a C10orf54-mediated disease and/or a symptom related thereto. In specific embodiments, the prophylactic agent is a humanized anti-C10orf54 antibody, such as a humanized anti-C10orf54 monoclonal antibody.

In certain embodiments, a "prophylactically effective serum titer" is the serum titer in a subject, preferably a human, that totally or partially inhibits the development, recurrence, onset or spread of a C10orf54-mediated disease and/or symptom related thereto in the subject.

The term "recombinant antibody" refers to an antibody that is prepared, expressed, created or isolated by recombinant means. Recombinant antibodies can be antibodies expressed using a recombinant expression vector transfected into a host cell, antibodies isolated from a recombinant, combinatorial antibody library, antibodies isolated from an animal (*e.g.*, a mouse or cow) that is transgenic and/or transchromosomal for human immunoglobulin genes (*see e.g.*, Taylor, L. D. *et al.* (1992) *Nucl. Acids Res.* 20:6287-6295) or antibodies prepared, expressed, created or isolated by any other means that involves splicing of immunoglobulin gene sequences to other DNA sequences. Such recombinant antibodies can have variable and constant regions derived from human germline immunoglobulin sequences (See Kabat, E. A. *et al.* (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242). In certain embodiments, however, such recombinant antibodies are subjected to *in vitro* mutagenesis (or, when an animal transgenic for human Ig sequences is used, *in vivo* somatic mutagenesis) and thus the amino acid sequences of the VH and VL regions of the recombinant antibodies are sequences that, while derived from and related to human germline VH and VL sequences, may not naturally exist within the human antibody germline repertoire *in vivo*.

The term "serum titer" as used herein refers to an average serum titer in a population of least 10, such as at least 20, or at least 40 subjects, up to about 100, 1000 or more.

As used herein, the term "side effects" encompasses unwanted and adverse effects of a therapy (*e.g.*, a prophylactic or therapeutic agent). Unwanted effects are not necessarily adverse. An adverse effect from a therapy (*e.g.*, a prophylactic or therapeutic agent) might be harmful or uncomfortable or risky. Examples of side effects include, diarrhea, cough, gastroenteritis, wheezing, nausea, vomiting, anorexia, abdominal cramping, fever, pain, loss of body weight, dehydration, alopecia, dyspenea, insomnia, dizziness, mucositis, nerve and muscle effects, fatigue, dry mouth, and loss of appetite, rashes or swellings at the site of administration, flu-like symptoms such as fever, chills and fatigue, digestive tract problems and allergic reactions. Additional undesired effects experienced by patients are numerous and known in the art. Many are described in the Physician's Desk Reference (67^{th} ed., 2013).

As used herein, the terms "subject" and "patient" are used interchangeably. As used herein, in certain embodiments, a subject is a mammal, such as a non-primate (*e.g.*, cows, pigs, horses, cats, dogs, rats, *etc.*) or a primate (*e.g.*, monkey and human). In specific embodiments, the subject is a human. In one embodiment, the subject is a mammal (*e.g.*, a human) having a C10orf54-mediated disease. In another embodiment, the subject is a mammal (*e.g.*, a human) at risk of developing a C10orf54-mediated disease.

As used herein "substantially all" refers to refers to at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or about 100%.

As used herein, the term "therapeutic agent" refers to any agent that can be used in treating, preventing or alleviating a disease, disorder or condition, including in the treatment, prevention or alleviation of one or more symptoms of a C10orf54-mediated disease, disorder, or condition and/or a symptom related thereto. In certain embodiments, a therapeutic agent refers to an antibody provided herein. In certain other embodiments, a therapeutic agent refers to an agent other than an antibody provided herein. In certain embodiments, a therapeutic agent is an agent which is known to be useful for, or has been or is currently being used for the treatment, prevention or alleviation of one or more symptoms of a C10orf54-mediated disease, disorder, condition, or a symptom related thereto.

The combination of therapies (*e.g.*, use of therapeutic agents) can be more effective than the additive effects of any two or more single therapy. For example, a synergistic effect of a combination of therapeutic agents permits the use of lower dosages of one or more of the agents and/or less frequent administration of the agents to a subject with a C10orf54-mediated disease. The ability to utilize lower dosages of therapeutic therapies and/or to administer the therapies less frequently reduces the toxicity associated with the administration of the therapies to a subject without reducing the efficacy of the therapies in the prevention, treatment or alleviation of one or more symptom of a C10orf54-mediated disease. In addition, a synergistic effect can result in improved efficacy of therapies in the prevention, treatment or alleviation of one or more symptom of a C10orf54-mediated disease. Finally, synergistic effect of a combination of therapies (*e.g.*, therapeutic agents) may avoid or reduce adverse or unwanted side effects associated with the use of any single therapy.

The term "therapeutically effective amount" as used herein refers to the amount of a therapeutic agent (*e.g.*, an antibody provided herein or any other therapeutic agent provided herein) that is sufficient to reduce and/or ameliorate the severity and/or duration of a given disease and/or a symptom related thereto. A therapeutically effective amount of a therapeutic agent can be an amount necessary for the reduction or amelioration of the advancement or progression of a given disease, reduction or amelioration of the recurrence, development or onset of a given disease, and/or to improve or enhance the prophylactic or therapeutic effect of another therapy (*e.g.*, a therapy other than the administration of an antibody provided herein).

In certain embodiments, a "therapeutically effective serum titer" is the serum titer in a subject, preferably a human, that reduces the severity, the duration and/or the symptoms associated with a C10orf54-mediated disease in the subject.

As used herein, the term "therapy" refers to any protocol, method and/or agent that can be used in the prevention, management, treatment and/or amelioration of a C10orf54-mediated disease. In certain embodiments, the terms "therapies" and "therapy" refer to a biological therapy, supportive therapy, and/or other therapies useful in the prevention, management, treatment and/or amelioration of a C10orf54-mediated disease known to one of skill in the art such as medical personnel.

The term "thiol," as used herein, refers to the radical -SH.

As used herein, the terms "treat," "treatment" and "treating" refer to the reduction or amelioration of the progression, severity, and/or duration of a C10orf54-mediated disease resulting from the administration of one or more therapies (including, but not limited to, the administration of one or more therapeutic agents, such as an antibody provided herein). In specific embodiments, such terms refer to the reduction or inhibition of cancer or tumor formation. In other specific embodiments, such term refers to the reduction or amelioration of the progression, severity and/or duration of graft-versus-host disease. In yet other specific embodiments, such terms refer to the reduction or amelioration of the progression, severity, and/or duration of a disease that is responsive to immune modulation, such modulation resulting from increasing T cell activation, increasing T cell proliferation or increasing cytokine production.

"Tubulysin" includes both the natural products described as tubulysins, such as by Sasse et al. and other authors mentioned in the Description of the related art, and also the tubulysin analogs described in US Patent Application Publication No. US 2011/0021568 A1. Tubulysins disclosed in the present application are noted herein and may include the tubulysins of the formulae T3 and T4, and other tubulysins where the terminal *N*-methylpiperidine has been replaced by an unsubstituted piperidine, allowing amide bond formation with a linker.

The term "variable domain" or "variable region" refers to a portion of the light or heavy chains of an antibody that is generally located at the amino-terminal of the light or heavy chain and has a length of about 120 to 130 amino acids in the heavy chain and about 100 to 110 amino acids in the light chain, and are used in the binding and specificity of each particular antibody for its particular antigen. The variable domains differ extensively in sequence between different antibodies. The variability in sequence is concentrated in the CDRs while the less variable portions in the variable domain are referred to as framework regions (FR). The CDRs of the light and heavy chains are primarily responsible for the interaction of the antibody with antigen. In specific embodiments, the variable region is a human variable region.

The term "variable domain residue numbering as in Kabat" or "amino acid position numbering as in Kabat", and variations thereof, refers to the numbering system used

for heavy chain variable domains or light chain variable domains of the compilation of antibodies in Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD. (1991). Using this numbering system, the actual linear amino acid sequence may contain fewer or additional amino acids corresponding to a shortening of, or insertion into, a FR or CDR of the variable domain. For example, a heavy chain variable domain may include a single amino acid insert (residue 52a according to Kabat) after residue 52 of H2 and inserted residues (*e.g.* residues 82a, 82b, and 82c, etc, according to Kabat) after heavy chain FR residue 82. The Kabat numbering of residues may be determined for a given antibody by alignment at regions of homology of the sequence of the antibody with a "standard" Kabat numbered sequence. The Kabat numbering system is generally used when referring to a residue in the variable domain (approximately residues 1-107 of the light chain and residues 1-113 of the heavy chain) (e.g, Kabat *et al., Sequences of Immunological Interest.* 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)). The "EU numbering system" or "EU index" is generally used when referring to a residue in an immunoglobulin heavy chain constant region (*e.g.,* the EU index reported in Kabat *et al., supra).* The "EU index as in Kabat" refers to the residue numbering of the human IgG 1 EU antibody. Unless stated otherwise herein, references to residue numbers in the variable domain of antibodies means residue numbering by the Kabat numbering system. Other numbering systems have been described, including, for example, by AbM, Chothia, Contact and IMGT. Various numbering systems are illustrated in **FIG. 16A** and **16B**.

The term "variant" when used in relation to C10orf54 or to an anti-C10orf54 antibody refers to a peptide or polypeptide comprising one or more (such as, for example, about 1 to about 25, about 1 to about 20, about 1 to about 15, about 1 to about 10, or about 1 to about 5) amino acid sequence substitutions, deletions, and/or additions as compared to a native or unmodified sequence. For example, a C10orf54 variant may result from one or more (such as, for example, about 1 to about 25, about 1 to about 20, about 1 to about 15, about 1 to about 10, or about 1 to about 5) changes to an amino acid sequence of native C10orf54. Also by way of example, a variant of an anti-C10orf54 antibody may result from one or more (such as, for example, about 1 to about 25, about 1 to about 20, about 1 to about 15, about 1 to about 10, or about 1 to

about 5) changes to an amino acid sequence of a native or previously unmodified anti-C10orf54 antibody. Variants may be naturally occurring, such as allelic or splice variants, or may be artificially constructed. Polypeptide variants may be prepared from the corresponding nucleic acid molecules encoding the variants. In specific embodiments, the C10orf54 variant or anti-C10orf54 antibody variant at least retains C10orf54 or anti-C10orf54 antibody functional activity, respectively. In specific embodiments, an anti-C10orf54 antibody variant binds C10orf54 and/or is antagonistic to C10orf54 activity. In specific embodiments, an anti-C10orf54 antibody variant binds C10orf54 and/or is agonistic to C10orf54 activity. In certain embodiments, the variant is encoded by a single nucleotide polymorphism (SNP) variant of a nucleic acid molecule that encodes C10orf54 or anti-C10orf54 antibody VH or VL regions or subregions.

The term "vector" refers to a substance that is used to introduce a nucleic acid molecule into a host cell. Vectors applicable for use include, for example, expression vectors, plasmids, phage vectors, viral vectors, episomes and artificial chromosomes, which can include selection sequences or markers operable for stable integration into a host cell's chromosome. Additionally, the vectors can include one or more selectable marker genes and appropriate expression control sequences. Selectable marker genes that can be included, for example, provide resistance to antibiotics or toxins, complement auxotrophic deficiencies, or supply critical nutrients not in the culture media. Expression control sequences can include constitutive and inducible promoters, transcription enhancers, transcription terminators, and the like which are well known in the art. When two or more nucleic acid molecules are to be co-expressed (*e.g.* both an antibody heavy and light chain), both nucleic acid molecules can be inserted, for example, into a single expression vector or in separate expression vectors. For single vector expression, the encoding nucleic acids can be operationally linked to one common expression control sequence or linked to different expression control sequences, such as one inducible promoter and one constitutive promoter. The introduction of nucleic acid molecules into a host cell can be confirmed using methods well known in the art. Such methods include, for example, nucleic acid analysis such as Northern blots or polymerase chain reaction (PCR) amplification of mRNA, or immunoblotting for expression of gene products, or other suitable analytical methods to test the expression of an introduced nucleic acid

sequence or its corresponding gene product. It is understood by those skilled in the art that the nucleic acid molecule is expressed in a sufficient amount to produce the desired product (*e.g.* an anti-C10orf54 antibody provided herein), and it is further understood that expression levels can be optimized to obtain sufficient expression using methods well known in the art.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. 1A and **1B** shows the protein expression level of C10orf54 that was identified and quantified by sTAg analysis in AML and BMMC samples and relevant control.

FIG. 2 shows FACS analysis of 23 primary AML-BM-MNC and 3 normal BM-MNC samples using anti-C10orf54 antibody 76E1.

FIGS. 3A and **3B** show humanized sequences for murine monoclonal antibody 76E1 VH region. SEQ ID NOS: 1, 7, 8, 12-15 and 82 are depicted.

FIGS. 4A and **4B** show humanized sequences for murine monoclonal antibody 141A VH region. SEQ ID NOS: 2, 7, 8, 16-19 and 82 are depicted.

FIGS. 5A and **5B** show humanized sequences for murine monoclonal antibody 175A VH region. SEQ ID NOS: 3, 7, 8, 20-23 and 82 are depicted.

FIGS. 6A and **6B** show humanized sequences for murine monoclonal antibody 76E1 VL region. SEQ ID NOS: 4, 9, 10, 24, 25 and 94 are depicted.

FIGS. 7A and **7B** show humanized sequences for murine monoclonal antibody 141A VL region. SEQ ID NOS: 5, 10, 11, 26, 27 and 94 are depicted.

FIGS. 8A and **8B** show humanized sequences for murine monoclonal antibody 175A VL region. SEQ ID NOS: 6, 9, 10, 28, 29 and 94 are depicted.

FIG. 9 shows pseudo-sequences of VH and VL domains of murine monoclonal antibodies 76E1, 141A and 175A (SEQ ID NOS: 1143-1148). CDRs are identified in bold.

FIG. 10 shows anti-C10orf54 antibody treatment induces strong tumor growth inhibition in established Kasumi-3 tumors.

FIG. 11 shows murine 175A anti-C10orf54 antibody treatment induces strong tumor growth inhibition in established Kasumi-3 tumors.

FIG. 12 shows results of a secondary ADC assay using anti-C10orf54 antibodies in a cell viability assay with C10orf54 expressing sarcoma line.

FIGS. 13 and **14** show activity of unconjugated and MMAF conjugated anti-C10orf54 antibodies in a cell viability assay using C10orf54 expressing sarcoma lines and parental sarcoma line.

FIG. 15 shows results of treatment with unconjugated and MMAF conjugated anti-C10orf54 antibodies in a tumor model using a C10orf54 expressing sarcoma line and parental sarcoma line.

FIG. 16A and **16B** shows a sequence alignment of the variable heavy chains and variable light chains of the anti-C10orf54 murine antibodies designated 76E1, 141A and 175A (SEQ ID NOS:1-6). Boundaries of CDR's are indicated by Kabat, AbM, Chothia, Contact and IMGT numbering.

FIG. 17A and **17B** shows a sequence alignment of the variable heavy chains and variable light chains of exemplary humanized anti-C10orf54 antibodies designated hu76E1, hu141A and hu175A (SEQ ID NOS: 1135-1137 for heavy chains; SEQ ID NOS: 1139-1141 for light chains) and the corresponding consensus sequences between hu76E1 and hu175A (SEQ ID NO: 1138 for the heavy chain; SEQ ID NO: 1142 for the light chain). Residues indicated just below that alignment indicate specific residues that can be varied at the above "X" position in the consensus sequence.

DETAILED DESCRIPTION

Provided herein are antibodies that bind to C10orf54, including a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope. Such antibodies include humanized anti-C10orf54 antibodies. Also provided are antibodies (*e.g.*, humanized anti-C10orf54 antibodies) that competitively block and anti-C10orf54 antibody provided herein from binding to a C10orf54 polypeptide. The anti-C10orf54 antibodies (*e.g.*, humanized anti-C10orf54 antibodies) provided herein can also be conjugated or recombinantly fused to a diagnostic agent, detectable agent or

therapeutic agent (*e.g.,* antibody-drug conjugate). Further provided are compositions comprising an anti-C10orf54 antibody (*e.g.*, a humanized anti-C10orf54 antibody). For example, a detectable agent may be a detectable probe.

Also provided herein 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 that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope. Further provided are vectors and host cells comprising nucleic acid molecules encoding anti-C10orf54 antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope. Also provided are methods of making antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope.

Methods of using the anti-C10orf54 antibodies (*e.g.*, humanized anti-C10orf54 antibodies) are provided. Methods include 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, including an antibody-drug conjugate (ADC) comprising an anti-C10orf54 antibody, provided herein 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 embodiments the anti-C10orf54 antibodies are humanized antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In one embodiment, 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 regulatory T cells (T regs)). In certain embodiments, the disease is a cancer, such as a leukemia, a bladder cancer or a fibrosarcoma. In one embodiment, the leukemia is an acute myeloid leukemia (AML). In other embodiments, the disease is graft-versus-host disease (GVHD). Additional methods provided include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells, provided herein, for 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 embodiments, the anti-C10orf54 antibodies, including ADCs comprising the anti-C10orf54 antibodies, provided herein

inhibit C10orf54-mediated suppressor activity on T cells (*e.g.*, to allow an effective anti-tumor immune response). In certain embodiments, the anti-C10orf54 antibodies provided herein 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 embodiments, antibody drug conjugates (ADCs) comprising anti-C10orf54 antibodies provided herein 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 embodiments, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In any of the above embodiments, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

Additional methods of using an anti-C10orf54 antibody arer provided.

The methods include 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 provided herein. In one embodiment, the cell is a regulatory T cell (*e.g.*, a $CD4^+$ $Foxp3^+$ regulatory T cell). In other embodiments, 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 embodiments, the cell is a cancerous or pre-cancerous cell. Additional methods provided include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells provided herein, 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 embodiments, the anti-C10orf54 antibodies, including ADCs comprising the anti-C10orf54 antibodies, provided herein inhibit C10orf54-mediated suppressor activity on T cells (*e.g.*, to allow an effective anti-tumor immune response). In certain embodiments, the anti-C10orf54

antibodies provided herein 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 embodiments, antibody drug conjugates (ADCs) comprising anti-C10orf54 antibodies provided herein 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 embodiments, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

The methods include 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) provided herein to a subject. In one embodiment, the modulating comprises increasing T cell activation. In other embodiment, the modulating comprises increasing T cell proliferation. In another embodiment, the modulating comprises increasing cytokine production.

The methods include methods for detecting C10orf54 in a sample comprising contacting the sample with an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody) provided herein, such as an antibody that comprises a detectible agent. In certain embodiments, the sample comprises a cell expressing C10orf54 on its surface.

The methods include methods of treating cancers comprising administering to a subject an anti-C10orf54 antibody or an antibody-drug conjugate (ADC) comprising an anti-C10orf54 (*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) 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 embodiments the cancer is acute myeloid leukemia (AML). In any of the above embodiments, the anti-C10orf54 antibody can

be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

The methods include 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 regs)) 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) 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 embodiments, the tumor cell is an AML cell. In any of the above embodiments, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In one embodiemnt, provided 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 provided herein. In some embodiments, the kits comprise an antibody-drug conjugate (ADC) wherein the antibody is an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody).

ANTIBODIES

In some embodiments, provided herein are antibodies that bind to C10orf54, including a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In some embodiments the anti-C10orf54 antibodies are humanized antibodies that bind C10orf54, including to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In certain embodiments, 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 the murine monoclonal antibody 175A, 76E1 or 141A as depicted in Table 2 and **FIGS. 3-8**. Accordingly, in some aspects, the VH domain comprises the amino acid sequence of SEQ ID NO:1. In some embodiments, the VH domain comprises the

amino acid sequence of SEQ ID NO:2. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:3. In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO:4. In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO:5. In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO:6.

Table 2. Murine Antibody Sequences

Murine Antibody	VH Domain*	VL Domain*
76E1	EVQLLQSGPELEKPGASVKISCKAS **GYSFTGYNMN**WVKQSNGKSLEWIG **NIDPYYDYTSYNLKFKD**KATLTVDK SSSTAYMQLKSLTSEDSAVYYCAT**S TMITPFDY**WGQGTTLTVSS (SEQ ID NO:1)	DVLMTQTPLSLPVSLGDQASISC**RSSQ SIVHSNGNTYLE**WYLQKPGQSPKLLIY **KVSNRFS**GVPDRFSGSGSGTDFTLKIN RVEAEDLGVYYC**FQGSHVPWT**FGGGT KLEIK (SEQ ID NO:4)
141A	QVQLQQSGAELMKPGASVKISCKAT **GYTFSRYWIE**WVKQRPGHGLEWIG **EILPGSGSTNYNEKFKG**KATFTADT SSNTAYMQLSSLTSEDSAVYYCAGE **EVYDGYPWFGY**WGQGTLVTVSA (SEQ ID NO:2)	QIVLSQSPAILSASPGEKVTMTC**RASSS LSYMH**WYQQKPGSSPKPWIY**ATSNLA S**GVPARFSGSGSGTSYSLTISRVEAED AATYYC**QQWSSNPYT**FGGGTKLEIK (SEQ ID NO:5)
175A	QVQLQQSGAELMKPGASVKISCKAT **GYTFSTHWIE**WVKQRPGHGLEWIG **EILPGSGSTSYNEKFKG**KATFTADT SSNTAYMQLSSLTSEDSAVYYCAR **WLLYYYAMDY**WGQGTSVTVSS (SEQ ID NO:3)	DVLMTQTPLSLPVSLGDQASISC**RSSQ SIVHSNGNTYLE**WYLQKPGQSPKLLIY **KLSNRFS**GVPDRFSGSGSGTDFTLKIS RVEAEDLGVYYC**FQGSHFPYT**FGGGT KLEIK (SEQ ID NO: 6)

*Bold amino acid residues represent CDR sequences (CDR1 - first bolded sequence; CDR2 - second bolded sequence; CDR3 - third bolded sequence)

In certain embodiments, the anti-C10orf54 antibody 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. For example, in some embodiments, the anti-C10orf54 antibody comprises a VH FR1, VH FR2, VH FR3, and/or VH FR4 depicted in a human germline sequence identified in Table 3. Accordingly, in some embodiments, the anti-C10orf54 antibody comprises a VH FR1, VH FR2, VH FR3, and/or VH FR4 of the human germline IGHV1-18 (SEQ ID NO:7) and IGHJ4-01 (SEQ ID NO: 82). In some embodiments, the anti-C10orf54 antibody comprises a VH FR1, VH FR2, VH FR3, and/or VH FR4 of the human germline IGHV3-48 (SEQ ID NO:8) and IGHJ4-01 (SEQ ID NO: 82). In some embodiments, the anti-C10orf54 antibody comprises a VL FR1, VL FR2, VL FR3, and/or VL FR4 of the human germline IGKV2-28 (SEQ ID NO:9) and IGKJ2-1 (SEQ ID NO:94). In

some embodiments, the anti-C10orf54 antibody comprises a VL FR1, VL FR2, VL FR3, and/or VL FR4 of the human germline IGKV1-39 (SEQ ID NO:10) and IGKJ2-1 (SEQ ID NO:94). In some embodiments, the anti-C10orf54 antibody comprises a VL FR1, VL FR2, VL FR3, and/or VL FR4 of the human germline IGKV3-20 (SEQ ID NO:10) and IGKJ2-1 (SEQ ID NO:94).

Table 3. Human Germline Immunoglobulin Amino Acid Sequences

Human Germline	Amino Acid Sequence	SEQ ID NO:
	Heavy Chain	
IMGT IGHV1-18	QVQLVQSGAEVKKPGASVKVSCKAS**GYTFT SYGIS**WVRQAPGQGLEWMG**WISAYNGNTN YAQKLQG**RVTMTTDTSTSTAYMELRSLRSD DTAVYYCAR	(SEQ ID NO:7)
IMGT IGHV3-48	EVQLVESGGGLVQPGGSLRLSCAAS**GFTFSS YSMN**WVRQAPGKGLEWVS**YISSSSSTIYYAD SVKG**RFTISRDNAKNSLYLQMNSLRAEDTAV YYCAR	(SEQ ID NO:8)
Joining region IMGT IGHJ4-01	YFDYWGQGTLVTVSS	(SEQ ID NO:82)
	Light Chain	
IMGT IGKV2-28	DIVMTQSPLSLPVTPGEPASISC**RSSQSLLHS NGYNYLD**WYLQKPGQSPQLLIY**LGSNRAS**G VPDRFSGSGSGTDFTLKISRVEAEDVGVYYC **MQALQTP**	(SEQ ID NO:9)
IMGT IGKV1-39	DIQMTQSPSSLSASVGDRVTITC**RASQSISSY LN**WYQQKPGKAPKLLIY**AASSLQS**GVPSRFS GSGSGTDFTLTISSLQPEDFATYYC**QQSYST P**	(SEQ ID NO:10)
IMGT IGKV3-20	EIVLTQSPGTLSLSPGERATLSC**RASQSVSSS YLA**WYQQKPGQAPRLLIY**GASSRAT**GIPDRF SGSGSGTDFTLTISRLEPEDFAVYYC**QQYGS SP**	(SEQ ID NO:11)
Joining region IMGT IGKJ2-01	YTFGQGTKLEIK	(SEQ ID NO: 94)

*Bold amino acid residues represent CDR sequences (CDR1 - first bolded sequence; CDR2 - second bolded sequence; CDR3 - third bolded sequence)

In certain embodiments, antibodies that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprise a VH domain having an amino acid sequence identified in Table 4 or **FIGS. 3-8** and/or a VL domain having an amino acid sequence identified in Table 4 or **FIGS. 3-8**.

Table 4. Humanized Antibody Amino Acid Sequences of VH and VL Domains

Murine Clone	Humanized VH Domains (SEQ ID NO:)	Humanized VL Domains (SEQ ID NO:)
76E1	QVQLVQSGAEVKKPGASVKVSCKA SGYSFTGYNMNWVRQAPGQGLEW MGNIDPYYDYTSYNLKFKDRVTMTT DTSTSTAYMELRSLRSDDTAVYYCA RSTMITPFDYWGQGTLVTVSS (SEQ ID NO:12)	DIVMTQSPLSLPVTPGEPASISCRSSQS IVHSNGNTYLEWYLQKPGQSPQLLIYK VSNRFSGVPDRFSGSGSGTDFTLKISR VEAEDVGVYYCFQGSHVPWTFGQGTK LEIK (SEQ ID NO:24)
	QVQLVQSGAEVKKPGASVKVSCKA SGYSFTGYNMNWVRQAPGQGLEW MGNIDPYYDYTSYAQKLQGRVTMT TDTSTSTAYMELRSLRSDDTAVYYC ARSTMITPFDYWGQGTLVTVSS (SEQ ID NO:13)	DIQMTQSPSSLSASVGDRVTITCRSSQ SIVHSNGNTYLEWYQQKPGKAPKLLIY KVSNRFSGVPSRFSGSGSGTDFTLTIS SLQPEDFATYYCFQGSHVPWTFGQGT KLEIK (SEQ ID NO:25)
	EVQLVESGGGLVQPGGSLRLSCAA SGYSFTGYNMNWVRQAPGKGLEW VSNIDPYYDYTSYNLKFKDRFTISRD NAKNSLYLQMNSLRAEDTAVYYCA RSTMITPFDYWGQGTLVTVSS (SEQ ID NO:14)	
	EVQLVESGGGLVQPGGSLRLSCAA SGYSFTGYNMNWVRQAPGKGLEW VSNIDPYYDYTSYADSVKGRFTISRD NAKNSLYLQMNSLRAEDTAVYYCA RSTMITPFDYWGQGTLVTVSS (SEQ ID NO:15)	
141A	QVQLVQSGAEVKKPGASVKVSCKA SGYTFSRYWIEWVRQAPGQGLEW MGEILPGSGSTNYNEKFKGRVTMTT DTSTSTAYMELRSLRSDDTAVYYCA REEVYDGYPWFGYWGQGTLVTVS S (SEQ ID NO:16)	EIVLTQSPGTLSLSPGERATLSCRASSS LSYMHWYQQKPGQAPRLLIYATSNLAS GIPDRFSGSGSGTDFTLTISRLEPEDFA VYYCQQWSSNPYTFGQGTKLEIK (SEQ ID NO:26)
	QVQLVQSGAEVKKPGASVKVSCKA SGYTFSRYWIEWVRQAPGQGLEW MGEILPGSGSTNYAQKLQGRVTMT TDTSTSTAYMELRSLRSDDTAVYYC AREEVYDGYPWFGYWGQGTLVTV SS (SEQ ID NO:17)	DIQMTQSPSSLSASVGDRVTITCRASS SLSYMHWYQQKPGKAPKLLIYATSNLA SGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQWSSNPYTFGQGTKLEIK (SEQ ID NO:27)
	EVQLVESGGGLVQPGGSLRLSCAA SGYTFSRYWIEWVRQAPGKGLEWV SEILPGSGSTNYNEKFKGRFTISRDN AKNSLYLQMNSLRAEDTAVYYCARE EVYDGYPWFGYWGQGTLVTVSS (SEQ ID NO:18)	
	EVQLVESGGGLVQPGGSLRLSCAA SGYTFSRYWIEWVRQAPGKGLEWV SEILPGSGSTNYADSVKGRFTISRD NAKNSLYLQMNSLRAEDTAVYYCA REEVYDGYPWFGYWGQGTLVTVS S (SEQ ID NO:19)	

Murine Clone	Humanized VH Domains (SEQ ID NO:)	Humanized VL Domains (SEQ ID NO:)
175A	QVQLVQSGAEVKKPGASVKVSCKA SGYTFSTHWIEWVRQAPGQGLEW MGEILPGSGSTSYNEKFKGRVTMTT DTSTSTAYMELRSLRSDDTAVYYCA RWLLYYYAMDYWGQGTLVTVSS (SEQ ID NO:20)	DIVMTQSPLSLPVTPGEPASISCRSSQS IVHSNGNTYLEWYLQKPGQSPQLLIYK LSNRFSGVPDRFSGSGSGTDFTLKISR VEAEDVGVYYCFQGSHFPYTFGQGTK LEIK(SEQ ID NO:28)
	QVQLVQSGAEVKKPGASVKVSCKA SGYTFSTHWIEWVRQAPGQGLEW MGEILPGSGSTSYAQKLQGRVTMTT DTSTSTAYMELRSLRSDDTAVYYCA RWLLYYYAMDYWGQGTLVTVSS (SEQ ID NO:21)	DIQMTQSPSSLSASVGDRVTITCRSSQ SIVHSNGNTYLEWYQQKPGKAPKLLIY KLSNRFSGVPSRFSGSGSGTDFTLTIS SLQPEDFATYYCFQGSHFPYTFGQGT KLEIK (SEQ ID NO:29)
	EVQLVESGGGLVQPGGSLRLSCAA SGYTFSTHWIEWVRQAPGKGLEWV SEILPGSGSTSYNEKFKGRFTISRDN AKNSLYLQMNSLRAEDTAVYYCAR WLLYYYAMDYWGQGTLVTVSS (SEQ ID NO:22)	
	EVQLVESGGGLVQPGGSLRLSCAA SGYTFSTHWIEWVRQAPGKGLEWV SEILPGSGSTSYADSVKGRFTISRDN AKNSLYLQMNSLRAEDTAVYYCAR WLLYYYAMDYWGQGTLVTVSS (SEQ ID NO:23)	

Accordingly, in some embodiments, antibodies that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprise a VH domain having the amino acid sequence of SEQ ID NOS:20, 21, 22 or 23 and/or a VL domain having the amino acid sequence of SEQ ID NO:28 or 29. In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:20 and/or a VL domain having the amino acid sequence of SEQ ID NO:28. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:21 and/or a VL domain having the amino acid sequence of SEQ ID NO:28. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:22 and/or a VL domain having the amino acid sequence of SEQ ID NO:28. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino

acid sequence of SEQ ID NO:23 and/or a VL domain having the amino acid sequence of SEQ ID NO:28. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:20 and/or a VL domain having the amino acid sequence of SEQ ID NO:29. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:21 and/or a VL domain having the amino acid sequence of SEQ ID NO:29. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:22 and/or a VL domain having the amino acid sequence of SEQ ID NO:29. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:23 and/or a VL domain having the amino acid sequence of SEQ ID NO:29.

In some embodiments, antibodies that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprise a VH domain having the amino acid sequence of SEQ ID NOS:12, 13, 14 or 15 and/or a VL domain having the amino acid sequence of SEQ ID NO:24 or 25. Accordingly, in one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:12 and/or a VL domain having the amino acid sequence of SEQ ID NO:24. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:13 and/or a VL domain having the amino acid sequence of SEQ ID NO:24. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:14 and/or a VL domain having the amino acid sequence of SEQ ID NO:24. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:15 and/or a VL domain having the amino acid sequence of SEQ ID NO:24. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54

polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:12 and/or a VL domain having the amino acid sequence of SEQ ID NO:25. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:13 and/or a VL domain having the amino acid sequence of SEQ ID NO:25. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:14 and/or a VL domain having the amino acid sequence of SEQ ID NO:25. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:15 and/or a VL domain having the amino acid sequence of SEQ ID NO:25.

In some embodiments, antibodies that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprise a VH domain having the amino acid sequence of SEQ ID NOS:16, 17, 18 or 19 and/or a VL domain having the amino acid sequence of SEQ ID NO:26 or 27. Accordingly, in one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:16 and/or a VL domain having the amino acid sequence of SEQ ID NO:26. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:17 and/or a VL domain having the amino acid sequence of SEQ ID NO:26. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:18 and/or a VL domain having the amino acid sequence of SEQ ID NO:26. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:19 and/or a VL domain having the amino acid sequence of SEQ ID NO:26. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:16 and/or a VL domain having the amino acid

sequence of SEQ ID NO:27. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:17 and/or a VL domain having the amino acid sequence of SEQ ID NO:27. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:18 and/or a VL domain having the amino acid sequence of SEQ ID NO:27. In one aspect an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH domain having the amino acid sequence of SEQ ID NO:19 and/or a VL domain having the amino acid sequence of SEQ ID NO:27.

In certain embodiments, antibodies provided herein that bind to a C10orf54 eptitope comprise a VH region having a VH CDR1, VH CDR2, and/or VH CDR3, that have an amino acid sequence indentified in Tables 5-7 below; and/or a VL region having VL CDR1, VL CDR 2 and/or VL CDR3 that have an amino acid sequence identified in Tables 5-7 below.

Table 5: Amino Acid Sequences derived from Murine 175A Antibody.

175A HUMANIZED ANTIBODY SEQUENCE: HEAVY CHAIN
175A-huVH1a Variable Region
QVQLVQSGAEVKKPGASVKVSCKASGYTFSTHWIEWVRQAPGQGLEWMGEILPGSGSTS YNEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWLLYYYAMDYWGQGTLVTVS S (SEQ ID NO:20)
175A-huVH1a VH FR1
QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO:51)
QVQLVQSGAEVKKPGASVK**I**SCKAS (SEQ ID NO:105)
175A-huVH1a VH CDR1
GYTFSTHWIE (SEQ ID NO:36)
175A-huVH1a VH FR2
WVRQAPGQGLEWMG (SEQ ID NO:52)
WVRQAPGQGLEW**I**G (SEQ ID NO:106)
175A-huVH1a VH CDR2
EILPGSGSTSYNEKFKG (SEQ ID NO:37)
EILPGSGSTSY**Q**EKFKG (SEQ ID NO:101)
EILPGSGSTSY**S**EKFKG (SEQ ID NO:102)
EILPGSGSTSY**D**EKFKG (SEQ ID NO:103)
EILPGSGSTSY**A**EKFKG (SEQ ID NO:104)

175A-huVH1a VH FR3
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:53)
RATMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:107)
RVTFTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:108)
RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:109)
RATFTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:110)
RVTFTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:111)
RATMTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:112)
RATFTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:113)
175A-huVH1a VH CDR3
WLLYYYAMDY(SEQ ID NO:38)
175A-huVH1a VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
175A-huVH1b Variable Region
QVQLVQSGAEVKKPGASVKVSCKASGYTFSTHWIEWVRQAPGQGLEWMGEILPGSGSTS YAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWLLYYYAMDYWGQGTLVTVS S (SEQ ID NO:21)
175A-huVH1b VH FR1
QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO:51)
QVQLVQSGAEVKKPGASVKISCKAS (SEQ ID NO:105)
175A-huVH1b VH CDR1
GYTFSTHWIE (SEQ ID NO:36)
175A-huVH1b VH FR2
WVRQAPGQGLEWMG (SEQ ID NO:52)
WVRQAPGQGLEWIG (SEQ ID NO:106)
175A-huVH1b VH CDR2*
EILPGSGSTSYAQKLQG (SEQ ID NO:50)
EILPGSGSTSYAQKFQG (SEQ ID NO:114)
175A-huVH1b VH FR3
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:53)
RATMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:107)
RVTFTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:108)
RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:109)
RATFTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:110)
RVTFTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:111)
RATMTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:112)
RATFTADTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:113)
175A-huVH1b VH CDR3
WLLYYYAMDY (SEQ ID NO:38)
175A-huVH1b VH FR4
WGQGTLVTVSS (SEQ ID NO:54)

175A-huVH3a Variable Region
EVQLVESGGGLVQPGGSLRLSCAASGYTFSTHWIEWVRQAPGKGLEWVSEILPGSGSTSY NEKFKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARWLLYYYAMDYWGQGTLVTVSS (SEQ ID NO:22)
175A-huVH3a VH FR1
EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO:55)
EVQLV**Q**SGGGLVQPGGSLRLSCAAS (SEQ ID NO:115)
EVQLVESGGGLVQPGGS**V**RLSCAAS (SEQ ID NO:116)
EVQLVESGGGLVQPGGSLR**I**SCAAS (SEQ ID NO:117)
EVQLV**Q**SGGGLVQPGGS**V**RLSCAAS (SEQ ID NO:118)
EVQLVESGGGLVQPGGS**V**R**I**SCAAS (SEQ ID NO:119)
EVQLV**Q**SGGGLVQPGGSLR**I**SCAAS (SEQ ID NO:120)
EVQLV**Q**SGGGLVQPGGS**V**R**I**SCAAS (SEQ ID NO:121)
175A-huVH3a VH CDR1
GYTFSTHWIE(SEQ ID NO:36)
175A-huVH3a VH FR2
WVRQAPGKGLEWVS (SEQ ID NO:56)
WVRQAPGKGLEW**I**S (SEQ ID NO:122)
WVRQAPGKGLEWV**G** (SEQ ID NO:123)
WVRQAPGKGLEW**IG** (SEQ ID NO:124)
175A-huVH3a VH CDR2
EILPGSGSTSYNEKFKG (SEQ ID NO:37)
EILPGSGSTSY**Q**EKFKG (SEQ ID NO:101)
EILPGSGSTSY**S**EKFKG (SEQ ID NO:102)
EILPGSGSTSY**D**EKFKG (SEQ ID NO:103)
EILPGSGSTSY**A**EKFKG (SEQ ID NO:104)
175A-huVH3a VH FR3
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:57)
R**A**TISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:125)
RFT**F**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:126)
RFTIS**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:127)
RFTISRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:128)
RFTISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:129)
RFTISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:130)
RFTISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:131)
R**A**T**F**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:132)
R**A**TIS**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:133)
R**A**TISRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:134)
R**A**TISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:135)
R**A**TISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:136)
R**A**TISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:137)
RFT**F**S**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:138)
RFT**F**SRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:139)
RFT**F**SRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:140)
RFT**F**SRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:141)
RFT**F**SRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:142)
RFTIS**A**D**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:143)
RFTIS**A**DNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:144)

RFTISADNAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:145)
RFTISADNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:146)
RFTISRDTAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:147)
RFTISRDTAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:148)
RFTISRDTAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:149)
RFTISRDNAKNSAYMQMNSLRAEDTAVYYCAR (SEQ ID NO:150)
RFTISRDNAKNSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:151)
RFTISRDNAKNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:152)
RATFSADNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:153)
RATFSRDTAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:154)
RATFSRDNAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:155)
RATFSRDNAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:156)
RATFSRDNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:157)
RATISADTAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:158)
RATISADNAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:159)
RATISADNAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:160)
RATISADNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:161)
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RATISADTAKNALYMQLNSLRAEDTAVYYCAR (SEQ ID NO:249)
RFTFSADTAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:250)

RATFSADTAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:251)
175A-huVH3a VH CDR3
WLLYYYAMDY(SEQ ID NO:38)
175A-huVH3a VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
175A-huVH3b Variable Region
EVQLVESGGGLVQPGGSLRLSCAASGYTFSTHWIEWVRQAPGKGLEWVSEILPGSGSTSY ADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARWLLYYYAMDYWGQGTLVTVSS (SEQ ID NO:23)
175A-huVH3b VH FR1
EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO:55)
EVQLV**Q**SGGGLVQPGGSLRLSCAAS (SEQ ID NO:115)
EVQLVESGGGLVQPGGS**V**RLSCAAS (SEQ ID NO:116)
EVQLVESGGGLVQPGGSLR**I**SCAAS (SEQ ID NO:117)
EVQLV**Q**SGGGLVQPGGS**V**RLSCAAS (SEQ ID NO:118)
EVQLVESGGGLVQPGGS**V**R**I**SCAAS (SEQ ID NO:119)
EVQLV**Q**SGGGLVQPGGSLR**I**SCAAS (SEQ ID NO:120)
EVQLV**Q**SGGGLVQPGGS**V**R**I**SCAAS (SEQ ID NO:121)
175A-huVH3b VH CDR1
GYTFSTHWIE(SEQ ID NO:36)
175A-huVH3b VH FR2
WVRQAPGKGLEWVS (SEQ ID NO:56)
WVRQAPGKGLEW**I**S (SEQ ID NO:122)
WVRQAPGKGLEWV**G** (SEQ ID NO:123)
WVRQAPGKGLEW**IG** (SEQ ID NO:124)
175A-huVH3b VH CDR2*
EILPGSGSTSYADSVKG (SEQ ID NO:99)
EILPGSGSTSYADS**F**KG (SEQ ID NO:100)
175A-huVH3b VH FR3
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:57)
R**A**TISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:125)
RFT**F**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:126)
RFTIS**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:127)
RFTISRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:128)
RFTISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:129)
RFTISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:130)
RFTISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:131)
R**A**T**F**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:132)
R**A**TIS**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:133)
R**A**TISRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:134)
R**A**TISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:135)
R**A**TISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:136)
R**A**TISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:137)
RFT**F**S**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:138)
RFT**F**SRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:139)

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RATISADNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:161)
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RATFSADTAKNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:246)
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RATFSRDTAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:248)
RATISADTAKNALYMQLNSLRAEDTAVYYCAR (SEQ ID NO:249)
RFTFSADTAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:250)
RATFSADTAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:251)
175A-huVH3b VH CDR3
WLLYYYAMDY(SEQ ID NO:38)
175A-huVH3b VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
175A HUMANIZED ANTIBODY SEQUENCE: LIGHT CHAIN
175A-huVK2 Variable Region
DIVMTQSPLSLPVTPGEPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKLSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHFPYTFGQGTKLEIK(SEQ ID NO:28)
175A-huVK2 VL FR1
DIVMTQSPLSLPVTPGEPASISC (SEQ ID NO:75)
DVVMTQSPLSLPVTPGEPASISC (SEQ ID NO:252)
175A-huVK2 VL CDR1
RSSQSIVHSNGNTYLE (SEQ ID NO:45)
RSSQSIVHSQGNTYLE (SEQ ID NO:253)
RSSQSIVHSSGNTYLE (SEQ ID NO:254)
RSSQSIVHSAGNTYLE (SEQ ID NO:255)
RSSQSIVHSNGQTYLE (SEQ ID NO:256)
RSSQSIVHSNGSTYLE (SEQ ID NO:257)
RSSQSIVHSNGATYLE (SEQ ID NO:258)
RSSQSIVHSNGDTYLE (SEQ ID NO:259)
RSSQSIVHSQGQTYLE (SEQ ID NO:260)
RSSQSIVHSQGSTYLE (SEQ ID NO:261)
RSSQSIVHSQGATYLE (SEQ ID NO:262)
RSSQSIVHSQGDTYLE (SEQ ID NO:263)
RSSQSIVHSSGQTYLE (SEQ ID NO:264)
RSSQSIVHSSGSTYLE (SEQ ID NO:265)
RSSQSIVHSSGATYLE (SEQ ID NO:266)
RSSQSIVHSSGDTYLE (SEQ ID NO:267)
RSSQSIVHSAGQTYLE (SEQ ID NO:268)
RSSQSIVHSAGSTYLE (SEQ ID NO:269)
RSSQSIVHSAGATYLE (SEQ ID NO:270)
RSSQSIVHSAGDTYLE (SEQ ID NO:271)
175A-huVK2 VL FR2
WYLQKPGQSPQLLIY (SEQ ID NO:76)
175A-huVK2 VL CDR2
KLSNRFS (SEQ ID NO:46)
KLSQRFS (SEQ ID NO:272)
KLSSRFS (SEQ ID NO:273)
KLSARFS (SEQ ID NO:274)

KLS**D**RFS (SEQ ID NO:275)
175A-huVK2 VL FR3
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC (SEQ ID NO:77)
GVPDRFSGSGSGTDFTLKISRVEAED**L**GVYYC (SEQ ID NO:276)
175A-huVK2 VL CDR3
FQGSHFPYT (SEQ ID NO:47)
175A-huVK2 VL FR4
FGQGTKLEIK (SEQ ID NO:78)
175A-huVK1 Variable Region
DIQMTQSPSSLSASVGDRVTITCRSSQSIVHSNGNTYLEWYQQKPGKAPKLLIYKLSNRFS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCFQGSHFPYTFGQGTKLEIK (SEQ ID NO:29)
175A-huVK1 VL FR1
DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO:79)
D**V**QMTQSPSSLSASVGDRVTITC (SEQ ID NO:277)
DIQMTQSPSSLS**V**SVGDRVTITC (SEQ ID NO:278)
DIQMTQSPSSLSASVGDR**A**TITC (SEQ ID NO:279)
D**V**QMTQSPSSLS**V**SVGDRVTITC (SEQ ID NO:280)
D**V**QMTQSPSSLSASVGDR**A**TITC (SEQ ID NO:281)
DIQMTQSPSSLS**V**SVGDR**A**TITC (SEQ ID NO:282)
D**V**QMTQSPSSLS**V**SVGDR**A**TITC (SEQ ID NO:283)
175A-huVK1 VL CDR1
RSSQSIVHSNGNTYLE (SEQ ID NO:45)
RSSQSIVHS**Q**GNTYLE (SEQ ID NO:253)
RSSQSIVHS**S**GNTYLE (SEQ ID NO:254)
RSSQSIVHS**A**GNTYLE (SEQ ID NO:255)
RSSQSIVHSNG**Q**TYLE (SEQ ID NO:256)
RSSQSIVHSNG**S**TYLE (SEQ ID NO:257)
RSSQSIVHSNG**A**TYLE (SEQ ID NO:258)
RSSQSIVHSNG**D**TYLE (SEQ ID NO:259)
RSSQSIVHS**Q**G**Q**TYLE (SEQ ID NO:260)
RSSQSIVHS**Q**G**S**TYLE (SEQ ID NO:261)
RSSQSIVHS**Q**G**A**TYLE (SEQ ID NO:262)
RSSQSIVHS**Q**G**D**TYLE (SEQ ID NO:263)
RSSQSIVHS**S**G**Q**TYLE (SEQ ID NO:264)
RSSQSIVHS**S**G**S**TYLE (SEQ ID NO:265)
RSSQSIVHS**S**G**A**TYLE (SEQ ID NO:266)
RSSQSIVHS**S**G**D**TYLE (SEQ ID NO:267)
RSSQSIVHS**A**G**Q**TYLE (SEQ ID NO:268)
RSSQSIVHS**A**G**S**TYLE (SEQ ID NO:269)
RSSQSIVHS**A**G**A**TYLE (SEQ ID NO:270)
RSSQSIVHS**A**G**D**TYLE (SEQ ID NO:271)
175A-huVK1 VL FR2
WYQQKPGKAPKLLIY(SEQ ID NO:80)
WYQQKPGK**S**PKLLIY(SEQ ID NO:284)

175A-huVK1 VL CDR2
KLSNRFS (SEQ ID NO:46)
KLS**Q**RFS (SEQ ID NO:272)
KLS**S**RFS (SEQ ID NO:273)
KLS**A**RFS (SEQ ID NO:274)
KLS**D**RFS (SEQ ID NO:275)
175A-huVK1 VL FR3
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:81)
GVPSRFSGSGSGTDFTLTISS**V**QPEDFATYYC (SEQ ID NO:285)
GVPSRFSGSGSGTDFTLTISSLQPED**L**ATYYC (SEQ ID NO:286)
GVPSRFSGSGSGTDFTLTISSLQPEDF**G**TYYC (SEQ ID NO:287)
GVPSRFSGSGSGTDFTLTISS**V**QPED**L**ATYYC (SEQ ID NO:288)
GVPSRFSGSGSGTDFTLTISS**V**QPEDF**G**TYYC (SEQ ID NO:289)
GVPSRFSGSGSGTDFTLTISSLQPED**LG**TYYC (SEQ ID NO:290)
GVPSRFSGSGSGTDFTLTISS**V**QPED**LG**TYYC (SEQ ID NO:291)
175A-huVK1 VL CDR3
FQGSHFPYT (SEQ ID NO:47)
175A-huVK1 VL FR4
FGQGTKLEIK (SEQ ID NO:78)

* Amino acid position numbering as in Kabat.

Table 6: Amino Acid Sequences derived from Murine 76E1 Antibody.

76E1 HUMANIZED ANTIBODY SEQUENCE: HEAVY CHAIN
76E1-huVH1a Variable Region
QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYNMNWVRQAPGQGLEWMGNIDPYYDYT SYNLKFKDRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARSTMITPFDYWGQGTLVTVSS (SEQ ID NO:12)
76E1-huVH1a VH FR1
QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO:51)
QVQLVQSGAEVKKPGASVK**I**SCKAS (SEQ ID NO:105)
76E1-huVH1a VH CDR1
GYSFTGYNMN (SEQ ID NO:30)
GYSFTGY**Q**MN (SEQ ID NO:59)
GYSFTGY**S**MN (SEQ ID NO:60)
GYSFTGY**D**MN (SEQ ID NO:61)
GYSFTGY**A**MN (SEQ ID NO:62)
76E1-huVH1a VH FR2
WVRQAPGQGLEWMG (SEQ ID NO:52)
WVRQAPGQ**S**LEWMG (SEQ ID NO:63)
WVRQAPGQGLEW**I**G (SEQ ID NO:106)
WVRQAPGQ**S**LEW**I**G (SEQ ID NO:64)
76E1-huVH1a VH CDR2
NIDPYYDYTSYNLKFKD (SEQ ID NO:31)
NI**E**PYYDYTSYNLKFKD (SEQ ID NO:65)

NI**S**PYYDYTSYNLKFKD (SEQ ID NO:66)
NI**A**PYYDYTSYNLKFKD (SEQ ID NO:67)
NIDPYYDYTSY**Q**LKFKD (SEQ ID NO:68)
NIDPYYDYTSY**S**LKFKD (SEQ ID NO:69)
NIDPYYDYTSY**D**LKFKD (SEQ ID NO:70)
NIDPYYDYTSY**A**LKFKD (SEQ ID NO:71)
NI**E**PYYDYTSY**Q**LKFKD (SEQ ID NO:72)
NI**E**PYYDYTSY**S**LKFKD (SEQ ID NO:73)
NI**E**PYYDYTSY**D**LKFKD (SEQ ID NO:74)
NI**E**PYYDYTSY**A**LKFKD (SEQ ID NO:83)
NI**S**PYYDYTSY**Q**LKFKD (SEQ ID NO:84)
NI**S**PYYDYTSY**S**LKFKD (SEQ ID NO:85)
NI**S**PYYDYTSY**D**LKFKD (SEQ ID NO:86)
NI**S**PYYDYTSY**A**LKFKD (SEQ ID NO:87)
NI**A**PYYDYTSY**Q**LKFKD (SEQ ID NO:88)
NI**A**PYYDYTSY**S**LKFKD (SEQ ID NO:89)
NI**A**PYYDYTSY**D**LKFKD (SEQ ID NO:90)
NI**A**PYYDYTSY**A**LKFKD (SEQ ID NO:95)
76E1-huVH1a VH FR3
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:53)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:107)
RVT**L**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:96)
RVTMT**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:97)
RVTMTTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:98)
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:292)
R**A**T**L**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:293)
R**A**TMT**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:294)
R**A**TMTTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:295)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:296)
RVT**L**T**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:297)
RVT**L**TTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:298)
RVT**L**TTDTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:299)
RVTMT**V**D**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:300)
RVTMT**V**DTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:301)
RVTMTTD**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:302)
R**A**T**L**T**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:303)
R**A**T**L**TTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:304)
R**A**T**L**TTDTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:305)
R**A**TMT**V**D**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:306)
R**A**TMT**V**DTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:307)
R**A**TMTTD**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:308)
RVT**L**T**V**D**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:309)
RVT**L**T**V**DTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:310)
RVT**L**TTD**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:311)
RVTMT**V**D**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:312)
R**A**T**L**T**V**D**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:313)
R**A**T**L**T**V**DTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:314)
R**A**T**L**TTD**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:315)
R**A**TMT**V**D**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:316)
RVT**L**T**V**D**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:317)
R**A**T**L**T**V**D**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:318)

76E1-huVH1a VH CDR3
STMITPFDY (SEQ ID NO:32)
ST**L**ITPFDY (SEQ ID NO:319)
76E1-huVH1a VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
WGQGTL**L**TVSS (SEQ ID NO:320)
76E1-huVH1b Variable Region
QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYNMNWVRQAPGQGLEWMGNIDPYYDYT SYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARSTMITPFDYWGQGTLVTVSS (SEQ ID NO:13)
76E1-huVH1b VH FR1
QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO:51)
QVQLVQSGAEVKKPGASVK**I**SCKAS (SEQ ID NO:105)
76E1-huVH1b VH CDR1
GYSFTGYNMN (SEQ ID NO:30)
GYSFTGY**Q**MN (SEQ ID NO:59)
GYSFTGY**S**MN (SEQ ID NO:60)
GYSFTGY**D**MN (SEQ ID NO:61)
GYSFTGY**A**MN (SEQ ID NO:62)
76E1-huVH1b VH FR2
WVRQAPGQGLEWMG (SEQ ID NO:52)
WVRQAPGQ**S**LEWMG (SEQ ID NO:63)
WVRQAPGQGLEW**I**G (SEQ ID NO:106)
WVRQAPGQ**S**LEW**I**G (SEQ ID NO:64)
76E1-huVH1b VH CDR2*
NIDPYYDYTSYAQKLQG (SEQ ID NO:321)
NIDPYYDYTSYAQK**F**QG (SEQ ID NO:322)
76E1-huVH1b VH FR3
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:53)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:107)
RVT**L**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:96)
RVTMT**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:97)
RVTMTTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:98)
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:292)
R**A**T**L**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:293)
R**A**TMT**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:294)
R**A**TMTTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:295)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:296)
RVT**L**T**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:297)
RVT**L**TTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:298)
RVT**L**TTDTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:299)
RVTMT**V**D**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:300)
RVTMT**V**DTSTSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:301)
RVTMTTD**K**STSTAYMELRSLRSDDTAVYYCA**T** (SEQ ID NO:302)
R**A**T**L**T**V**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:303)
R**A**T**L**TTD**K**STSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:304)

RATLTTDTSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:305)
RATMTVDKSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:306)
RATMTVDTSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:307)
RATMTTDKSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:308)
RVTLTVDKSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:309)
RVTLTVDTSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:310)
RVTLTTDKSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:311)
RVTMTVDKSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:312)
RATLTVDKSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:313)
RATLTVDTSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:314)
RATLTTDKSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:315)
RATMTVDKSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:316)
RVTLTVDKSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:317)
RATLTVDKSTSTAYMELRSLRSDDTAVYYCAT (SEQ ID NO:318)
76E1-huVH1b VH CDR3
STMITPFDY (SEQ ID NO:32)
STLITPFDY (SEQ ID NO:319)
76E1-huVH1b VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
WGQGTLLTVSS (SEQ ID NO:320)
76E1-huVH3a Variable Region
EVQLVESGGGLVQPGGSLRLSCAASGYSFTGYNMNWVRQAPGKGLEWVSNIDPYYDYTS YNLKFKDRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARSTMITPFDYWGQGTLVTVSS (SEQ ID NO:14)
76E1-huVH3a VH FR1
EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO:55)
EVQLVQSGGGLVQPGGSLRLSCAAS (SEQ ID NO:115)
EVQLVESGGGLVQPGGSVRLSCAAS (SEQ ID NO:116)
EVQLVESGGGLVQPGGSLRISCAAS (SEQ ID NO:117)
EVQLVQSGGGLVQPGGSVRLSCAAS (SEQ ID NO:118)
EVQLVESGGGLVQPGGSVRISCAAS (SEQ ID NO:119)
EVQLVQSGGGLVQPGGSLRISCAAS (SEQ ID NO:120)
EVQLVQSGGGLVQPGGSVRISCAAS (SEQ ID NO:121)
76E1-huVH3a VH CDR1
GYSFTGYNMN (SEQ ID NO:30)
GYSFTGYQMN (SEQ ID NO:59)
GYSFTGYSMN (SEQ ID NO:60)
GYSFTGYDMN (SEQ ID NO:61)
GYSFTGYAMN (SEQ ID NO:62)
76E1-huVH3a VH FR2
WVRQAPGKGLEWVS (SEQ ID NO:56)
WVRQAPGKSLEWVS (SEQ ID NO:323)
WVRQAPGKGLEWIS (SEQ ID NO:122)
WVRQAPGKGLEWVG (SEQ ID NO:123)
WVRQAPGKSLEWIS (SEQ ID NO:324)
WVRQAPGKSLEWVG (SEQ ID NO:325)
WVRQAPGKGLEWIG (SEQ ID NO:124)

WVRQAPGK**S**LEW**IG** (SEQ ID NO:326)
76E1-huVH3a VH CDR2
NIDPYYDYTSYNLKFKD (SEQ ID NO:31)
NI**E**PYYDYTSYNLKFKD (SEQ ID NO:65)
NI**S**PYYDYTSYNLKFKD (SEQ ID NO:66)
NI**A**PYYDYTSYNLKFKD (SEQ ID NO:67)
NIDPYYDYTSY**Q**LKFKD (SEQ ID NO:68)
NIDPYYDYTSY**S**LKFKD (SEQ ID NO:69)
NIDPYYDYTSY**D**LKFKD (SEQ ID NO:70)
NIDPYYDYTSY**A**LKFKD (SEQ ID NO:71)
NI**E**PYYDYTSY**Q**LKFKD (SEQ ID NO:72)
NI**E**PYYDYTSY**S**LKFKD (SEQ ID NO:73)
NI**E**PYYDYTSY**D**LKFKD (SEQ ID NO:74)
NI**E**PYYDYTSY**A**LKFKD (SEQ ID NO:83)
NI**S**PYYDYTSY**Q**LKFKD (SEQ ID NO:84)
NI**S**PYYDYTSY**S**LKFKD (SEQ ID NO:85)
NI**S**PYYDYTSY**D**LKFKD (SEQ ID NO:86)
NI**S**PYYDYTSY**A**LKFKD (SEQ ID NO:87)
NI**A**PYYDYTSY**Q**LKFKD (SEQ ID NO:88)
NI**A**PYYDYTSY**S**LKFKD (SEQ ID NO:89)
NI**A**PYYDYTSY**D**LKFKD (SEQ ID NO:90)
NI**A**PYYDYTSY**A**LKFKD (SEQ ID NO:95)
76E1-huVH3a VH FR3
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:57)
R**A**TISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:327)
RFT**L**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:328)
RFTIS**V**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:329)
RFTISRD**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:330)
RFTISRDNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:331)
RFTISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:332)
RFTISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:333)
RFTISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:334)
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:335)
R**A**T**L**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:336)
R**A**TIS**V**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:337)
R**A**TISRD**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:338)
R**A**TISRDNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:339)
R**A**TISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:340)
R**A**TISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:341)
R**A**TISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:342)
R**A**TISRDNAKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:343)
RFT**L**S**V**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:344)
RFT**L**SRD**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:345)
RFT**L**SRDNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:346)
RFT**L**SRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:347)
RFT**L**SRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:348)
RFT**L**SRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:349)
RFT**L**SRDNAKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:350)
RFTIS**V**D**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:351)
RFTIS**V**DNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:352)
RFTIS**V**DNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:353)

RFTISVDNAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:354)
RFTISVDNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:355)
RFTISVDNAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:356)
RFTISRDKAKSSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:357)
RFTISRDKAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:358)
RFTISRDKAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:359)
RFTISRDKAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:360)
RFTISRDKAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:361)
RFTISRDNAKSSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:362)
RFTISRDNAKSSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:363)
RFTISRDNAKSSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:364)
RFTISRDNAKSSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:365)
RFTISRDNAKNSAYMQMNSLRAEDTAVYYCAR (SEQ ID NO:366)
RFTISRDNAKNSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:367)
RFTISRDNAKNSAYLQMNSLRAEDTAVYYCAT (SEQ ID NO:368)
RFTISRDNAKNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:369)
RFTISRDNAKNSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:370)
RFTISRDNAKNSLYLQLNSLRAEDTAVYYCAT (SEQ ID NO:371)
RATLSVDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:372)
RATLSRDKAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:373)
RATLSRDNAKSSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:374)
RATLSRDNAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:375)
RATLSRDNAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:376)
RATLSRDNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:377)
RATLSRDNAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:378)
RATISVDKAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:379)
RATISVDNAKSSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:380)
RATISVDNAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:381)
RATISVDNAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:382)
RATISVDNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:383)
RATISVDNAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:384)
RATISRDKAKSSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:385)
RATISRDKAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:386)
RATISRDKAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:387)
RATISRDKAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:388)
RATISRDKAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:389)
RATISRDNAKSSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:390)
RATISRDNAKSSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:391)
RATISRDNAKSSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:392)
RATISRDNAKSSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:393)
RATISRDNAKNSAYMQMNSLRAEDTAVYYCAR (SEQ ID NO:394)
RATISRDNAKNSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:395)
RATISRDNAKNSAYLQMNSLRAEDTAVYYCAT (SEQ ID NO:396)
RATISRDNAKNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:397)
RATISRDNAKNSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:398)
RATISRDNAKNSLYLQLNSLRAEDTAVYYCAT (SEQ ID NO:399)
RFTLSVDKAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:400)
RFTLSVDNAKSSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:401)
RFTLSVDNAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:402)
RFTLSVDNAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:403)
RFTLSVDNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:404)
RFTLSVDNAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:405)
RFTLSRDKASNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:406)

RFTLSRDKAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:407)
RFTLSRDKAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:408)
RFTLSRDKAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:409)
RFTLSRDKAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:410)
RFTLSRDNAKSSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:411)
RFTLSRDNAKSSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:412)
RFTLSRDNAKSSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:413)
RFTLSRDNAKSSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:414)
RFTLSRDNAKNSAYMQMNSLRAEDTAVYYCAR (SEQ ID NO:415)
RFTLSRDNAKNSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:416)
RFTLSRDNAKNSAYLQMNSLRAEDTAVYYCAT (SEQ ID NO:417)
RFTLSRDNAKNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:418)
RFTLSRDNAKNSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:419)
RFTLSRDNAKNSLYLQLNSLRAEDTAVYYCAT (SEQ ID NO:420)
RFTISVDKAKSSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:421)
RFTISVDKAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:422)
RFTISVDKAKNSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:423)
RFTISVDKAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:424)
RFTISVDKAKNSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:425)
RFTISVDNAKSSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:426)
RFTISVDNAKSSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:427)
RFTISVDNAKSSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:428)
RFTISVDNAKSSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:429)
RFTISVDNAKNSAYMQMNSLRAEDTAVYYCAR (SEQ ID NO:430)
RFTISVDNAKNSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:431)
RFTISVDNAKNSAYLQMNSLRAEDTAVYYCAT (SEQ ID NO:432)
RFTISVDNAKNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:433)
RFTISVDNAKNSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:434)
RFTISVDNAKNSLYLQLNSLRAEDTAVYYCAT (SEQ ID NO:435)
RFTISRDKAKSSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:436)
RFTISRDKAKSSLYMQMNSLRAEDTAVYYCAR (SEQ ID NO:437)
RFTISRDKAKSSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:438)
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RATISVDKAKSSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:741)
RATISVDKAKSSAYLQMNSLRAEDTAVYYCAT (SEQ ID NO:742)
RATISVDKAKSSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:743)
RATISVDKAKSSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:744)
RATISVDKAKSSLYLQLNSLRAEDTAVYYCAT (SEQ ID NO:745)
RATISVDKAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:746)
RATISVDKAKNSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:747)
RATISVDKAKNSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:748)
RATISVDKAKNSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:749)
RATISVDNAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:750)
RATISVDNAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:751)
RATISVDNAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:752)
RATISVDNAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:753)
RATISVDNAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:754)
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RATISRDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:759)
RATISRDNAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:760)
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RFTLSVDKAKSSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:762)
RFTLSVDKAKSSAYLQMNSLRAEDTAVYYCAT (SEQ ID NO:763)
RFTLSVDKAKSSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:764)
RFTLSVDKAKSSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:765)
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RFTLSVDKAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:767)
RFTLSVDKAKNSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:768)
RFTLSVDKAKNSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:769)
RFTLSVDKAKNSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:770)
RFTLSVDNAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:771)
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RFTLSVDNAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:775)
RFTLSRDKASNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:776)
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RFTLSRDKASNSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:778)
RFTLSRDKASNSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:779)
RFTLSRDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:780)
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RFTISVDKAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:784)
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RFTISVDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:786)
RFTISRDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:787)
RATLSVDKASNSAYMQMNSLRAEDTAVYYCAR (SEQ ID NO:788)
RATLSVDKASNSAYLQLNSLRAEDTAVYYCAR (SEQ ID NO:789)
RATLSVDKASNSAYLQMNSLRAEDTAVYYCAT (SEQ ID NO:790)
RATLSVDKASNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:791)
RATLSVDKASNSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:792)
RATLSVDKASNSLYLQLNSLRAEDTAVYYCAT (SEQ ID NO:793)
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RATLSVDKAKNSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:796)
RATLSVDKAKNSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:797)
RATLSVDNAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:798)
RATLSVDNAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:799)
RATLSVDNAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:800)
RATLSVDNAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:801)
RATLSVDNAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:802)
RATLSRDKAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:803)
RATLSRDKAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:804)
RATLSRDKAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:805)
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RATLSRDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:807)
RATLSRDNAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:808)
RATISVDKAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:809)
RATISVDKAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:810)
RATISVDKAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:811)
RATISVDKAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:812)
RATISVDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:813)
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RFTLSVDKAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:818)
RFTLSVDKAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:819)
RFTLSVDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:820)
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RFTLSRDKASNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:822)
RFTISVDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:823)
RATLSVDKASNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:824)
RATLSVDKASNSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:825)
RATLSVDKASNSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:826)
RATLSVDKASNSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:827)
RATLSVDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:828)
RATLSVDNAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:829)
RATLSRDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:830)

RATISVDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:831)
RFTLSVDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:832)
RATLSVDKASNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:833)
76E1-huVH3a VH CDR3
STMITPFDY (SEQ ID NO:32)
STLITPFDY (SEQ ID NO:319)
76E1-huVH3a VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
WGQGTLLTVSS (SEQ ID NO:320)
76E1-huVH3b Variable Region
EVQLVESGGGLVQPGGSLRLSCAASGYSFTGYNMNWVRQAPGKGLEWVSNIDPYYDYTS YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARSTMITPFDYWGQGTLVTVSS (SEQ ID NO:15)
76E1-huVH3b VH FR1
EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO:55)
EVQLVQSGGGLVQPGGSLRLSCAAS (SEQ ID NO:115)
EVQLVESGGGLVQPGGSVRLSCAAS (SEQ ID NO:116)
EVQLVESGGGLVQPGGSLRISCAAS (SEQ ID NO:117)
EVQLVQSGGGLVQPGGSVRLSCAAS (SEQ ID NO:118)
EVQLVESGGGLVQPGGSVRISCAAS (SEQ ID NO:119)
EVQLVQSGGGLVQPGGSLRISCAAS (SEQ ID NO:120)
EVQLVQSGGGLVQPGGSVRISCAAS (SEQ ID NO:121)
76E1-huVH3b VH CDR1
GYSFTGYNMN (SEQ ID NO:30)
GYSFTGYQMN (SEQ ID NO:59)
GYSFTGYSMN (SEQ ID NO:60)
GYSFTGYDMN (SEQ ID NO:61)
GYSFTGYAMN (SEQ ID NO:62)
76E1-huVH3b VH FR2
WVRQAPGKGLEWVS (SEQ ID NO:56)
WVRQAPGKSLEWVS (SEQ ID NO:323)
WVRQAPGKGLEWIS (SEQ ID NO:122)
WVRQAPGKGLEWVG (SEQ ID NO:123)
WVRQAPGKSLEWIS (SEQ ID NO:324)
WVRQAPGKSLEWVG (SEQ ID NO:325)
WVRQAPGKGLEWIG (SEQ ID NO:124)
WVRQAPGKSLEWIG (SEQ ID NO:326)
76E1-huVH3b VH CDR2*
NIDPYYDYTSYADSVKG (SEQ ID NO:835)
NIEPYYDYTSYADSVKG (SEQ ID NO:836)
NISPYYDYTSYADSVKG (SEQ ID NO:837)
NIAPYYDYTSYADSVKG (SEQ ID NO:838)
NIDPYYDYTSYADSVKG (SEQ ID NO:839)
NIEPYYDYTSYADSVKG (SEQ ID NO:840)
NISPYYDYTSYADSVKG (SEQ ID NO:841)
NIAPYYDYTSYADSVKG (SEQ ID NO:842)

76E1-huVH3b VH FR3
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:57)
R**A**TISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:327)
RFT**L**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:328)
RFTIS**V**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:329)
RFTISRD**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:330)
RFTISRDNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:331)
RFTISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:332)
RFTISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:333)
RFTISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:334)
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:335)
R**A**T**L**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:336)
R**A**TIS**V**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:337)
R**A**TISRD**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:338)
R**A**TISRDNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:339)
R**A**TISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:340)
R**A**TISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:341)
R**A**TISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:342)
R**A**TISRDNAKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:343)
RFT**L**S**V**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:344)
RFT**L**SRD**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:345)
RFT**L**SRDNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:346)
RFT**L**SRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:347)
RFT**L**SRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:348)
RFT**L**SRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:349)
RFT**L**SRDNAKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:350)
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RFTIS**V**DNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:352)
RFTIS**V**DNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:353)
RFTIS**V**DNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:354)
RFTIS**V**DNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:355)
RFTIS**V**DNAKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:356)
RFTISRD**K**AK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:357)
RFTISRD**K**AKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:358)
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RFTISRD**K**AKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:360)
RFTISRD**K**AKNSLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:361)
RFTISRDNAK**S**S**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:362)
RFTISRDNAK**S**SLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:363)
RFTISRDNAK**S**SLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:364)
RFTISRDNAK**S**SLYLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:365)
RFTISRDNAKNS**A**Y**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:366)
RFTISRDNAKNS**A**YLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:367)
RFTISRDNAKNS**A**YLQMNSLRAEDTAVYYCA**T** (SEQ ID NO:368)
RFTISRDNAKNSLY**M**QL**N**SLRAEDTAVYYCAR (SEQ ID NO:369)
RFTISRDNAKNSLY**M**QMNSLRAEDTAVYYCA**T** (SEQ ID NO:370)
RFTISRDNAKNSLYLQ**L**NSLRAEDTAVYYCA**T** (SEQ ID NO:371)
R**A**T**L**S**V**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:372)
R**A**T**L**SRD**K**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:373)
R**A**T**L**SRDNAK**S**SLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:374)
R**A**T**L**SRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:375)
R**A**T**L**SRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:376)

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RATISVDNAKSSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:380)
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RFTISVDKAKNSAYLQMNSLRAEDTAVYYCAR (SEQ ID NO:422)
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RFTISVDNAKSSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:428)
RFTISVDNAKSSLYLQMNSLRAEDTAVYYCAT (SEQ ID NO:429)

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RATLSVDKASNSLYMQLNSLRAEDTAVYYCAR (SEQ ID NO:791)
RATLSVDKASNSLYMQMNSLRAEDTAVYYCAT (SEQ ID NO:792)
RATLSVDKASNSLYLQLNSLRAEDTAVYYCAT (SEQ ID NO:793)
RATLSVDKAKNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:794)
RATLSVDKAKNSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:795)
RATLSVDKAKNSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:796)
RATLSVDKAKNSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:797)
RATLSVDNAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:798)
RATLSVDNAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:799)
RATLSVDNAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:800)

RATLSVDNAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:801)
RATLSVDNAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:802)
RATLSRDKAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:803)
RATLSRDKAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:804)
RATLSRDKAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:805)
RATLSRDKAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:806)
RATLSRDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:807)
RATLSRDNAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:808)
RATISVDKAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:809)
RATISVDKAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:810)
RATISVDKAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:811)
RATISVDKAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:812)
RATISVDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:813)
RATISVDNAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:814)
RATISRDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:815)
RFTLSVDKAKSSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:816)
RFTLSVDKAKSSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:817)
RFTLSVDKAKSSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:818)
RFTLSVDKAKSSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:819)
RFTLSVDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:820)
RFTLSVDNAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:821)
RFTLSRDKASNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:822)
RFTISVDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:823)
RATLSVDKASNSAYMQLNSLRAEDTAVYYCAR (SEQ ID NO:824)
RATLSVDKASNSAYMQMNSLRAEDTAVYYCAT (SEQ ID NO:825)
RATLSVDKASNSAYLQLNSLRAEDTAVYYCAT (SEQ ID NO:826)
RATLSVDKASNSLYMQLNSLRAEDTAVYYCAT (SEQ ID NO:827)
RATLSVDKAKNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:828)
RATLSVDNAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:829)
RATLSRDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:830)
RATISVDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:831)
RFTLSVDKAKSSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:832)
RATLSVDKASNSAYMQLNSLRAEDTAVYYCAT (SEQ ID NO:833)
76E1-huVH3b VH CDR3
STMITPFDY (SEQ ID NO:32)
STLITPFDY (SEQ ID NO:319)
76E1-huVH3b VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
WGQGTLLTVSS (SEQ ID NO:320)
76E1 HUMANIZED ANTIBODY SEQUENCE: LIGHT CHAIN
76E1-huVK2 Variable Region
DIVMTQSPLSLPVTPGEPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPWTFGQGTKLEIK (SEQ ID NO:24)
76E1-huVK2 VL FR1
DIVMTQSPLSLPVTPGEPASISC (SEQ ID NO:75)
DVVMTQSPLSLPVTPGEPASISC (SEQ ID NO:252)

76E1-huVK2 VL CDR1
RSSQSIVHSNGNTYLE (SEQ ID NO:45)
RSSQSIVHS**Q**GNTYLE (SEQ ID NO:253)
RSSQSIVHS**S**GNTYLE (SEQ ID NO:254)
RSSQSIVHS**A**GNTYLE (SEQ ID NO:255)
RSSQSIVHSNG**Q**TYLE (SEQ ID NO:256)
RSSQSIVHSNG**S**TYLE (SEQ ID NO:257)
RSSQSIVHSNG**A**TYLE (SEQ ID NO:258)
RSSQSIVHSNG**D**TYLE (SEQ ID NO:259)
RSSQSIVHS**Q**G**Q**TYLE (SEQ ID NO:260)
RSSQSIVHS**Q**G**S**TYLE (SEQ ID NO:261)
RSSQSIVHS**Q**G**A**TYLE (SEQ ID NO:262)
RSSQSIVHS**Q**G**D**TYLE (SEQ ID NO:263)
RSSQSIVHS**S**G**Q**TYLE (SEQ ID NO:264)
RSSQSIVHS**S**G**S**TYLE (SEQ ID NO:265)
RSSQSIVHS**S**G**A**TYLE (SEQ ID NO:266)
RSSQSIVHS**S**G**D**TYLE (SEQ ID NO:267)
RSSQSIVHS**A**G**Q**TYLE (SEQ ID NO:268)
RSSQSIVHS**A**G**S**TYLE (SEQ ID NO:269)
RSSQSIVHS**A**G**A**TYLE (SEQ ID NO:270)
RSSQSIVHS**A**G**D**TYLE (SEQ ID NO:271)
76E1-huVK2 VL FR2
WYLQKPGQSPQLLIY (SEQ ID NO:76)
76E1-huVK2 VL CDR2
KVSNRFS (SEQ ID NO:40)
KVS**Q**RFS (SEQ ID NO:843)
KVS**S**RFS (SEQ ID NO:844)
KVS**D**RFS (SEQ ID NO:845)
KVS**A**RFS (SEQ ID NO:846)
76E1-huVK2 VL FR3
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC (SEQ ID NO:77)
GVPDRFSGSGSGTDFTLKISRVEAED**L**GVYYC (SEQ ID NO:276)
76E1-huVK2 VL CDR3
FQGSHVPWT (SEQ ID NO:41)
76E1-huVK2 VL FR4
FGQGTKLEIK (SEQ ID NO:78)
76E1-huVK1 Variable Region
DIQMTQSPSSLSASVGDRVTITCRSSQSIVHSNGNTYLEWYQQKPGKAPKLLIYKVSNRFS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCFQGSHVPWTFGQGTKLEIK (SEQ ID NO:25)
76E1-huVK1 VL FR1
DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO:79)
D**V**QMTQSPSSLSASVGDRVTITC (SEQ ID NO:277)
DIQMTQSPSSLS**V**SVGDRVTITC (SEQ ID NO:278)
DIQMTQSPSSLSASVGDR**A**TITC (SEQ ID NO:279)
D**V**QMTQSPSSLS**V**SVGDRVTITC (SEQ ID NO:280)

D**V**QMTQSPSSLSASVGDR**A**TITC (SEQ ID NO:281)
DIQMTQSPSSLS**V**SVGDR**A**TITC (SEQ ID NO:282)
D**V**QMTQSPSSLS**V**SVGDR**A**TITC (SEQ ID NO:283)
76E1-huVK1 VL CDR1
RSSQSIVHSNGNTYLE (SEQ ID NO:45)
RSSQSIVHS**Q**GNTYLE (SEQ ID NO:253)
RSSQSIVHS**S**GNTYLE (SEQ ID NO:254)
RSSQSIVHS**A**GNTYLE (SEQ ID NO:255)
RSSQSIVHSNG**Q**TYLE (SEQ ID NO:256)
RSSQSIVHSNG**S**TYLE (SEQ ID NO:257)
RSSQSIVHSNG**A**TYLE (SEQ ID NO:258)
RSSQSIVHSNG**D**TYLE (SEQ ID NO:259)
RSSQSIVHS**Q**G**Q**TYLE (SEQ ID NO:260)
RSSQSIVHS**Q**G**S**TYLE (SEQ ID NO:261)
RSSQSIVHS**Q**G**A**TYLE (SEQ ID NO:262)
RSSQSIVHS**Q**G**D**TYLE (SEQ ID NO:263)
RSSQSIVHS**S**G**Q**TYLE (SEQ ID NO:264)
RSSQSIVHS**S**G**S**TYLE (SEQ ID NO:265)
RSSQSIVHS**S**G**A**TYLE (SEQ ID NO:266)
RSSQSIVHS**S**G**D**TYLE (SEQ ID NO:267)
RSSQSIVHS**A**G**Q**TYLE (SEQ ID NO:268)
RSSQSIVHS**A**G**S**TYLE (SEQ ID NO:269)
RSSQSIVHS**A**G**A**TYLE (SEQ ID NO:270)
RSSQSIVHS**A**G**D**TYLE (SEQ ID NO:271)
76E1-huVK1 VL FR2
WYQQKPGKAPKLLIY(SEQ ID NO:80)
WYQQKPGK**S**PKLLIY(SEQ ID NO:284)
76E1-huVK1 VL CDR2
KVSNRFS (SEQ ID NO:40)
KVS**Q**RFS (SEQ ID NO:843)
KVS**S**RFS (SEQ ID NO:844)
KVS**D**RFS (SEQ ID NO:845)
KVS**A**RFS (SEQ ID NO:846)
76E1-huVK1 VL FR3
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:81)
GVPSRFSGSGSGTDFTLTISS**V**QPEDFATYYC (SEQ ID NO:285)
GVPSRFSGSGSGTDFTLTISSLQPED**L**ATYYC (SEQ ID NO:286)
GVPSRFSGSGSGTDFTLTISSLQPEDF**G**TYYC (SEQ ID NO:287)
GVPSRFSGSGSGTDFTLTISS**V**QPED**L**ATYYC (SEQ ID NO:288)
GVPSRFSGSGSGTDFTLTISS**V**QPEDF**G**TYYC (SEQ ID NO:289)
GVPSRFSGSGSGTDFTLTISSLQPED**LG**TYYC (SEQ ID NO:290)
GVPSRFSGSGSGTDFTLTISS**V**QPED**LG**TYYC (SEQ ID NO:291)
76E1-huVK1 VL CDR3
FQGSHVPWT (SEQ ID NO:41)
76E1-huVK1 VL FR4
FGQGTKLEIK (SEQ ID NO:78)

* Amino acid position numbering as in Kabat.

Table 7: Amino Acid Sequences derived from Murine 141A Antibody.

141A HUMANIZED ANTIBODY SEQUENCE: HEAVY CHAIN
141A-huVH1a Variable Region
QVQLVQSGAEVKKPGASVKVSCKAS**GYTFSRYWIE**WVRQAPGQGLEWMG**EILPGSGST** **NYNEKFKG**RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR**EEVYDGYPWFGY**WGQGTLV TVSS (SEQ ID NO:16)
141A-huVH1a VH FR1
QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO:51)
QVQLVQSGAEV**M**KPGASVKVSCKAS (SEQ ID NO:39)
QVQLVQSGAEVKKPGASVK**I**SCKAS (SEQ ID NO:105)
QVQLVQSGAEV**M**KPGASVK**I**SCKAS (SEQ ID NO:58)
141A-huVH1a VH CDR1
GYTFSRYWIE (SEQ ID NO:33)
141A-huVH1a VH FR2
WVRQAPGQGLEWMG (SEQ ID NO:52)
WVRQAPGQGLEW**I**G (SEQ ID NO:106)
141A-huVH1a VH CDR2
EILPGSGSTNYNEKFKG (SEQ ID NO:34)
EILPGSGST**Q**YNEKFKG (SEQ ID NO:847)
EILPGSGST**S**YNEKFKG (SEQ ID NO:848)
EILPGSGST**D**YNEKFKG (SEQ ID NO:849)
EILPGSGST**A**YNEKFKG (SEQ ID NO:850)
EILPGSGSTNY**Q**EKFKG (SEQ ID NO:851)
EILPGSGSTNY**S**EKFKG (SEQ ID NO:852)
EILPGSGSTNY**D**EKFKG (SEQ ID NO:853)
EILPGSGSTNY**A**EKFKG (SEQ ID NO:854)
EILPGSGST**Q**Y**Q**EKFKG (SEQ ID NO:855)
EILPGSGST**S**Y**S**EKFKG (SEQ ID NO:856)
EILPGSGST**D**Y**D**EKFKG (SEQ ID NO:857)
EILPGSGST**A**Y**A**EKFKG (SEQ ID NO:858)
141A-huVH1a VH FR3
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:53)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:107)
RVT**F**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:108)
RVTMT**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:109)
RVTMTTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:859)
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:860)
R**A**T**F**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:110)
R**A**TMT**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:112)
R**A**TMTTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:861)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:862)
RVT**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:111)
RVT**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:863)
RVT**F**TTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:864)

RVTMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:865)
RVTMT**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:866)
RVTMTTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:867)
R**A**T**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:113)
R**A**T**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:868)
R**A**T**F**TTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:869)
R**A**TMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:870)
R**A**TMT**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:871)
R**A**TMTTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:872)
RVT**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:873)
RVT**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:874)
RVT**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:875)
RVTMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:876)
R**A**T**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:877)
R**A**T**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:878)
R**A**T**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:879)
R**A**TMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:880)
RVT**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:881)
R**A**T**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:882)
141A-huVH1a VH CDR3
EEVYDGYPWFGY (SEQ ID NO:35)
EEVY**E**GYPWFGY (SEQ ID NO:883)
EEVY**S**GYPWFGY (SEQ ID NO:884)
EEVY**A**GYPWFGY (SEQ ID NO:885)
141A-huVH1a VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
141A-huVH1b Variable Region
QVQLVQSGAEVKKPGASVKVSCKAS**GYTFSRYWIE**WVRQAPGQGLEWMG**EILPGSGST** **N**YAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR**EEVYDGYPWFGY**WGQGTLV TVSS (SEQ ID NO:17)
141A-huVH1b VH FR1
QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO:51)
QVQLVQSGAEV**M**KPGASVKVSCKAS (SEQ ID NO:39)
QVQLVQSGAEVKKPGASVK**I**SCKAS (SEQ ID NO:105)
QVQLVQSGAEV**M**KPGASVK**I**SCKAS (SEQ ID NO:58)
141A-huVH1b VH CDR1
GYTFSRYWIE (SEQ ID NO:33)
141A-huVH1b VH FR2
WVRQAPGQGLEWMG (SEQ ID NO:52)
WVRQAPGQGLEW**I**G (SEQ ID NO:106)
141A-huVH1b VH CDR2*
EILPGSGSTNYAQKLQG (SEQ ID NO:49)
EILPGSGST**Q**YAQKLQG (SEQ ID NO:886)
EILPGSGST**S**YAQKLQG (SEQ ID NO:887)
EILPGSGST**D**YAQKLQG (SEQ ID NO:888)
EILPGSGST**A**YAQKLQG (SEQ ID NO:889)

EILPGSGSTNYAQK**F**QG (SEQ ID NO:890)
EILPGSGST**Q**YAQK**F**QG (SEQ ID NO:891)
EILPGSGST**S**YAQK**F**QG (SEQ ID NO:892)
EILPGSGST**D**YAQK**F**QG (SEQ ID NO:893)
EILPGSGST**A**YAQK**F**QG (SEQ ID NO:894)
141A-huVH1b VH FR3
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:53)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:107)
RVT**F**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:108)
RVTMT**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:109)
RVTMTTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:859)
RVTMTTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:860)
R**A**T**F**TTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:110)
R**A**TMT**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:112)
R**A**TMTTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:861)
R**A**TMTTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:862)
RVT**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:111)
RVT**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:863)
RVT**F**TTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:864)
RVTMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:865)
RVTMT**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:866)
RVTMTTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:867)
R**A**T**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:113)
R**A**T**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:868)
R**A**T**F**TTDTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:869)
R**A**TMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:870)
R**A**TMT**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:871)
R**A**TMTTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:872)
RVT**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:873)
RVT**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:874)
RVT**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:875)
RVTMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:876)
R**A**T**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:877)
R**A**T**F**T**A**DTSTSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:878)
R**A**T**F**TTDT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:879)
R**A**TMT**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:880)
RVT**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:881)
R**A**T**F**T**A**DT**N**TSTAYMELRSLRSDDTAVYYCA**G** (SEQ ID NO:882)
141A-huVH1b VH CDR3
EEVYDGYPWFGY (SEQ ID NO:35)
141A-huVH1b VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
141A-huVH3a Variable Region
EVQLVESGGGLVQPGGSLRLSCAAS**GYTFSRYWIE**WVRQAPGKGLEWVS**EILPGSGSTN YNEKFKG**RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR**EEVYDGYPWFGY**WGQGTLVT VSS (SEQ ID NO:18)
141A-huVH3a VH FR1
EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO:55)

EVQLV**Q**SGGGLVQPGGSLRLSCAAS (SEQ ID NO:115)
EVQLVESGGGLVQPGGS**V**RLSCAAS (SEQ ID NO:116)
EVQLVESGGGLVQPGGSLR**I**SCAAS (SEQ ID NO:117)
EVQLV**Q**SGGGLVQPGGS**V**RLSCAAS (SEQ ID NO:118)
EVQLVESGGGLVQPGGS**V**R**I**SCAAS (SEQ ID NO:119)
EVQLV**Q**SGGGLVQPGGSLR**I**SCAAS (SEQ ID NO:120)
EVQLV**Q**SGGGLVQPGGS**V**R**I**SCAAS (SEQ ID NO:121)
EVQLVESGGGL**M**QPGGSLRLSCAAS (SEQ ID NO:895)
EVQLV**Q**SGGGL**M**QPGGSLRLSCAAS (SEQ ID NO:896)
EVQLVESGGGL**M**QPGGS**V**RLSCAAS (SEQ ID NO:897)
EVQLVESGGGL**M**QPGGSLR**I**SCAAS (SEQ ID NO:898)
EVQLV**Q**SGGGL**M**QPGGS**V**RLSCAAS (SEQ ID NO:899)
EVQLV**Q**SGGGL**M**QPGGSLR**I**SCAAS (SEQ ID NO:900)
EVQLVESGGGL**M**QPGGS**V**R**I**SCAAS (SEQ ID NO:901)
EVQLV**Q**SGGGL**M**QPGGS**V**R**I**SCAAS (SEQ ID NO:902)
141A-huVH3a VH CDR1
GYTFSRYWIE (SEQ ID NO:33)
141A-huVH3a VH FR2
WVRQAPGKGLEWVS (SEQ ID NO:56)
WVRQAPGKGLEW**I**S (SEQ ID NO:122)
WVRQAPGKGLEWV**G** (SEQ ID NO:123)
WVRQAPGKGLEW**IG** (SEQ ID NO:124)
141A-huVH3a VH CDR2
EILPGSGSTNYNEKFKG (SEQ ID NO:34)
EILPGSGST**Q**YNEKFKG (SEQ ID NO:847)
EILPGSGST**S**YNEKFKG (SEQ ID NO:848)
EILPGSGST**D**YNEKFKG (SEQ ID NO:849)
EILPGSGST**A**YNEKFKG (SEQ ID NO:850)
EILPGSGSTNY**Q**EKFKG (SEQ ID NO:851)
EILPGSGSTNY**S**EKFKG (SEQ ID NO:852)
EILPGSGSTNY**D**EKFKG (SEQ ID NO:853)
EILPGSGSTNY**A**EKFKG (SEQ ID NO:854)
EILPGSGST**Q**Y**Q**EKFKG (SEQ ID NO:855)
EILPGSGST**S**Y**S**EKFKG (SEQ ID NO:856)
EILPGSGST**D**Y**D**EKFKG (SEQ ID NO:857)
EILPGSGST**A**Y**A**EKFKG (SEQ ID NO:858)
141A-huVH3a VH FR3
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:57)
R**A**TISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:125)
RFT**F**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:126)
RFTIS**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:127)
RFTISRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:128)
RFTISRDNAKNS**A**YLQMNSLRAEDTAVYYCAR (SEQ ID NO:129)
RFTISRDNAKNSLY**M**QMNSLRAEDTAVYYCAR (SEQ ID NO:130)
RFTISRDNAKNSLYLQ**L**NSLRAEDTAVYYCAR (SEQ ID NO:131)
R**A**T**F**SRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:132)
R**A**TIS**A**DNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:133)
R**A**TISRD**T**AKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:134)
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RATFSADTAKNSAYMQLNSLRAEDTAVYYCAG (SEQ ID NO:1030)
141A-huVH3a VH CDR3
EEVYDGYPWFGY (SEQ ID NO:35)
EEVYEGYPWFGY (SEQ ID NO:883)
EEVYSGYPWFGY (SEQ ID NO:884)
EEVYAGYPWFGY (SEQ ID NO:885)
141A-huVH3a VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
141A-huVH3b Variable Region
EVQLVESGGGLVQPGGSLRLSCAAS**GYTFSRYWIE**WVRQAPGKGLEWVS**EILPGSGSTN** YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR**EEVYDGYPWFGY**WGQGTLVT VSS (SEQ ID NO:19)
141A-huVH3b VH FR1
EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO:55)
EVQLVQSGGGLVQPGGSLRLSCAAS (SEQ ID NO:115)
EVQLVESGGGLVQPGGSVRLSCAAS (SEQ ID NO:116)
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141A-huVH3b VH CDR1
GYTFSRYWIE (SEQ ID NO:33)
141A-huVH3b VH FR2
WVRQAPGKGLEWVS (SEQ ID NO:56)
WVRQAPGKGLEWIS (SEQ ID NO:122)
WVRQAPGKGLEWVG (SEQ ID NO:123)
WVRQAPGKGLEWIG (SEQ ID NO:124)
141A-huVH3b VH CDR2*
EILPGSGSTNYADSVKG (SEQ ID NO:1070)
EILPGSGSTQYADSVKG (SEQ ID NO:1071)
EILPGSGSTSYADSVKG (SEQ ID NO:99)
EILPGSGSTDYADSVKG (SEQ ID NO:1072)
EILPGSGSTAYADSVKG (SEQ ID NO:1073)
EILPGSGSTNYADSFKG (SEQ ID NO:1074)
EILPGSGSTQYADSFKG (SEQ ID NO:1075)
EILPGSGSTSYADSFKG (SEQ ID NO:1076)
EILPGSGSTDYADSFKG (SEQ ID NO:1077)
EILPGSGSTAYADSFKG (SEQ ID NO:1078)
141A-huVH3b VH FR3
RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:57)
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RFTFSRDNAKNSLYLQLNSLRAEDTAVYYCAR (SEQ ID NO:142)

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141A-huVH3b VH CDR3
EEVYDGYPWFGY (SEQ ID NO:35)
EEVYEGYPWFGY (SEQ ID NO:883)
EEVYSGYPWFGY (SEQ ID NO:884)
EEVYAGYPWFGY (SEQ ID NO:885)
141A-huVH3b VH FR4
WGQGTLVTVSS (SEQ ID NO:54)
141A HUMANIZED ANTIBODY SEQUENCE: LIGHT CHAIN
141A-huVK3 Variable Region
EIVLTQSPGTLSLSPGERATLSC**RASSSLSYMH**WYQQKPGQAPRLLIY**ATSNLAS**GIPDRF SGSGSGTDFTLTISRLEPEDFAVYYC**QQWSSNPYT**FGQGTKLEIK (SEQ ID NO:26)
141A-huVK3 VL FR1
EIVLTQSPGTLSLSPGERATLSC (SEQ ID NO:91)
EIVLTQSPGTLSASPGERATLSC (SEQ ID NO:1031)
EIVLTQSPGTLSLSPGERVTLSC (SEQ ID NO:1032)
EIVLTQSPGTLSLSPGERATMSC (SEQ ID NO:1033)
EIVLTQSPGTLSASPGERVTLSC (SEQ ID NO:1034)
EIVLTQSPGTLSASPGERATMSC (SEQ ID NO:1035)
EIVLTQSPGTLSLSPGERVTMSC (SEQ ID NO:1036)
EIVLTQSPGTLSASPGERVTMSC (SEQ ID NO:1037)
141A-huVK3 VL CDR1
RASSSLSYMH (SEQ ID NO:42)

141A-huVK3 VL FR2
WYQQKPGQAPRLLIY (SEQ ID NO:92)
WYQQKPGQ**S**PRLLIY (SEQ ID NO:1038)
WYQQKPGQAPR**P**LIY (SEQ ID NO:1039)
WYQQKPGQAPRL**W**IY (SEQ ID NO:1040)
WYQQKPGQ**S**PR**P**LIY (SEQ ID NO:1041)
WYQQKPGQ**S**PRL**W**IY (SEQ ID NO:1042)
WYQQKPGQAPR**PW**IY (SEQ ID NO:1043)
WYQQKPGQ**S**PR**PW**IY (SEQ ID NO:1044)
141A-huVK3 VL CDR2
ATSNLAS (SEQ ID NO:43)
ATS**Q**LAS (SEQ ID NO:1045)
ATS**S**LAS (SEQ ID NO:1046)
ATS**D**LAS (SEQ ID NO:1047)
ATS**A**LAS (SEQ ID NO:1048)
141A-huVK3 VL FR3
GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO:93)
G**V**PDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO:1049)
GIPDRFSGSGSGTD**Y**TLTISRLEPEDFAVYYC (SEQ ID NO:1050)
GIPDRFSGSGSGTDFTLTISR**V**EPEDFAVYYC (SEQ ID NO:1051)
G**V**PDRFSGSGSGTD**Y**TLTISRLEPEDFAVYYC (SEQ ID NO:1052)
G**V**PDRFSGSGSGTDFTLTISR**V**EPEDFAVYYC (SEQ ID NO:1053)
GIPDRFSGSGSGTD**Y**TLTISR**V**EPEDFAVYYC (SEQ ID NO:1054)
G**V**PDRFSGSGSGTD**Y**TLTISR**V**EPEDFAVYYC (SEQ ID NO:1055)
141A-huVK3 VL CDR3
QQWSSNPYT (SEQ ID NO:44)
QQWSS**Q**PYT (SEQ ID NO:1056)
QQWSS**S**PYT (SEQ ID NO:1057)
QQWSS**A**PYT (SEQ ID NO:1058)
141A-huVK3 VL FR4
FGQGTKLEIK (SEQ ID NO:78)
141A-huVK1 Variable Region
DIQMTQSPSSLSASVGDRVTITC**RASSSLSYMH**WYQQKPGKAPKLLIY**ATSNLAS**GVPSR FSGSGSGTDFTLTISSLQPEDFATYYC**QQWSSNPYT**FGQGTKLEIK (SEQ ID NO:27)
141A-huVK1 VL FR1
DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO:79)
DIQ**L**TQSPSSLSASVGDRVTITC (SEQ ID NO:1059)
DIQMTQSPSSLSASVGDRVT**M**TC (SEQ ID NO:1060)
DIQ**L**TQSPSSLSASVGDRVT**M**TC (SEQ ID NO:1061)
141A-huVK1 VL CDR1
RASSSLSYMH (SEQ ID NO:42)
141A-huVK1 VL FR2
WYQQKPGKAPKLLIY (SEQ ID NO:80)
WYQQKPGK**S**PKLLIY (SEQ ID NO:284)

WYQQKPGKAPK**P**LIY (SEQ ID NO:1062)
WYQQKPGKAPKL**W**IY (SEQ ID NO:1063)
WYQQKPGK**S**PK**P**LIY (SEQ ID NO:1064)
WYQQKPGK**S**PKL**W**IY (SEQ ID NO:1065)
WYQQKPGKAPK**PW**IY (SEQ ID NO:1066)
WYQQKPGK**S**PK**PW**IY (SEQ ID NO:1067)
141A-huVK1 VL CDR2
ATSNLAS (SEQ ID NO:43)
ATS**Q**LAS (SEQ ID NO:1045)
ATS**S**LAS (SEQ ID NO:1046)
ATS**D**LAS (SEQ ID NO:1047)
ATS**A**LAS (SEQ ID NO:1048)
141A-huVK1 VL FR3
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:81)
GVPSRFSGSGSGTD**Y**TLTISSLQPEDFATYYC (SEQ ID NO:1068)
GVPSRFSGSGSGTDFTLTISS**V**QPEDFATYYC (SEQ ID NO:285)
GVPSRFSGSGSGTD**Y**TLTISS**V**QPEDFATYYC (SEQ ID NO:1069)
141A-huVK1 VL CDR3
QQWSSNPYT (SEQ ID NO:44)
QQWSS**Q**PYT (SEQ ID NO:1056)
QQWSS**S**PYT (SEQ ID NO:1057)
QQWSS**A**PYT (SEQ ID NO:1058)
141A-huVK1 VL FR4
FGQGTKLEIK (SEQ ID NO:78)

* Amino acid position numbering as in Kabat.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:36; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:37; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:38. In certain embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:47. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:6. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:28. In yet other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:29. In some embodiments, the antibody comprises (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:36;

(2) a VH CDR2 having an amino acid sequence of SEQ ID NO:37; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:38; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:47. To the extent an antibody provided herein is the to "bind to a C10orf54 epitope", it is envisioned those antibodies also bind to a C10orf54 polypeptide, polypeptide fragment, or antigen thereof.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:36; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:50; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:38. In certain embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:47. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:6. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:28. In yet other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:29. In some embodiments, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:36; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:50; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:38; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:47.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:36; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:99; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:38. In certain embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino

acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:47. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:6. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:28. In yet other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:29. In some embodiments, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:36; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:99; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:38; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:47.

In another embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:47. In some embodiments, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:20. In another embodiment, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:21. In other embodiments, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:22. In other embodiments, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:23.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:30; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:31; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:32. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:41. In other embodiments, the antibody further comprises a VL region having the

amino acid sequence of SEQ ID NO:24. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:25. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:30; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:31; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:32; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:41.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:30; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:321; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:32. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:41. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:24. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:25. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:30; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:321; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:32; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:41.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:30; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:835; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:32. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino

acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:41. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:24. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:25. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:30; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:835; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:32; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:41.

In some embodiments, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:41. In some embodiments, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:12. In another embodiment, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:13. In other embodiments, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:14. In other embodiments, the antibody further comprises a VH region having the amino acid sequence of SEQ ID NO:15.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:34; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:35. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:44. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:26. In another embodiment, the antibody further

comprises a VL region having the amino acid sequence of SEQ ID NO:27. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:34; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:35; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:44.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:49; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:35. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:44. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:26. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:27. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:49; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:35; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:44.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:1070; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:35. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:42; (2) a VL CDR2 having an amino acid sequence of

SEQ ID NO:43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:44. In other embodiments, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:26. In another embodiment, the antibody further comprises a VL region having the amino acid sequence of SEQ ID NO:27. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO:33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO:1070; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO:35; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO:42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO:43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO:44.

As will be understood by a person skilled in the art, the boundaries between the CDRs and framework sequences for any of the VH regions and VL regions described herein can be determined using any one of the well-known methods in the art, including IMGT, Kabat, Chothia, Contact, AbM or Kabat plus Chothia. Accordingly, any anti-C10orf54 antibody having one or more CDR or framework sequence as described herein includes a CDR or framework amino acid sequence as determined using IMGT, Kabat, Chothia, Contact, AbM or Kabat plus Chothis. For instance, exemplary CDR sequences for both VH and VL regions that can be included in an anti-C10orf54 antibody of the invention are depicted in Tables 8-10 for the [INSERT FULL NAMES OF CLONES] as disclosed in Tables 5-7. Table 8 cdr sequences based on a 175A-huVH1a variable region sequence as shown in Table 5.

Table 8: Antibody 175A-huVH1A CDR Sequences

		Exemplary*	IMGT	Kabat	Chothia	Contact	AbM
VH CDR Seq.	*VH CDR1*	GYTFSTHWIE (SEQ ID NO. 36)	GYTFSTHW (SEQ ID NO. 1081)	THWIE (SEQ ID NO. 1086)	GYTFSTH (SEQ ID NO. 1087)	STHWIE (SEQ ID NO. 1092)	GYTFSTHWIE (SEQ ID NO. 36)
	VH CDR2	EILPGSGSTSYN EKFKG (SEQ ID NO. 37)	ILPGSGST (SEQ ID NO. 1082)	EILPGSGSTSYN EKFKG (SEQ ID NO. 37)	PGSG (SEQ ID NO. 1088)	WIGEILPGSGST S (SEQ ID NO. 1093)	EILPGSGSTS (SEQ ID NO. 1098)
	VH CDR3	WLLYYYAMDY (SEQ ID NO. 38)	ARWLLYYYAMD Y (SEQ ID NO. 1083)	WLLYYYAMDY (SEQ ID NO. 38)	LLYYYAMD (SEQ ID NO. 1089)	ARWLLYYYAMD (SEQ ID NO. 1094)	WLLYYYAMDY (SEQ ID NO. 38)
VL CDR Seq.	*VL CDR1*	RSSQSIVHSNGN TYLE (SEQ ID NO. 45)	QSIVHSNGNTY (SEQ ID NO. 1084)	RSSQSIVHSNGN TYLE (SEQ ID NO. 45)	SQSIVHSNGNTY (SEQ ID NO. 1090)	VHSNGNTYLEW Y (SEQ ID NO. 1095)	RSSQSIVHSNGN TYLE (SEQ ID NO. 45)
	VL CDR2	KLSNRFS (SEQ ID NO. 46)	KLS (SEQ ID NO. 1085)	KLSNRFS (SEQ ID NO. 46)	KLS (SEQ ID NO. 1085)	LLIYKLSNRF (SEQ ID NO. 1096)	KLSNRFS (SEQ ID NO. 46)
	VL CDR3	FQGSHFPYT (SEQ ID NO. 47)	FQGSHFPYT (SEQ ID NO. 47)	FQGSHFPYT (SEQ ID NO. 47)	GSHFPY (SEQ ID NO. 1091)	FQGSHFPY (SEQ ID NO. 1097)	FQGSHFPYT (SEQ ID NO. 47)
VH Sequence: QVQLQQSGAELMKPGASVKISCKATGYTFSTHWIEWVKQRPGHGLEWIGEILPGSGSTSYNEKFKGKATFTADTSSNTAYMQLSSLTSEDSAVYY CARWLLYYYAMDYWGQGTSVTVSS (SEQ ID NO: 3)						
VL Sequence: DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKLSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYYCFQG SHFPYTFGGGTKLEIK (SEQ ID NO: 6)						

*Exemplary CDR sequences encompass amino acids as determined by Kabat plus Chothia.

Table 9: Antibody 76E1-huVH1a CDR Sequences

		Exemplary*	IMGT	Kabat	Chothia	Contact	AbM
VH CDR Seq.	*VH CDR1*	GYSFTGYNMN (SEQ ID NO. 30)	GYSFTGYN (SEQ ID NO. 1099)	GYNMN (SEQ ID NO. 1104)	GYSFTGY (SEQ ID NO. 1105)	TGYNMN (SEQ ID NO. 1110)	GYSFTGYNMN (SEQ ID NO. 30)
	VH CDR2	NIDPYYDYTSYN LKFKD (SEQ ID NO. 31)	IDPYYDYT (SEQ ID NO. 1100)	NIDPYYDYTSYN LKFKD (SEQ ID NO. 31)	PYYD (SEQ ID NO. 1106)	WIGNIDPYYDYT S (SEQ ID NO. 1111)	NIDPYYDYTS (SEQ ID NO. 1116)
	VH CDR3	STMITPFDY (SEQ ID NO. 32)	ATSTMITPFDY (SEQ ID NO. 1101)	STMITPFDY (SEQ ID NO. 32)	TMITPFD (SEQ ID NO. 1107)	ATSTMITPFD (SEQ ID NO. 1112)	STMITPFDY (SEQ ID NO. 32)
VL CDR Seq.	*VL CDR1*	RSSQSIVHSNGN TYLE (SEQ ID NO. 45)	QSIVHSNGNTY (SEQ ID NO. 1102)	RSSQSIVHSNGN TYLE (SEQ ID NO. 45)	SQSIVHSNGNTY (SEQ ID NO. 1108)	VHSNGNTYLEW Y (SEQ ID NO. 1113)	RSSQSIVHSNGN TYLE (SEQ ID NO. 45)
	VL CDR2	KVSNRFS (SEQ ID NO. 40)	KVS (SEQ ID NO. 1103)	KVSNRFS (SEQ ID NO. 40)	KVS (SEQ ID NO. 1103)	LLIYKVSNRF (SEQ ID NO. 1114)	KVSNRFS (SEQ ID NO. 40)
	VL CDR3	FQGSHVPWT (SEQ ID NO. 41)	FQGSHVPWT (SEQ ID NO. 41)	FQGSHVPWT (SEQ ID NO. 41)	GSHVPW (SEQ ID NO. 1109)	FQGSHVPW (SEQ ID NO. 1115)	FQGSHVPWT (SEQ ID NO. 41)
VH Sequence: EVQLLQSGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNIDPYYDYTSYNLKFKDKATLTVDKSSSTAYMQLKSLTSEDSAVYY CATSTMITPFDYWGQGTTLTVSS (SEQ ID NO: 1)						
VL Sequence: DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKINRVEAEDLGVYYCFQG SHVPWTFGGGTKLEIK (SEQ ID NO: 4)						

*Exemplary CDR sequences encompass amino acids as determined by Kabat plus Chothia.

Table 10: Antibody 141A-huVH1a CDR Sequences

		Exemplary*	IMGT	Kabat	Chothia	Contact	AbM
VH CDR Seq.	*VH CDR1*	GYTFSRYWIE (SEQ ID NO. 33)	GYTFSRYW (SEQ ID NO. 1117)	RYWIE (SEQ ID NO. 1122)	GYTFSRY (SEQ ID NO. 1123)	SRYWIE (SEQ ID NO. 1128)	GYTFSRYWIE (SEQ ID NO. 33)
	VH CDR2	EILPGSGSTNYN EKFKG (SEQ ID NO. 34)	ILPGSGST (SEQ ID NO. 1118)	EILPGSGSTNYN EKFKG (SEQ ID NO. 34)	PGSG (SEQ ID NO. 1124)	WIGEILPGSGST N (SEQ ID NO. 1129)	EILPGSGSTN (SEQ ID NO. 1134)
	VH CDR3	EEVYDGYPWFG Y (SEQ ID NO. 35)	AGEEVYDGYPW FGY (SEQ ID NO. 1119)	EEVYDGYPWFG Y (SEQ ID NO. 35)	EVYDGYPWFG (SEQ ID NO. 1125)	AGEEVYDGYPW FG (SEQ ID NO. 1130)	EEVYDGYPWFG Y (SEQ ID NO. 35)
VL CDR Seq.	*VL CDR1*	RASSSLSYMH (SEQ ID NO. 42)	SSLSY (SEQ ID NO. 1120)	RASSSLSYMH (SEQ ID NO. 42)	SSSLSY (SEQ ID NO. 1126)	SYMHWY (SEQ ID NO. 1131)	RASSSLSYMH (SEQ ID NO. 42)
	VL CDR2	ATSNLAS (SEQ ID NO. 43)	ATS (SEQ ID NO. 1121)	ATSNLAS (SEQ ID NO. 43)	ATS (SEQ ID NO. 1121)	PWIYATSNLA (SEQ ID NO. 1132)	ATSNLAS (SEQ ID NO. 43)
	VL CDR3	QQWSSNPYT (SEQ ID NO. 44)	QQWSSNPYT (SEQ ID NO. 44)	QQWSSNPYT (SEQ ID NO. 44)	WSSNPY (SEQ ID NO. 1127)	QQWSSNPY (SEQ ID NO. 1133)	QQWSSNPYT (SEQ ID NO. 44)
VH Sequence: QVQLQQSGAELMKPGASVKISCKATGYTFSRYWIEWVKQRPGHGLEWIGEILPGSGSTNYNEKFKGKATFTADTSSNTAYMQLSSLTSEDSAVYY CAGEEVYDGYPWFGYWGQGTLVTVSA (SEQ ID NO: 2)						
VL Sequence: QIVLSQSPAILSASPGEKVTMTCRASSSLSYMHWYQQKPGSSPKPWIYATSNLASGVPARFSGSGSGTSYSLTISRVEAEDAATYYCQQWSSNPY TFGGGTKLEIK (SEQ ID NO: 5)						

*Exemplary CDR sequences encompass amino acids as determined by Kabat plus Chothia.

In accordance with the amino acid sequences disclosed in Tables 8-10, in some embodiments, an antibody that binds to a C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 36, 1081, 1086, 1087, 1092, 30, 1099, 1104, 1105, 1110, 33, 1117, 1122, 1123 or 1128; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 37, 1082, 1088, 1093, 1098, 31, 1100, 1106, 1111, 1116, 34, 1118, 1124, 1129 or 1134; and/or (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 38, 1083, 1089, 1094, 32, 1101, 1107, 1112, 35, 1119, 1125 or 1130. In certain embodiments, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45, 1084, 1090, 1095, 1102, 1108, 1113, 42, 1120, 1126 or 1131; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 46, 1085, 1096, 40, 1103, 1114, 43, 1121 and 1132; and/or (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47, 1091, 1097, 41, 1109, 1115, 44, 1127 or 1133. In some embodiments, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 36, 1081, 1086, 1087, 1092, 30, 1099, 1104, 1105, 1110, 33, 1117, 1122, 1123 or 1128; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 37, 1082, 1088, 1093, 1098, 31, 1100, 1106, 1111, 1116, 34, 1118, 1124, 1129 or 1134; and/or (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 38, 1083, 1089, 1094, 32, 1101, 1107, 1112, 35, 1119, 1125 or 1130; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45, 1084, 1090, 1095, 1102, 1108, 1113, 42, 1120, 1126 or 1131; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 46, 1085, 1096, 40, 1103, 1114, 43, 1121 or 1132; and/or (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47, 1091, 1097, 41, 1109, 1115, 44, 1127 or 1133.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1081; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1082; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1083. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an

amino acid sequence of SEQ ID NO: 1084; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1085; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1081; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1082; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1083; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1084; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1085; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1086; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 37; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 38. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1086; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 37; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 38; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1087; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1088; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1089. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1090; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1085; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1091. In one embodiment, the antibody comprises: (a) a VH region

comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1087; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1088; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1089; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1090; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1085; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1091.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1092; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1093; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1094. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1095; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1096; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1097. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1092; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1093; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1094; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1095; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1096; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1097.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 36; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1098; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 38. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 36; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1098; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 38; and (b) a VL region comprising: (1) a VL CDR1

having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 46; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 47.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1099; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1100; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1101. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1102; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1103; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 41. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1099; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1100; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1101; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1102; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1103; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 41.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1104; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 31; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 32. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 41. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1104; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 31; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 32; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 41.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1105; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1106; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1107. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1108; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1103; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1109. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1105; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1106; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1107; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1108; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1103; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1109.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1110; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1111; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1112. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1113; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1114; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1115. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1110; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1111; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1112; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1113; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1114; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1115.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 30; (2) a

VH CDR2 having an amino acid sequence of SEQ ID NO: 1116; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 32. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 41. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 30; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1116; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 32; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 45; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 40; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 41.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1117; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1118; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1119. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1120; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1121; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 44. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1117; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1118; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1119; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1120; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1121; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 44.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1122; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 34; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 35. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino

acid sequence of SEQ ID NO: 42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 44. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1122; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 34; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 35; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 44.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1123; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1124; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1125. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1126; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1121; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1127. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1123; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1124; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1125; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1126; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1121; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1127.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1128; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1129; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1130. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1131; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1132; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1133. In one embodiment, the antibody comprises: (a) a VH region

comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 1128; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1129; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 1130; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 1131; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 1132; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 1133.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1134; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 35. In some embodiments, the antibody further comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 44. In one embodiment, the antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of SEQ ID NO: 33; (2) a VH CDR2 having an amino acid sequence of SEQ ID NO: 1134; and (3) a VH CDR3 having an amino acid sequence of SEQ ID NO: 35; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of SEQ ID NO: 42; (2) a VL CDR2 having an amino acid sequence of SEQ ID NO: 43; and (3) a VL CDR3 having an amino acid sequence of SEQ ID NO: 44.

In certain embodiments, a humanized anti-C10orf54 antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises one or more consensus sequences derived from related antibodies as depicted in **FIG. 17A** and **17B**. As described herein, a "consensus sequence" refers to amino acid sequences having conserved amino acids common among a number of sequences and variable amino acids that vary within a given amino acid sequences. The CDR consensus sequences provided include CDRs corresponding to CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. Consensus sequences of CDRs of anti-C10orf54 antibodies are shown in **FIG. 17A** and **17B**. Accordingly, in some embodiments, a humanized anti-C10orf54 antibody comprises a VH region comprising: (1) a VH CDR1 having an amino acid sequence of GYTFSX_1X_2WIE (SEQ ID NO: 1149), wherein X_1 is a R or T and X_2 is a Y or H; (2) a VH CDR2 having an

amino acid sequence of EILPGSGSTX$_1$YNEKFKG (SEQ ID NO: 1150), wherein X$_1$ is a N or S; and/or (3) a VH CDR3 having an amino acid sequence of xxxxxxxxxX$_1$X$_2$Y (SEQ ID NO: 1151), wherein x is any amino acid residue, X$_1$ is a M or F, and X$_2$ is G or D. In certain embodiments, a humanized anti-C10orf54 antibody comprises a VL region comprising: (1) a VL CDR1 having an amino acid sequence of RSSQSIVHSNGNTYLE (SEQ ID NO: 45); (2) a VL CDR2 having an amino acid sequence of KX$_1$SNRFS (SEQ ID NO: 1152), wherein X$_1$ is a V or L; and/or (3) a VL CDR3 having an amino acid sequence of FQGSHX$_1$PX$_2$T (SEQ ID NO: 1153), wherein X$_1$ is V or F and X$_2$ is a W or Y. In certain embodiments, a humanized anti-C10orf54 antibody comprises: (a) a VH region comprising: (1) a VH CDR1 having an amino acid sequence of GYTFSX$_1$X$_2$WIE (SEQ ID NO: 1149), wherein X$_1$ is a R or T and X$_2$ is a Y or H; (2) a VH CDR2 having an amino acid sequence of EILPGSGSTX$_1$YNEKFKG (SEQ ID NO: 1150), wherein X$_1$ is a N or S; and/or (3) a VH CDR3 having an amino acid sequence of xxxxxxxxxX$_1$X$_2$Y (SEQ ID NO: 1151), wherein x is any amino acid residue, X$_1$ is a M or F, and X$_2$ is G or D; and (b) a VL region comprising: (1) a VL CDR1 having an amino acid sequence of RSSQSIVHSNGNTYLE (SEQ ID NO: 45); (2) a VL CDR2 having an amino acid sequence of KX$_1$SNRFS (SEQ ID NO: 1152), wherein X$_1$ is a V or L; and/or (3) a VL CDR3 having an amino acid sequence of FQGSHX$_1$PX$_2$T (SEQ ID NO: 1153), wherein X$_1$ is V or F and X$_2$ is a W or Y.

In some embodiments, the antibodies provided herein comprise a VH region that comprises or consists of a VH domain. In other embodiments, the antibodies provided herein comprise a VH region that comprises or consists of a VH chain. In some embodiments, the antibodies provided herein comprise a VL region that comprises or consists of a VL domain. In other embodiments, the antibodies provided herein comprise a VL region that comprises or consists of a VL chain. In some embodiments, the antibodies provided herein have a combination of (i) a VH domain or VH chain; and/or (ii) a VL domain or VL chain.

In some embodiments, an antibody provided herein comprises or consists six CDRs, for example, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 identified in Tables 5-10. In certain embodiments, an antibody provided herein can comprise less than six CDRs. In some embodiments, 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 embodiments, 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 murine monoclonal antibody 175A, 76E1 or 141A described herein, or a humanized variant thereof, as identified in Tables 5-10. Accordingly, in some embodiments, the antibody comprises or consists of one, two, three four or five CDRs of anyone of the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 identified in Tables 5-10.

In some embodiments, the antibodies provided herein comprise one or more (*e.g.*, one, two or three) VH CDRs listed in Tables 5-10. In other embodiments, the antibodies provided herein comprise one or more (*e.g.*, one, two or three) VL CDRs listed in Tables 5-10. In yet other embodiments, the antibodies provided herein comprise one or more (*e.g.*, one, two or three) VH CDRs listed in Tables 5-10 and one or more VL CDRs listed in Tables 5-10. Accordingly, in certain embodiments, the antibodies comprise a VH CDR1 having the amino acid sequence of any one of SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 and 1128. In another embodiment, the antibodies comprise a VH CDR2 having the amino acid sequence of any one of SEQ ID NOS: 37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 and 1134. In another embodiment, the antibodies comprise a VH CDR3 having the amino acid sequence of any one of SEQ ID NOS: 38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 and 1130. In certain embodiments, the antibodies comprise a VH CDR1 and/or a VH CDR2 and/or a VH CDR3 independently selected from a VH CDR1, VH CDR2, VH CDR3 as depicted in any one of the VH regions depicted in Table 5-10. In certain embodiments, the antibodies comprise a VL CDR1 having the amino acid sequence of any one of SEQ ID NOS: 45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 and 1131. In another embodiment, the antibodies comprise a VL CDR2 having the amino acid sequence of any one of SEQ ID NOS: 46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 and 1132. In another embodiment, the antibodies comprise a VL CDR3 having the amino acid sequence of any one of SEQ ID NOS: 47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 and 1133. In certain

embodiments, the antibodies comprise a VL CDR1 and/or a VL CDR2 and/or a VL CDR3 independently selected from a VL CDR1, VL CDR2, VL CDR3 as depicted in any one of the VL regions depicted in Tables 5-10.

Also provided herein are antibodies comprising one or more VH CDRs and one or more (*e.g.*, one, two or three) VL CDRs listed in Tables 5-10. In particular, provided herein is an antibody comprising a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128) and a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134) and a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131); a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115,

1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134) and a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133);a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113,

1120, 1126 or 1131) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-

846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR3 (SEQ ID

NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID

NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132) and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR2 (SEQ ID NOS:37, 101-104, 50,

114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132), and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR1 (SEQ ID NOS:36, 30, 59-62, 33, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123 or 1128), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132), and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); a VH CDR2 (SEQ ID NOS:37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894, 1070-1078, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129 or 1134), a VH CDR3 (SEQ ID NOS:38, 32, 319, 35, 883-885, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 or 1130), a VL CDR1 (SEQ ID NOS:45, 253-271, 42, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126 or 1131), a VL CDR2 (SEQ ID NOS:46, 272-275, 40, 843-846, 43, 1045-1048, 1085, 1096, 1103, 1114, 1121 or 1132), and a VL CDR3 (SEQ ID NOS:47, 41, 44, 1056-1058, 1091, 1097, 1109, 1115, 1127 or 1133); or any combination thereof of the VH CDRs (SEQ ID NOS:36, 30, 59-62, 33, 37, 101-104, 50, 114, 99, 100, 31, 65-74, 83-90, 95, 321, 322, 835-842, 34, 847-858, 49, 886-894 1070-1078, 38, 32, 319, 35, 883-885, 1081, 1086, 1087, 1092, 1099, 1104, 1105, 1110, 1117, 1122, 1123, 1128, 1082, 1088, 1093, 1098, 1100, 1106, 1111, 1116, 1118, 1124, 1129, 1134, 1083, 1089, 1094, 1101, 1107, 1112, 1119, 1125 and 1130) and VL CDRs (SEQ ID NOS:45, 253-271, 42, 46, 272-275, 40, 843-846, 43, 1045-1048, 47, 41, 44, 1056-1058, 1084, 1090, 1095, 1102, 1108, 1113, 1120, 1126, 1131, 1085, 1096, 1103, 1114, 1121, 1132, 1091, 1097, 1109, 1115, 1127 and 1133) listed in Tables 5-10.

In certain embodiments, humanized anti-C10orf54 antibodies bind to a C10orf54 polypeptide, polypeptide fragment or epitope with an affinity comparable to that of one or more of the murine monoclonal antibodies designated 175A, 76E1 or 141A. The humanized anti-C10orf54 the antibodies can also comprise one, two, three or four

human or humanized framework regions of the immunoglobulin heavy chain variable region and/or one, two, three or four human or humanized framework regions of the immunoglobulin light chain variable region. Also provided are heavy and/or light chain FR regions that contain one or more back-mutations in which a human FR residue is exchanged for the corresponding residue present in the parental murine heavy or light chain or another residue comparable residue. In some aspects, the amino acid sequences for CDR1, CDR2, and CDR3 of the heavy and light chains for some of the humanized anti-C10orf54 the antibodies can also include one or more mutations in which a CDR residue as identified in Tables 5-10. The amino acid sequences for FR1, FR2, FR3 and FR4 of the heavy and light chains that can be used for the humanized anti-C10orf54 the antibodies are identified in Tables 5-7 and FiGs. 3-9 and 17.

In certain embodiments, a humanized antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region that comprises: (1) a VH FR1 having an amino acid sequence selected from the group consisting of SEQ ID NOS:51, 105, 55, 115-121, 39, 58, and 895-902; (2) a VH FR2 having an amino acid sequence selected from the group consisting of SEQ ID NOS:52, 106, 56, 122-124, 63, 64, and 323-326; (3) a VH FR3 having an amino acid sequence selected from the group consisting of SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882, and 903-1030; and/or (4) a VH FR4 having an amino acid sequence of SEQ ID NO:54 or 320. Accordingly, in some embodiments, the humanized antibody comprises a VH region that includes a VH FR1 having an amino acid sequence selected from the group consisting of SEQ ID NOS:51, 105, 55, 115-121, 39, 58, and 895-902. In some embodiments, the humanized antibody comprises a VH region that includes a VH FR2 having an amino acid sequence selected from the group consisting of SEQ ID NOS:52, 106, 56, 122-124, 63, 64, and 323-326. In some embodiments, the humanized antibody comprises a VH region that includes a VH FR3 having an amino acid sequence selected from the group consisting of SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882, and 903-1030. In some embodiments, the humanized antibody comprises a VH region that includes a VH FR4 having an amino acid sequence of SEQ ID NO:54 or 320.

In certain embodiments, a humanized antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VL region that comprises: (1) a VL FR1 having an amino acid sequence selected from the group consisting of SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037, and 1059-1061; (2) a VL FR2 having an amino acid sequence selected from the group consisting of SEQ ID NOS:76, 80, 284, 92, 1038-1044, and 1062-1067; (3) a VL FR3 having an amino acid sequence selected from the group consisting of SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068, and 1069; and/or (4) a VL FR4 having an amino acid of SEQ ID NO:78. Accordingly, in some aspects, the humanized antibody comprises a VL region that includes a VL FR1 having an amino acid sequence selected from the group consisting of SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037, and 1059-1061. In some aspects, the humanized antibody comprises a VL region that includes a VL FR2 having an amino acid sequence selected from the group consisting of SEQ ID NOS:76, 80, 284, 92, 1038-1044, and 1062-1067. In some aspects, the humanized antibody comprises a VL region that includes a VL FR3 having an amino acid sequence selected from the group consisting of SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068, and 1069. In some aspects, the humanized antibody comprises a VL region that includes a VL FR4 having an amino acid of SEQ ID NO:78.

In certain embodiments, a humanized antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH region and a VL region, wherein the VH region further comprises: (1) a VH FR1 having an amino acid sequence selected from the group consisting of SEQ ID NOS:51, 105, 55, 115-121, 39, 58, and 895-902; (2) a VH FR2 having an amino acid sequence selected from the group consisting of SEQ ID NOS:52, 106, 56, 122-124, 63, 64, and 323-326; (3) a VH FR3 having an amino acid sequence selected from the group consisting of SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882, and 903-1030; and/or (4) a VH FR4 having an amino acid sequence of SEQ ID NO:54 or 320; and wherein the VL region further comprises: (1) a VL FR1 having an amino acid sequence selected from the group consisting of SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037, and 1059-1061; (2) a VL FR2 having an amino acid sequence selected from the group consisting of SEQ ID NOS:76, 80, 284, 92, 1038-1044, and 1062-1067; (3) a VL FR3 having an amino acid sequence

selected from the group consisting of SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068, and 1069; and/or (4) a VL FR4 having an amino acid of SEQ ID NO:78.

Also provided herein are antibodies comprising one or more (*e.g.*, one, two, three or four) VH FRs and one or more VL FRs listed in Tables 5-7. In particular, provided herein is an antibody comprising a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902) and a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902) and a VL FR4 (SEQ ID NO:78); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR4 (SEQ ID NO:78); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069);a VH FR1 (SEQ ID

NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326) and a VL FR4 (SEQ ID NO:78);a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR4 (SEQ ID NO:78); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR4 (SEQ ID NO:78); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and

a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR4 (SEQ ID NO:78); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR4 (SEQ ID NO:78); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR4 (SEQ ID NO:78); a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067); a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061) and a VL FR4 (SEQ ID NO:78); a VH FR4 (SEQ ID NO:54 or 320), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR4 (SEQ ID NO:54 or 320), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030) and a VL

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106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VH FR4 (SEQ ID NO:54 or 320), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), a VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-

326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VH FR4 (SEQ ID NO:54 or 320), VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VH FR4 (SEQ ID NO:54 or 320), VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VH FR4 (SEQ ID NO:54 or 320), VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR1 (SEQ ID NOS:51, 105, 55, 115-121, 39, 58 or 895-902), a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); a VH FR2 (SEQ ID NOS:52, 106, 56, 122-124, 63, 64 or 323-326), a VH FR3 (SEQ ID NOS:53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 or 903-1030), a VH FR4 (SEQ ID NO:54 or 320), a VL FR1 (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037 or 1059-1061), VL FR2 (SEQ ID NOS:76, 80, 284, 92, 1038-1044 or 1062-1067), VL FR3 (SEQ ID NOS:77, 276, 81, 285-291, 93, 1049-1055, 1068 or 1069) and a VL FR4 (SEQ ID NO:78); or any combination thereof of the VH FRs (SEQ ID NOS:51, 105, 55, 115-121, 39, 58, 895-902, 52, 106, 56, 122-124, 63, 64, 323-326, 53, 107-113, 57, 125-251, 96-98, 292-318, 327-833, 53, 859-882 903-

1030, 54 or 320) and VL FRs (SEQ ID NOS:75, 252, 79, 277-283, 91, 1031-1037, 1059-1061, 76, 80, 284, 92, 1038-1044, 1062-1067, 77, 276, 81, 285-291, 93, 1049-1055, 1068, 1069, or 78) listed in Tables 5-7.

In some embodiments, antibodies provided herein are antibodies that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope), and include antibodies comprising derivatives of the VH domains, VH CDRs, VL domains, and VL CDRs described herein that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope). Also provided herein are antibodies comprising derivatives of the murine monoclonal antibody 175A, 76E1 or 141A, wherein the antibodies bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope). Standard techniques known to those of skill in the art can be used to introduce mutations in the nucleotide sequence encoding an antibody, or fragment thereof, provided herein, including, for example, site-directed mutagenesis and PCR-mediated mutagenesis which results in amino acid substitutions. In certain embodiments, the derivatives include less than 25 amino acid substitutions, less than 20 amino acid substitutions, less than 15 amino acid substitutions, less than 10 amino acid substitutions, less than 5 amino acid substitutions, less than 4 amino acid substitutions, less than 3 amino acid substitutions, or less than 2 amino acid substitutions relative to the original molecule. In a specific embodiment, the derivatives have conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a side chain with a similar charge. Families of amino acid residues having side chains with similar charges have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Alternatively, mutations can be introduced randomly along all or part of the coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for biological activity to identify mutants that retain activity.

Following mutagenesis, the encoded protein can be expressed and the activity of the protein can be determined.

In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises an amino acid sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to the amino acid sequence of the murine monoclonal antibody 175A, 76E1 or 141A, or an antigen-binding fragment thereof, such as a VH domain or VL domain. In one embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises an amino acid sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to an amino acid sequence depicted in SEQ ID NOS:12-29. In another embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises an amino acid sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to an amino acid sequence depicted in Tables 5-10. In yet another embodiment, an antibody that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises a VH CDR and/or a VL CDR amino acid sequence that is at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to a VH CDR amino acid sequence depicted in Tables 5-10 and/or a VL CDR amino acid sequence depicted in Tables 5-10.

In certain embodiments, the antibodies used in accordance with the methods provided herein have a high affinity for a C10orf54 polypeptide, or polypeptide fragment or epitope thereof. In one embodiment, the antibodies used in accordance with the methods provided herein have a higher affinity for a C10orf54 antibody than known antibodies (*e.g.*, commercially available monoclonal antibodies discussed elsewhere herein). In a specific embodiment, the antibodies used in accordance with the methods provided herein have a 2- to 10-fold (or more) higher affinity for a

C10orf54 antigen than a known anti-C10orf54 antibody as assessed by techniques described herein or known to one of skill in the art (*e.g.*, a BIAcore assay). In accordance with these embodiments, the affinity of the antibodies are, in one embodiment, assessed by a BIAcore assay.

In a specific embodiment, an antibody that binds C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises an amino acid sequence of a VH domain and/or an amino acid sequence a VL domain encoded by a nucleotide sequence that hybridizes to (1) the complement of a nucleotide sequence encoding any one of the VH and/or VL domains depicted in Tables 2 and 4-10 under stringent conditions (*e.g.*, hybridization to filter-bound DNA in 6x sodium chloride/sodium citrate (SSC) at about 45° C followed by one or more washes in 0.2xSSC/0.1% SDS at about 50-65° C) under highly stringent conditions (*e.g.*, hybridization to filter-bound nucleic acid in 6xSSC at about 45° C followed by one or more washes in 0.1xSSC/0.2% SDS at about 68° C), or under other stringent hybridization conditions which are known to those of skill in the art (see, for example, Ausubel, F.M. *et al.*, eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc. and John Wiley & Sons, Inc., New York at pages 6.3.1-6.3.6 and 2.10.3).

In another embodiment, an antibody that binds C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) comprises an amino acid sequence of a VH CDR or an amino acid sequence of a VL CDR encoded by a nucleotide sequence that hybridizes to the complement of a nucleotide sequence encoding any one of the VH CDRs and/or VL CDRs depicted in Tables 2 and 4-10 under stringent conditions (*e.g.*, hybridization to filter-bound DNA in 6X SSC at about 45° C followed by one or more washes in 0.2X SSC/0.1% SDS at about 50-65° C), under highly stringent conditions (*e.g.*, hybridization to filter-bound nucleic acid in 6X SSC at about 45° C followed by one or more washes in 0.1X SSC/0.2% SDS at about 68° C), or under other stringent hybridization conditions which are known to those of skill in the art (see, for example, Ausubel, F.M. *et al.*, eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc. and John Wiley & Sons, Inc., New York at pages 6.3.1-6.3.6 and 2.10.3)

In some embodiments, antibodies provided herein are chemically modified, *e.g.,* by the covalent attachment of any type of molecule to the antibody. For example, but not by way of limitation, the antibody derivatives include antibodies that have been chemically modified, *e.g.,* by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, *etc.* Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formulation, metabolic synthesis of tunicamycin, *etc.* Additionally, the antibody may contain one or more non-classical amino acids.

Also provided herein are antibodies that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope) which comprises a framework region known to those of skill in the art (*e.g.,* a human or non-human fragment). The framework region may, for example, be naturally occurring or consensus framework regions. In specific embodiments, the framework region of an antibody provided herein is human (see, *e.g.,* Chothia *et al.*, 1998, *J. Mol. Biol.* 278:457-479 for a listing of human framework regions, which is incorporated by reference herein in its entirety). See also Kabat *et al.* (1991) Sequences of Proteins of Immunological Interest (U.S. Department of Health and Human Services, Washington, D.C.) 5th ed.

Also provided herein are antibodies that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope), the antibodies comprising the amino acid sequence of one or more of the CDRs of the murine monoclonal antibody 175A, 76E1 or 141A, including those also provided in Tables 5-10, or humanized variants thereof (*e.g.,* VH CDRs or VL CDRs of Tables 5-7), and human framework regions with one or more amino acid substitutions at one, two, three or more of the following residues: (a) rare framework residues that differ between the murine antibody framework (*e.g.,* donor antibody framework) and the human antibody framework (*e.g.,* acceptor antibody framework); (b) Venier zone residues when differing between donor antibody framework and acceptor antibody framework; (c) interchain packing residues at the VH/VL interface that differ between the donor antibody framework and the acceptor antibody framework; (d) canonical residues which differ between the donor antibody framework and the acceptor antibody framework sequences, particularly the framework regions crucial for the definition of

the canonical class of the murine antibody CDR loops; (e) residues that are adjacent to a CDR; (g) residues capable of interacting with the antigen; (h) residues capable of interacting with the CDR; and (i) contact residues between the VH domain and the VL domain. In certain embodiments, antibodies that bind to a C10orf54 antigen comprising the human framework regions with one or more amino acid substitutions at one, two, three or more of the above-identified residues are antagonistic C10orf54 antibodies. In certain embodiments, antibodies that bind to a C10orf54 antigen comprising the human framework regions with one or more amino acid substitutions at one, two, three or more of the above-identified residues are agonistic C10orf54 antibodies.

Antibodies provided herein include, but are not limited to, synthetic antibodies, monoclonal antibodies, recombinantly produced antibodies, multispecific antibodies (including bi-specific antibodies), human antibodies, humanized antibodies, camelized antibodies, chimeric antibodies, intrabodies, anti-idiotypic (anti-Id) antibodies, and functional fragments of any of the above. Non-limiting examples of functional fragments include single-chain Fvs (scFv) (*e.g.*, including monospecific, bispecific, *etc.*), Fab fragments, F(ab') fragments, $F(ab)_2$ fragments, $F(ab')_2$ fragments, disulfide-linked Fvs (sdFv), Fd fragments, Fv fragments, diabody, triabody, tetrabody and minibody.

In particular, antibodies provided herein include immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, *e.g.*, molecules that contain an antigen binding site that bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope). The immunoglobulin molecules provided herein can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA and IgY), class (*e.g.*, IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule.

Variants and derivatives of antibodies include antibody functional fragments that retain the ability to bind to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope). Exemplary functional fragments include Fab fragments (an antibody fragment that contains the antigen-binding domain and comprises a light chain and part of a heavy chain bridged by a disulfide bond); Fab' (an antibody fragment containing a single anti-binding domain comprising an Fab and an additional portion of the heavy chain through the hinge region); $F(ab')_2$ (two Fab'

molecules joined by interchain disulfide bonds in the hinge regions of the heavy chains; the Fab' molecules may be directed toward the same or different epitopes); a bispecific Fab (a Fab molecule having two antigen binding domains, each of which may be directed to a different epitope); a single chain Fab chain comprising a variable region, also known as, a sFv (the variable, antigen-binding determinative region of a single light and heavy chain of an antibody linked together by a chain of 10-25 amino acids); a disulfide-linked Fv, or dsFv (the variable, antigen-binding determinative region of a single light and heavy chain of an antibody linked together by a disulfide bond); a camelized VH (the variable, antigen-binding determinative region of a single heavy chain of an antibody in which some amino acids at the VH interface are those found in the heavy chain of naturally occurring camel antibodies); a bispecific sFv (a sFv or a dsFv molecule having two antigen-binding domains, each of which may be directed to a different epitope); a diabody (a dimerized sFv formed when the VH domain of a first sFv assembles with the VL domain of a second sFv and the VL domain of the first sFv assembles with the VH domain of the second sFv; the two antigen-binding regions of the diabody may be directed towards the same or different epitopes); and a triabody (a trimerized sFv, formed in a manner similar to a diabody, but in which three antigen-binding domains are created in a single complex; the three antigen binding domains may be directed towards the same or different epitopes). Derivatives of antibodies also include one or more CDR sequences of an antibody combining site. The CDR sequences may be linked together on a scaffold when two or more CDR sequences are present. In certain embodiments, the antibody comprises a single-chain Fv ("scFv"). scFvs are antibody fragments comprising the VH and VL domains of an antibody, wherein these domains are present in a single polypeptide chain. Generally, the scFv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the scFv to form the desired structure for antigen binding. For a review of scFvs see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore eds. Springer-Verlag, New York, pp. 269-315 (1994).

The antibodies provided herein may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a C10orf54 polypeptide or may be specific for both a C10orf54 polypeptide as well as for a heterologous epitope, such as a heterologous polypeptide or solid support

material. In specific embodiments, the antibodies provided herein are monospecific for a given epitope of a C10orf54 polypeptide and do not bind to other epitopes.

Also provided herein are fusion proteins comprising an antibody provided herein that binds to a C10orf54 antigen and a heterologous polypeptide. In some embodiments, the heterologous polypeptide to which the antibody is fused is useful for targeting the antibody to cells having cell surface-expressed C10orf54.

Also provided herein are panels of antibodies that bind to a C10orf54 antigen. In specific embodiments, panels of antibodies have different association rate constants different dissociation rate constants, different affinities for C10orf54 antigen, and/or different specificities for a C10orf54 antigen. In some embodiments, the panels comprise or consist of about 10, about 25, about 50, about 75, about 100, about 125, about 150, about 175, about 200, about 250, about 300, about 350, about 400, about 450, about 500, about 550, about 600, about 650, about 700, about 750, about 800, about 850, about 900, about 950, or about 1000 antibodies or more. Panels of antibodies can be used, for example, in 96 well or 384 well plates, such as for assays such as ELISAs.

ANTIBODY CONJUGATES AND FUSION PROTEINS

In some embodiments, antibodies provided herein are conjugated or recombinantly fused to a diagnostic, detectable or therapeutic agent or any other molecule. The conjugated or recombinantly fused antibodies can be useful, *e.g.*, for monitoring or prognosing the onset, development, progression and/or severity of a C10orf54-mediated disease as part of a clinical testing procedure, such as determining the efficacy of a particular therapy.

Such diagnosis and detection can accomplished, for example, by coupling the antibody to detectable substances including, but not limited to, various enzymes, such as, but not limited to, horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; prosthetic groups, such as, but not limited to, streptavidin/biotin and avidin/biotin; fluorescent materials, such as, but not limited to, umbelliferone, fluorescein, fluorescein isothiocynate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; luminescent materials, such as, but not limited to, luminol; bioluminescent materials, such as but

not limited to, luciferase, luciferin, and aequorin; chemiluminescent material, such as but not limited to, an acridinium based compound or a HALOTAG; radioactive materials, such as, but not limited to, iodine (^{131}I, ^{125}I, ^{123}I, and ^{121}I,), carbon (^{14}C), sulfur (^{35}S), tritium (^{3}H), indium (^{115}In, ^{113}In, ^{112}In, and ^{111}In,), technetium (^{99}Tc), thallium (^{201}Ti), gallium (^{68}Ga, ^{67}Ga), palladium (^{103}Pd), molybdenum (^{99}Mo), xenon (^{133}Xe), fluorine (^{18}F), ^{153}Sm, ^{177}Lu, ^{159}Gd, ^{149}Pm, ^{140}La, ^{175}Yb, ^{166}Ho, ^{90}Y, ^{47}Sc, ^{186}Re, ^{188}Re, ^{142}Pr, ^{105}Rh, ^{97}Ru, ^{68}Ge, ^{57}Co, ^{65}Zn, ^{85}Sr, ^{32}P, ^{153}Gd, ^{169}Yb, ^{51}Cr, ^{54}Mn, ^{75}Se, ^{113}Sn, and ^{117}Sn; and positron emitting metals using various positron emission tomographies, and non-radioactive paramagnetic metal ions.

Also provided herein are antibodies that are conjugated or recombinantly fused to a therapeutic moiety (or one or more therapeutic moieties), as well as uses thereof. The antibody may be conjugated or recombinantly fused to a therapeutic moiety, such as a cytotoxin, *e.g.,* a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, *e.g.,* alpha-emitters. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Therapeutic moieties include, but are not limited to, antimetabolites (*e.g.,* methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine); alkylating agents (*e.g.,* mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BCNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cisdichlorodiamine platinum (II) (DDP), and cisplatin); anthracyclines (*e.g.,* daunorubicin (formerly daunomycin) and doxorubicin); antibiotics (*e.g.,* d actinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)); Auristatin molecules (*e.g.,* auristatin PHE, auristatin F, monomethyl auristatin E, bryostatin 1, and solastatin 10; see Woyke *et al.*, Antimicrob. Agents Chemother. 46:3802-8 (2002), Woyke *et al.*, Antimicrob. Agents Chemother. 45:3580-4 (2001), Mohammad *et al.*, Anticancer Drugs 12:735-40 (2001), Wall *et al.*, Biochem. Biophys. Res. Commun. 266:76-80 (1999), Mohammad *et al.*, Int. J. Oncol. 15:367-72 (1999), all of which are incorporated herein by reference); hormones (*e.g.,* glucocorticoids, progestins, androgens, and estrogens), DNA-repair enzyme inhibitors (*e.g.,* etoposide or topotecan), kinase inhibitors (*e.g.,* compound ST1571, imatinib mesylate (Kantarjian *et al.*, Clin Cancer Res. 8(7):2167-76 (2002)); cytotoxic agents (*e.g.,* paclitaxel, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin,

dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof and those compounds disclosed in U.S. Patent Nos. 6,245,759, 6,399,633, 6,383,790, 6,335,156, 6,271,242, 6,242,196, 6,218,410, 6,218,372, 6,057,300, 6,034,053, 5,985,877, 5,958,769, 5,925,376, 5,922,844, 5,911,995, 5,872,223, 5,863,904, 5,840,745, 5,728,868, 5,648,239, 5,587,459); farnesyl transferase inhibitors (*e.g.*, R115777, BMS-214662, and those disclosed by, for example, U.S. Patent Nos: 6,458,935, 6,451,812, 6,440,974, 6,436,960, 6,432,959, 6,420,387, 6,414,145, 6,410,541, 6,410,539, 6,403,581, 6,399,615, 6,387,905, 6,372,747, 6,369,034, 6,362,188, 6,342,765, 6,342,487, 6,300,501, 6,268,363, 6,265,422, 6,248,756, 6,239,140, 6,232,338, 6,228,865, 6,228,856, 6,225,322, 6,218,406, 6,211,193, 6,187,786, 6,169,096, 6,159,984, 6,143,766, 6,133,303, 6,127,366, 6,124,465, 6,124,295, 6,103,723, 6,093,737, 6,090,948, 6,080,870, 6,077,853, 6,071,935, 6,066,738, 6,063,930, 6,054,466, 6,051,582, 6,051,574, and 6,040,305); topoisomerase inhibitors (*e.g.*, camptothecin; irinotecan; SN-38; topotecan; 9-aminocamptothecin; GG-211 (GI 147211); DX-8951f; IST-622; rubitecan; pyrazoloacridine; XR-5000; saintopin; UCE6; UCE1022; TAN-1518A; TAN 1518B; KT6006; KT6528; ED-110; NB-506; ED-110; NB-506; and rebeccamycin); bulgarein; DNA minor groove binders such as Hoescht dye 33342 and Hoechst dye 33258; nitidine; fagaronine; epiberberine; coralyne; beta-lapachone; BC-4-1; bisphosphonates (*e.g.*, alendronate, cimadronte, clodronate, tiludronate, etidronate, ibandronate, neridronate, olpandronate, risedronate, piridronate, pamidronate, zolendronate) HMG-CoA reductase inhibitors, (*e.g.*, lovastatin, simvastatin, atorvastatin, pravastatin, fluvastatin, statin, cerivastatin, lescol, lupitor, rosuvastatin and atorvastatin); antisense oligonucleotides (*e.g.*, those disclosed in the U.S. Patent Nos. 6,277,832, 5,998,596, 5,885,834, 5,734,033, and 5,618,709); adenosine deaminase inhibitors (*e.g.*, Fludarabine phosphate and 2-Chlorodeoxyadenosine); ibritumomab tiuxetan (Zevalin®); tositumomab (Bexxar®)) and pharmaceutically acceptable salts, solvates, clathrates, and prodrugs thereof.

Further, an antibody provided herein may be conjugated or recombinantly fused to a therapeutic moiety or drug moiety that modifies a given biological response. Therapeutic moieties or drug moieties are not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein,

peptide, or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, cholera toxin, or diphtheria toxin; a protein such as tumor necrosis factor, γ-interferon, α-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, *e.g.*, TNF-γ, TNF-γ, AIM I (see, International Publication No. WO 97/33899), AIM II (see, International Publication No. WO 97/34911), Fas Ligand (Takahashi *et al.*, 1994, J. Immunol., 6:1567-1574), and VEGF (see, International Publication No. WO 99/23105), an anti-angiogenic agent, *e.g.*, angiostatin, endostatin or a component of the coagulation pathway (*e.g.*, tissue factor); or, a biological response modifier such as, for example, a lymphokine (*e.g.*, interferon gamma, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-5 ("IL-5"), interleukin-6 ("IL-6"), interleukin-7 ("IL-7"), interleukin 9 ("IL-9"), interleukin-10 ("IL-10"), interleukin-12 ("IL-12"), interleukin-15 ("IL-15"), interleukin-23 ("IL-23"), granulocyte macrophage colony stimulating factor ("GM-CSF"), and granulocyte colony stimulating factor ("G-CSF")), or a growth factor (*e.g.*, growth hormone ("GH")), or a coagulation agent (*e.g.*, calcium, vitamin K, tissue factors, such as but not limited to, Hageman factor (factor XII), high-molecular-weight kininogen (HMWK), prekallikrein (PK), coagulation proteins-factors II (prothrombin), factor V, XIIa, VIII, XIIIa, XI, XIa, IX, IXa, X, phospholipid, and fibrin monomer).

Also provided herein are antibodies that are recombinantly fused or chemically conjugated (covalent or non-covalent conjugations) to a heterologous protein or polypeptide (or fragment thereof, for example, to a polypeptide of about 10, about 20, about 30, about 40, about 50, about 60, about 70, about 80, about 90 or about 100 amino acids) to generate fusion proteins, as well as uses thereof. In particular, provided herein are fusion proteins comprising an antigen-binding fragment of an antibody provided herein (*e.g.*, a Fab fragment, Fd fragment, Fv fragment, $F(ab)_2$ fragment, a VH domain, a VH CDR, a VL domain or a VL CDR) and a heterologous protein, polypeptide, or peptide. In one embodiment, the heterologous protein, polypeptide, or peptide that the antibody is fused to is useful for targeting the antibody to a particular cell type, such as a cell that expresses C10orf54 or an C10orf54 receptor. For example, an antibody that binds to a cell surface receptor expressed by a particular cell type (*e.g.*, an immune cell) may be fused or conjugated to a modified antibody provided herein.

A conjugated or fusion protein can comprise any antibody provided herein described herein and a heterologous polypeptide. In one embodiment, a conjugated or fusion protein provided herein comprises the VH or VL domain of any one of the murine monoclonal antibodies 175A, 76E1 or 141A, as depicted in Table 2, and a heterologous polypeptide. In another embodiment, a conjugated or fusion protein provided herein comprises a VH domain having the amino acid sequence of any one of the VH domains depicted in Tables 5-10, and/or a VL domain having the amino acid sequence of any one of the VL domains depicted Tables 5-10, and a heterologous polypeptide. In another embodiment, a conjugated or fusion protein provided herein comprises one or more VH CDRs having the amino acid sequence of any one of the VH CDRs depicted in Tables 5-10, and a heterologous polypeptide. In another embodiment, a conjugated or fusion protein comprises one or more VL CDRs having the amino acid sequence of any one of the VL CDRs depicted in Tables 5-10, and a heterologous polypeptide. In another embodiment, a conjugated or fusion protein provided herein comprises at least one VH domain and at least one VL domain depicted in Tables 5-10, and a heterologous polypeptide. In yet another embodiment, a conjugated or fusion protein provided herein comprises at least one VH CDR and at least one VL CDR depicted in Tables 5-10, and a heterologous polypeptide.

In addition, an antibody provided herein can be conjugated to therapeutic moieties such as a radioactive metal ion, such as alpha-emitters such as ^{213}Bi or macrocyclic chelators useful for conjugating radiometal ions, including but not limited to, ^{131}In, ^{131}LU, ^{131}Y, ^{131}Ho, ^{131}Sm, to polypeptides. In certain embodiments, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane-N,N',N",N"'-tetraacetic acid (DOTA) which can be attached to the antibody via a linker molecule. Such linker molecules are commonly known in the art and described in Denardo *et al.*, 1998, *Clin Cancer Res.* 4(10):2483-90; Peterson *et al.*, 1999, *Bioconjug. Chem.* 10(4):553-7; and Zimmerman *et al.*, 1999, *Nucl. Med. Biol.* 26(8):943-50, each incorporated by reference in their entireties.

Moreover, antibodies provided herein can be fused to marker sequences, such as a peptide to facilitate purification. In specific embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc.), among others, many of which are commercially available. As

described in Gentz *et al.*, 1989, Proc. Natl. Acad. Sci. USA 86:821-824, for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the hemagglutinin ("HA") tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson *et al.*, 1984, Cell 37:767), and the "FLAG" tag.

Methods for fusing or conjugating therapeutic moieties (including polypeptides) to antibodies are well known, see, *e.g.*, Arnon *et al.*, "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld *et al.* (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom *et al.*, "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson *et al.* (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies 84: Biological And Clinical Applications, Pinchera *et al.* (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin *et al.* (eds.), pp. 303-16 (Academic Press 1985), Thorpe *et al.*, 1982, Immunol. Rev. 62:119-58; U.S. Pat. Nos. 5,336,603, 5,622,929, 5,359,046, 5,349,053, 5,447,851, 5,723,125, 5,783,181, 5,908,626, 5,844,095, and 5,112,946; EP 307,434; EP 367,166; EP 394,827; PCT publications WO 91/06570, WO 96/04388, WO 96/22024, WO 97/34631, and WO 99/04813; Ashkenazi *et al.*, Proc. Natl. Acad. Sci. USA, 88: 10535-10539, 1991; Traunecker *et al.*, Nature, 331:84-86, 1988; Zheng *et al.*, J. Immunol., 154:5590-5600, 1995; Vil *et al.*, Proc. Natl. Acad. Sci. USA, 89:11337-11341, 1992, which are incorporated herein by reference in their entireties.

Fusion proteins may be generated, for example, through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to alter the activities of antibodies provided herein (*e.g.*, antibodies with higher affinities and lower dissociation rates). See, generally, U.S. Patent Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458; Patten *et al.*, 1997, Curr. Opinion Biotechnol. 8:724-33; Harayama, 1998, Trends Biotechnol. 16(2):76-82; Hansson *et al.*, 1999, J. Mol. Biol. 287:265-76; and Lorenzo and Blasco, 1998, Biotechniques 24(2):308- 313 (each of these patents and publications are hereby incorporated by reference in its

entirety). Antibodies, or the encoded antibodies, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. A polynucleotide encoding an antibody provided herein may be recombined with one or more components, motifs, sections, parts, domains, fragments, *etc.* of one or more heterologous molecules.

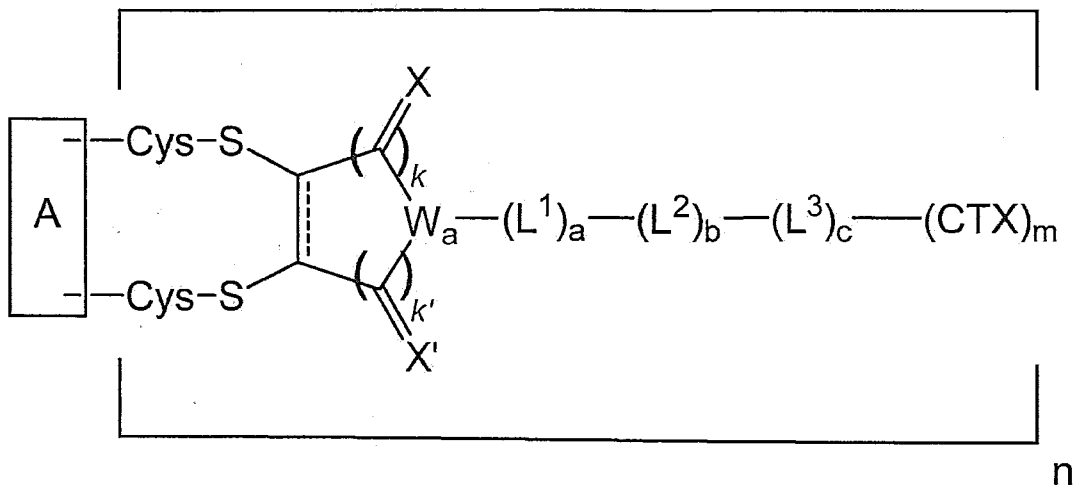
An antibody provided herein can also be conjugated to a second antibody to form an antibody heteroconjugate as described in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

The therapeutic moiety or drug conjugated or recombinantly fused to an antibody provided herein that binds to a C10orf54 antigen should be chosen to achieve the desired prophylactic or therapeutic effect(s). In certain embodiments, the antibody is a modified antibody. A clinician or other medical personnel should consider the following when deciding on which therapeutic moiety or drug to conjugate or recombinantly fuse to an antibody provided herein: the nature of the disease, the severity of the disease, and the condition of the subject.

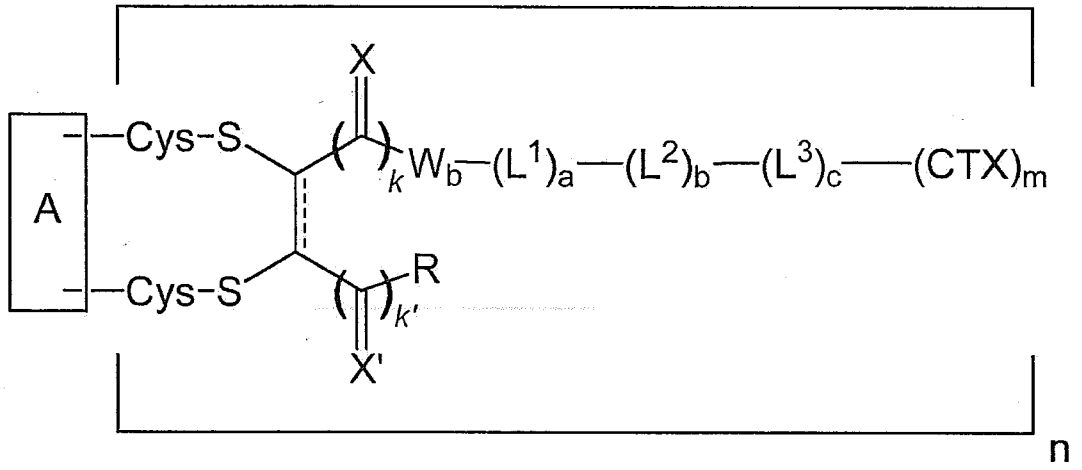
Antibodies provided herein may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

ANTIBODY-DRUG CONJUGATE (ADC)

In some embodiments, provided herein are antibody-drug conjugates, including an antibody-drug conjugate of the following formulas (Ia) and (Ib):



(Ia),



(Ib);

or a pharmaceutically acceptable salt thereof;

wherein:

A is an antibody or antibody fragment;

the two depicted cysteine residues are from an opened cysteine-cysteine disulfide bond in A;

each X and X' is independently O, S, NH, or NR^1 wherein R^1 is C_{1-6} alkyl;

W_a is =N-, =CH-, $=CHCH_2$-, $=C(R^2)$-, or $=CHCH(R^2)$-; W_b -NH-, $-N(R^1)$-, $-CH_2$-, $-CH_2$-NH-, $-CH_2-N(R^1)$-, $-CH_2CH_2$-, $-CH(R^2)$-, or $-CH_2CH(R^2)$-; wherein R^1 and R^2 are independently C_{1-6} alkyl;

CTX is a cytotoxin;

R is any chemical group; or R is absent;

each L^1, L^2 and L^3 is independently a linker selected from the group consisting of -O-, -C(O)-, -S-, -S(O)-, $-S(O)_2$-, -NH-, $-NCH_3$-, $-(CH_2)_q$-, $-NH(CH_2)_2NH$-,

-OC(O)-, -CO_2-, -$NHCH_2CH_2C(O)$-, -$C(O)NHCH_2CH_2NH$-, -$NHCH_2C(O)$-, -NHC(O)-, -C(O)NH-, -$NCH_3C(O)$-, -$C(O)NCH_3$-, -$(CH_2CH_2O)_p$, -$(CH_2CH_2O)_pCH_2CH_2$-, -CH_2CH_2-$(CH_2CH_2O)_p$-, -$OCH(CH_2O$-$)_2$, -$(AA)_r$-, cyclopentanyl, cyclohexanyl, unsubstituted phenylenyl, and phenylenyl substituted by 1 or 2 substituents selected from the group consisting of halo, CF_3-, CF_3O-, CH_3O-, -C(O)OH, -$C(O)OC_{1-3}$ alkyl, -$C(O)CH_3$, -CN, -NH-, -NH_2, -O-, -OH, -$NHCH_3$, -$N(CH_3)_2$, and C_{1-3} alkyl;

a, b and c are each independently an integer of 0, 1, 2 or 3, provided that at least one of a, b or c is 1;

each *k* and *k'* is independently an integer of 0 or 1;

each p is independently an integer of 1 to 14;

each q is independently an integer from 1 to 12;

each AA is independently an amino acid;

each r is 1 to 12;

m is an integer of 1 to 4;

n is an integer of 1 to 4; and

the ------ bond represents a single or a double bond.

In certain embodiments of the antibody-drug conjugate of formula (Ib), R is selected from the group consisting of W, $(L^1)_a$, $(L^2)_b$, $(L^3)_c$, Z, W-$(L^1)_a$-$(L^2)_b$-$(L^3)_c$, $(L^1)_a$-$(L^2)_b$-$(L^3)_c$-Z, and W-$(L^1)_a$-$(L^2)_b$-$(L^3)_c$-Z, as defined herein. In certain embodiments, R is selected from the group consisting of W, $(L^1)_a$, $(L^2)_b$, $(L^3)_c$, and W-$(L^1)_a$-$(L^2)_b$-$(L^3)_c$. In certain embodiments, R is selected from the group consisting of Z, $(L^1)_a$-$(L^2)_b$-$(L^3)_c$-Z, and W-$(L^1)_a$-$(L^2)_b$-$(L^3)_c$-Z.

In certain embodiments of the antibody-drug conjugate of formula (Ib), R is a detectable probe. In certain embodiments, R is a fluorophore, chromophore, radiolabel, enzyme, ligand, antibody or antibody fragment. In certain embodiments, R is a ligand (*e.g.*, a ligand specific for a receptor on a tumor cell, such as a prostate specific membrane antigen, or a virally infected cell, such as an HIV infected cell).

In certain embodiments of the antibody-drug conjugate of formula (Ib), R is bonded to the rest of the linker molecule via an amide, an N-(C_{1-6} alkyl)amide, a carbamate, an N-(C_{1-6} alkyl)carbamate, an amine, an N-(C_{1-6} alkyl)amine, an ether, a thioether, an urea, an N-(C_{1-6} alkyl)urea, or an N,N-di(C_{1-6} alkyl)urea bond.

In certain embodiments of the antibody-drug conjugate of formula (Ia) or (Ib), each L^1, L^2 and L^3 is independently selected from the group consisting of -NHC(O)-, -C(O)NH-, $-(CH_2CH_2O)_p$, $-(CH_2CH_2O)_pCH_2CH_2$-, $-CH_2CH_2-(CH_2CH_2O)_p$-, $-OCH(CH_2O-)_2$, $-(AA)_r$-, unsubstituted phenylenyl, and phenylenyl substituted by 1 or 2 substituents selected from the group consisting of halo, CF_3-, CF_3O-, CH_3O-, -C(O)OH, $-C(O)OC_{1-3}$ alkyl, $-C(O)CH_3$, -CN, -NH-, $-NH_2$, -O-, -OH, $-NHCH_3$, $-N(CH_3)_2$, and C_{1-3} alkyl; where a, b and c are each independently 0 or 1; and each p and r is independently 1, 2 or 3. In certain embodiments, one or more of the L^1, L^2 and L^3 is $-(AA)_r$-, wherein $-(AA)_r$- is ValCit (*e.g.*, the first amino acid is Valine, the second amino acid is Citrulline, and r is 1). In certain embodiments, one or more of the L^1, L^2 and L^3 is $-(AA)_r$-, wherein $-(AA)_r$- is ValAla (*e.g.*, the first amino acid is Valine, the second amino acid is Alanine, and r is 1). In certain embodiments, one or more of the L^1, L^2 and L^3 is phenylenyl substituted by -C(O)OH and $-NH_2$. In certain embodiments, one or more of the L^1, L^2 and L^3 is phenylenyl substituted by -C(O)O- and -NH-. In certain embodiments, one or more of the L^1, L^2 and L^3 is phenylenyl substituted by -OC(O)- and -NH-. In certain embodiments, one or more of the L^1, L^2 and L^3 is phenylenyl substituted by -O- and -NH-. In certain embodiments, one or more of the L^1, L^2 and L^3 is para aminobenzyl (PAB), which is optionally substituted with -C(O)O-, -OC(O)- or -O-. In certain embodiments, L^1 is $-(CH_2)_q$-, L^2 is absent, L^3 is absent, and the CTX is bonded to $(L^1)_a-(L^2)_b-(L^3)_c$ via an amide bond. In certain embodiments, L^1 is $-(CH_2)_q$-, L^2 is $-(OCH_2CH_2)_p$-, L^3 is absent, and the CTX is bonded to $(L^1)_a-(L^2)_b-(L^3)_c$ via an amide bond. In certain embodiments, L^1 is $-(CH_2CH_2O)_p$-, L^2 is $-(CH_2)_q$-, L^3 is absent, and the CTX is bonded to $(L^1)_a-(L^2)_b-(L^3)_c$ via an amide bond. In certain embodiments, each L^1 is independently selected from the group consisting of $-(CH_2CH_2O)_pCH_2CH_2$- and $-CH_2CH_2-(CH_2CH_2O)_p$-, L^2 is absent, L^3 is absent, and the CTX is bonded to $(L^1)_a-(L^2)_b-(L^3)_c$ via an amide bond. In certain embodiments, each L^1 is independently selected from the group consisting of $-(CH_2)_q$-, $-(CH_2CH_2O)_p$, $-(CH_2CH_2O)_pCH_2CH_2$-, $-CH_2CH_2-(CH_2CH_2O)_p$-, and -C(O)-, L^2 is Val-Cit, L^3 is PAB, and the CTX is bonded to $(L^1)_a-(L^2)_b-(L^3)_c$ via an amide bond. In certain embodiments, each L^1 is independently selected from the group consisting of $-(CH_2)_q$-, $-(CH_2CH_2O)_p$, $-(CH_2CH_2O)_pCH_2CH_2$-, $-CH_2CH_2-(CH_2CH_2O)_p$-, and -C(O)-, L^2 is Val-Cit, L^3 is PAB, and the CTX is bonded to $(L^1)_a-(L^2)_b-(L^3)_c$ via an amide bond. In certain embodiments, each L^1 is independently selected from the group consisting of $-(CH_2)_q$-

, $-(CH_2CH_2O)_p$, $-(CH_2CH_2O)_pCH_2CH_2-$, $-CH_2CH_2-(CH_2CH_2O)_p-$, and -C(O)-, L^2 is Val-Ala, L^3 is PAB, and the CTX is bonded to $(L^1)_a-(L^2)_b-(L^3)_c$ via an amide bond.

In certain embodiments of the antibody-drug conjugate of formula (Ia) or (Ib), CTX is selected from a from the group consisting of a tubulin stabilizer, a tubulin destabilizer, a DNA alkylator, a DNA minor groove binder, a DNA intercalator, a topoisomerase I inhibitor, a topoisomerase II inhibitor, a gyrase inhibitor, a protein synthesis inhibitor, a proteosome inhibitor, and an anti-metabolite.

In certain embodiments of the antibody-drug conjugate of formula (Ia) or (Ib), the CTX is a chemotherapeutic agent. Those of ordinary skill in the art will be aware of appropriate chemotherapeutic agents as disclosed, for example, in Chu, E., DeVite, V. T., 2012, Physicians' Cancer Chemotherapy Drug Manual 2012 (Jones & Bartlett Learning Oncology), and similar documents.

In certain embodiments, the CTX may be any FDA-approved chemotherapeutic agent. In certain embodiments, the CTX may be any FDA-approved chemotherapeutic agent available for cancer treatment.

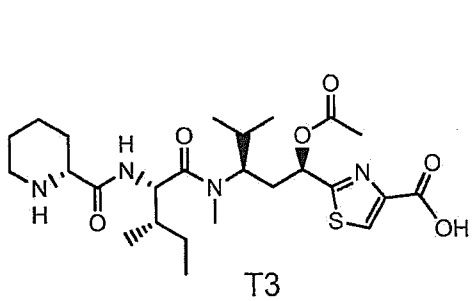
In certain embodiments, the CTX is selected from the group consisting of an alkylating agents, an anthracyclines, a cytoskeletal disruptors (taxanes), an epothilones, an histone deacetylase Inhibitor (HDAC), an inhibitor of Topoisomerase I, an Inhibitor of Topoisomerase II, a kinase inhibitor, a monoclonal antibodies, a nucleotide analog, a peptide antibiotic, a platinum-based agent, a retinoids, a Vinca alkaloid or a derivative thereof, and radioisotope.

In certain embodiments, the CTX is selected from the group consising of Actinomycin, all-trans retinoic acid, Azacitidine, Azathioprine, Bleomycin, Bortezomib, Carboplatin, Capecitabine, Cisplatin, Chlorambucil, Cyclophosphamide, Cytarabine, Daunorubicin, Docetaxel, Doxifluridine, Doxorubicin, Epirubicin, Epothilone, Etoposide, Fluorouracil, Gemcitabine, Hydroxyurea, Idarubicin, Imatinib, Irinotecan, Mechlorethamine, Mercaptopurine, Methotrexate, Mitoxantrone, Oxaliplatin, Paclitaxel, Pemetrexed, Teniposide, Tioguanine, Topotecan, Valrubicin, Vinblastine, Vincristine, Vindesine, and Vinorelbine.

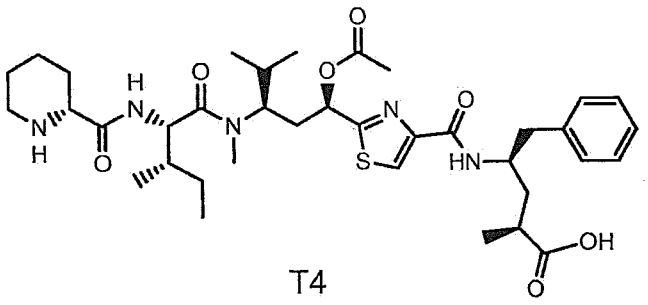
In certain embodiments, the CTX is selected from the group consisting of a tubulin stabilizer, a tubulin destabilizer, a DNA alkylator, a DNA minor groove binder, a DNA intercalator, a topoisomerase I inhibitor, a topoisomerase II inhibitor, a gyrase inhibitor, a protein synthesis inhibitor, a proteosome inhibitor, and an anti-metabolite.

In certain embodiments, the CTX is selected from the group consisting of Actinomycin D, Amonafide, an auristatin, benzophenone, benzothiazole, a calicheamicin, Camptothecin, CC-1065 (NSC 298223), Cemadotin, Colchicine, Combretastatin A4, Dolastatin, Doxorubicin, Elinafide, Emtansine (DM1), Etoposide, KF-12347 (Leinamycin), a maytansinoid, Methotrexate, Mitoxantrone, Nocodazole, Proteosome Inhibitor 1 (PSI 1), Roridin A, T-2 Toxin (trichothecene analog), Taxol, a tubulysin, Velcade®, and Vincristine. In certain embodiments, the CTX is an auristatin, a calicheamicin, a maytansinoid, or a tubulysin.

In certain embodiments, the CTX is monomethylauristatin E (MMAE), monomethylauristatin F (MMAF), a pyrrolobenzodiazepine (PDB), calicheamicin γ, mertansine, or tubulysin T2. In certain embodiments, the CTX is MMAE or MMAF. In certain embodiments, the CTX is a PDB. In certain embodiments, the CTX is tubulysin T2. In certain embodiments, the CTX is tubulysin T3, or tubulysin T4, the structures for which are provided below:



T3



T4

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PHARMACEUTICAL COMPOSITIONS

Therapeutic formulations containing one or more of the antibodies provided herein can be prepared for storage by mixing the antibody having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers,

excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (*e.g.,* Zn-protein complexes); and/or non-ionic surfactants such as TWEEN™, PLURONICS™ or polyethylene glycol (PEG).

The antibodies provided herein can also, for example, be formulated in liposomes. Liposomes containing the molecule of interest are prepared by methods known in the art, such as described in Epstein *et al.* (1985) *Proc. Natl. Acad. Sci. USA* 82:3688; Hwang *et al.* (1980) *Proc. Natl. Acad. Sci. USA* 77:4030; and U.S. Patent Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent No. 5,013,556.

Particularly useful immunoliposomes can be generated by the reverse phase evaporation method with a lipid composition containing phosphatidylcholine, cholesterol and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of an antibody provided herein can be conjugated to the liposomes as described in Martin *et al.* (1982) *J. Biol. Chem.* 257:286-288 via a disulfide interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome; See Gabizon *et al.*, (1989) *J. National Cancer Inst.* 81(19):1484.

Formulations, such as those described herein, can also contain more than one active compound as necessary for the particular indication being treated. In certain

embodiments, formulations comprise an antibody provided herein and one or more active compounds with complementary activities that do not adversely affect each other. Such molecules are suitably present in combination in amounts that are effective for the purpose intended. For example, an antibody provided herein can be combined with one or more other therapeutic agents. Such combined therapy can be administered to the patient serially or simultaneously or in sequence.

An antibody provided herein can also be entrapped in microcapsule prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsule and poly-(methylmethacylate) microcapsule, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA.

The formulations to be used for *in vivo* administration can be sterile. This is readily accomplished by filtration through, *e.g.,* sterile filtration membranes.

Sustained-release preparations can also be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the polypeptide, which matrices are in the form of shaped articles, *e.g.,* films, or microcapsule. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Patent No. 3,773,919), copolymers of L-glutamic acid and ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT™ (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S--S bond formation

through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

In some embodiments, the pharmaceutical compositions provided herein contain therapeutically effective amounts of one or more of the antibodies provided herein, and optionally one or more additional prophylactic of therapeutic agents, in a pharmaceutically acceptable carrier. Such pharmaceutical compositions are useful in the prevention, treatment, or alleviation of one or more symptom of a C10orf54-mediated disease.

Pharmaceutical carriers suitable for administration of the compounds provided herein include any such carriers known to those skilled in the art to be suitable for the particular mode of administration.

In addition, the antibodies provided herein may be formulated as the sole pharmaceutically active ingredient in the composition or may be combined with other active ingredients (such as one or more other prophylactic or therapeutic agents).

The compositions can contain one or more antibodies provided herein. In one embodiment, the antibodies are formulated into suitable pharmaceutical preparations, such as solutions, suspensions, tablets, dispersible tablets, pills, capsules, powders, sustained release formulations or elixirs, for oral administration or in sterile solutions or suspensions for parenteral administration, as well as transdermal patch preparation and dry powder inhalers. In one embodiment, the antibodies described above are formulated into pharmaceutical compositions using techniques and procedures well known in the art (see, *e.g.*, Ansel (1985) Introduction to Pharmaceutical Dosage Forms, 4th Ed., p. 126).

In certain embodiments of the compositions, effective concentrations of one or more antibodies or derivatives thereof is (are) mixed with a suitable pharmaceutical carrier. In specific embodiments, concentrations of the compounds in the compositions are effective for delivery of an amount, upon administration, that treats, prevents, or ameliorates a C10orf54-mediated disease or symptom thereof.

In one embodiment, the compositions are formulated for single dosage administration. To formulate a composition, the weight fraction of compound is dissolved, suspended, dispersed or otherwise mixed in a selected carrier at an effective concentration such that the treated condition is relieved, prevented, or one or more symptoms are ameliorated.

In some embodiments, the antibody provided herein is included in the pharmaceutically acceptable carrier in an effective amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the patient treated. The therapeutically effective concentration can be determined empirically by testing the compounds in *in vitro* and *in vivo* systems using routine methods and then extrapolated therefrom for dosages for humans.

The concentration of antibody in the pharmaceutical composition will depend on, *e.g.*, the physicochemical characteristics of the antibody, the dosage schedule, and amount administered as well as other factors known to those of skill in the art.

In one embodiment, a therapeutically effective dosage produces a serum concentration of antibody of from about 0.1 ng/ml to about 50-100 µg/ml. The pharmaceutical compositions, in another embodiment, provide a dosage of from about 0.001 mg to about 2000 mg of antibody per kilogram of body weight per day. Pharmaceutical dosage unit forms can be prepared to provide from about 0.01 mg, 0.1 mg or 1 mg to about 500 mg, 1000 mg or 2000 mg, and in one embodiment from about 10 mg to about 500 mg of the antibody and/or a combination of other optional essential ingredients per dosage unit form.

The antibody can be administered at once, or may be divided into a number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment is a function of the disease being treated and can be determined empirically using known testing protocols or by extrapolation from *in vivo* or *in vitro* test data. It is to be noted that concentrations and dosage values can also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens can be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that

the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

Upon mixing or addition of the antibody, the resulting mixture can be a solution, suspension, emulsion or the like. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. The effective concentration is sufficient for ameliorating the symptoms of the disease, disorder or condition treated and may be empirically determined.

In some embodiments, the pharmaceutical compositions are provided for administration to humans and animals in unit dosage forms, such as tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil-water emulsions containing suitable quantities of the compounds or pharmaceutically acceptable derivatives thereof. The antibody is, in one embodiment, formulated and administered in unit-dosage forms or multiple-dosage forms. "Unit-dose" forms as used herein refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art. Each unit-dose contains a predetermined quantity of the antibody sufficient to produce the desired therapeutic effect, in association with the required pharmaceutical carrier, vehicle or diluent. Examples of unit-dose forms include ampoules and syringes and individually packaged tablets or capsules. Unit-dose forms can be administered in fractions or multiples thereof. A "multiple-dose" form is a plurality of identical unit-dosage forms packaged in a single container to be administered in segregated unit-dose form. Examples of multiple-dose forms include vials, bottles of tablets or capsules or bottles of pints or gallons. Hence, multiple dose form is a multiple of unit-doses which are not segregated in packaging.

In specific embodiments, one or more anti-C10orf54 antibodies provided herein are in a liquid pharmaceutical formulation. Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, or otherwise mixing an active compound as defined above and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, glycols, ethanol, and the like, to thereby form a solution or suspension. If desired, the pharmaceutical composition to be administered can also contain minor amounts of

nontoxic auxiliary substances such as wetting agents, emulsifying agents, solubilizing agents, pH buffering agents and the like, for example, acetate, sodium citrate, cyclodextrine derivatives, sorbitan monolaurate, triethanolamine sodium acetate, triethanolamine oleate, and other such agents.

Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA.

Dosage forms or compositions containing antibody in the range of 0.005% to 100% with the balance made up from non-toxic carrier can be prepared. Methods for preparation of these compositions are known to those skilled in the art.

Oral pharmaceutical dosage forms are either solid, gel or liquid. The solid dosage forms include tablets, capsules, granules, and bulk powders. Types of oral tablets include compressed, chewable lozenges and tablets which may be enteric-coated, sugar-coated or film-coated. Capsules can be hard or soft gelatin capsules, while granules and powders can be provided in non-effervescent or effervescent form with the combination of other ingredients known to those skilled in the art.

In certain embodiments, the formulations are solid dosage forms. In certain embodiments, the formulations are capsules or tablets. The tablets, pills, capsules, troches and the like can contain one or more of the following ingredients, or compounds of a similar nature: a binder; a lubricant; a diluent; a glidant; a disintegrating agent; a coloring agent; a sweetening agent; a flavoring agent; a wetting agent; an emetic coating; and a film coating. Examples of binders include microcrystalline cellulose, gum tragacanth, glucose solution, acacia mucilage, gelatin solution, molasses, polvinylpyrrolidine, povidone, crospovidones, sucrose and starch paste. Lubricants include talc, starch, magnesium or calcium stearate, lycopodium and stearic acid. Diluents include, for example, lactose, sucrose, starch, kaolin, salt, mannitol and dicalcium phosphate. Glidants include, but are not limited to, colloidal silicon dioxide. Disintegrating agents include crosscarmellose sodium, sodium starch glycolate, alginic acid, corn starch, potato starch, bentonite, methylcellulose, agar and carboxymethylcellulose. Coloring agents include, for example, any of the approved certified water soluble FD and C dyes, mixtures thereof; and water insoluble FD and

C dyes suspended on alumina hydrate. Sweetening agents include sucrose, lactose, mannitol and artificial sweetening agents such as saccharin, and any number of spray dried flavors. Flavoring agents include natural flavors extracted from plants such as fruits and synthetic blends of compounds which produce a pleasant sensation, such as, but not limited to peppermint and methyl salicylate. Wetting agents include propylene glycol monostearate, sorbitan monooleate, diethylene glycol monolaurate and polyoxyethylene laural ether. Emetic-coatings include fatty acids, fats, waxes, shellac, ammoniated shellac and cellulose acetate phthalates. Film coatings include hydroxyethylcellulose, sodium carboxymethylcellulose, polyethylene glycol 4000 and cellulose acetate phthalate.

The antibodies provided herein can be provided in a composition that protects it from the acidic environment of the stomach. For example, the composition can be formulated in an enteric coating that maintains its integrity in the stomach and releases the active compound in the intestine. The composition can also be formulated in combination with an antacid or other such ingredient.

When the dosage unit form is a capsule, it can contain, in addition to material of the above type, a liquid carrier such as a fatty oil. In addition, dosage unit forms can contain various other materials which modify the physical form of the dosage unit, for example, coatings of sugar and other enteric agents. The compounds can also be administered as a component of an elixir, suspension, syrup, wafer, sprinkle, chewing gum or the like. A syrup may contain, in addition to the active compounds, sucrose as a sweetening agent and certain preservatives, dyes and colorings and flavors.

The antibody can also be mixed with other active materials which do not impair the desired action, or with materials that supplement the desired action, such as antacids, H2 blockers, and diuretics. The active ingredient is an antibody or pharmaceutically acceptable derivative thereof as described herein. Higher concentrations, up to about 98% by weight of the active ingredient may be included.

In all embodiments, tablets and capsules formulations can be coated as known by those of skill in the art in order to modify or sustain dissolution of the active ingredient. Thus, for example, they may be coated with a conventional enterically digestible coating, such as phenylsalicylate, waxes and cellulose acetate phthalate.

In specific embodiments, the formulations are liquid dosage forms. Liquid oral dosage forms include aqueous solutions, emulsions, suspensions, solutions and/or suspensions reconstituted from non-effervescent granules and effervescent preparations reconstituted from effervescent granules. Aqueous solutions include, for example, elixirs and syrups. Emulsions are either oil-in-water or water-in-oil.

Elixirs are clear, sweetened, hydroalcoholic preparations. Pharmaceutically acceptable carriers used in elixirs include solvents. Syrups are concentrated aqueous solutions of a sugar, for example, sucrose, and may contain a preservative. An emulsion is a two-phase system in which one liquid is dispersed in the form of small globules throughout another liquid. Pharmaceutically acceptable carriers used in emulsions are non-aqueous liquids, emulsifying agents and preservatives. Suspensions use pharmaceutically acceptable suspending agents and preservatives. Pharmaceutically acceptable substances used in non-effervescent granules, to be reconstituted into a liquid oral dosage form, include diluents, sweeteners and wetting agents. Pharmaceutically acceptable substances used in effervescent granules, to be reconstituted into a liquid oral dosage form, include organic acids and a source of carbon dioxide. Coloring and flavoring agents are used in all of the above dosage forms.

Solvents include glycerin, sorbitol, ethyl alcohol and syrup. Examples of preservatives include glycerin, methyl and propylparaben, benzoic acid, sodium benzoate and alcohol. Examples of non-aqueous liquids utilized in emulsions include mineral oil and cottonseed oil. Examples of emulsifying agents include gelatin, acacia, tragacanth, bentonite, and surfactants such as polyoxyethylene sorbitan monooleate. Suspending agents include sodium carboxymethylcellulose, pectin, tragacanth, Veegum and acacia. Sweetening agents include sucrose, syrups, glycerin and artificial sweetening agents such as saccharin. Wetting agents include propylene glycol monostearate, sorbitan monooleate, diethylene glycol monolaurate and polyoxyethylene lauryl ether. Organic acids include citric and tartaric acid. Sources of carbon dioxide include sodium bicarbonate and sodium carbonate. Coloring agents include any of the approved certified water soluble FD and C dyes, and mixtures thereof. Flavoring agents include natural flavors extracted from plants such fruits, and synthetic blends of compounds which produce a pleasant taste sensation.

For a solid dosage form, the solution or suspension, in for example propylene carbonate, vegetable oils or triglycerides, is, in one embodiment, encapsulated in a gelatin capsule. Such solutions, and the preparation and encapsulation thereof, are disclosed in U.S. Patent Nos. 4,328,245; 4,409,239; and 4,410,545. For a liquid dosage form, the solution, *e.g.*, for example, in a polyethylene glycol, can be diluted with a sufficient quantity of a pharmaceutically acceptable liquid carrier, *e.g.*, water, to be easily measured for administration.

Alternatively, liquid or semi-solid oral formulations can be prepared by dissolving or dispersing the active compound or salt in vegetable oils, glycols, triglycerides, propylene glycol esters (*e.g.*, propylene carbonate) and other such carriers, and encapsulating these solutions or suspensions in hard or soft gelatin capsule shells. Other useful formulations include those set forth in U.S. Patent Nos. RE28,819 and 4,358,603. Briefly, such formulations include, but are not limited to, those containing a compound provided herein, a dialkylated mono- or poly-alkylene glycol, including, but not limited to, 1,2-dimethoxymethane, diglyme, triglyme, tetraglyme, polyethylene glycol-350-dimethyl ether, polyethylene glycol-550-dimethyl ether, polyethylene glycol-750-dimethyl ether wherein 350, 550 and 750 refer to the approximate average molecular weight of the polyethylene glycol, and one or more antioxidants, such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), propyl gallate, vitamin E, hydroquinone, hydroxycoumarins, ethanolamine, lecithin, cephalin, ascorbic acid, malic acid, sorbitol, phosphoric acid, thiodipropionic acid and its esters, and dithiocarbamates.

Other formulations include, but are not limited to, aqueous alcoholic solutions including a pharmaceutically acceptable acetal. Alcohols used in these formulations are any pharmaceutically acceptable water-miscible solvents having one or more hydroxyl groups, including, but not limited to, propylene glycol and ethanol. Acetals include, but are not limited to, di(lower alkyl) acetals of lower alkyl aldehydes such as acetaldehyde diethyl acetal.

Parenteral administration, in one embodiment, is characterized by injection, either subcutaneously, intramuscularly or intravenously is also contemplated herein. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to injection,

or as emulsions. The injectables, solutions and emulsions also contain one or more excipients. Suitable excipients are, for example, water, saline, dextrose, glycerol or ethanol. In addition, if desired, the pharmaceutical compositions to be administered can also contain minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents, stabilizers, solubility enhancers, and other such agents, such as for example, sodium acetate, sorbitan monolaurate, triethanolamine oleate and cyclodextrins.

Implantation of a slow-release or sustained-release system, such that a constant level of dosage is maintained (see, *e.g.,* U.S. Patent No. 3,710,795) is also contemplated herein. Briefly, a compound provided herein is dispersed in a solid inner matrix, *e.g.,* polymethylmethacrylate, polybutylmethacrylate, plasticized or unplasticized polyvinylchloride, plasticized nylon, plasticized polyethyleneterephthalate, natural rubber, polyisoprene, polyisobutylene, polybutadiene, polyethylene, ethylene-vinylacetate copolymers, silicone rubbers, polydimethylsiloxanes, silicone carbonate copolymers, hydrophilic polymers such as hydrogels of esters of acrylic and methacrylic acid, collagen, cross-linked polyvinylalcohol and cross-linked partially hydrolyzed polyvinyl acetate, that is surrounded by an outer polymeric membrane, *e.g.,* polyethylene, polypropylene, ethylene/propylene copolymers, ethylene/ethyl acrylate copolymers, ethylene/vinylacetate copolymers, silicone rubbers, polydimethyl siloxanes, neoprene rubber, chlorinated polyethylene, polyvinylchloride, vinylchloride copolymers with vinyl acetate, vinylidene chloride, ethylene and propylene, ionomer polyethylene terephthalate, butyl rubber epichlorohydrin rubbers, ethylene/vinyl alcohol copolymer, ethylene/vinyl acetate/vinyl alcohol terpolymer, and ethylene/vinyloxyethanol copolymer, that is insoluble in body fluids. The antibody diffuses through the outer polymeric membrane in a release rate controlling step. The amount of antibody contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the compound and the needs of the subject.

Preparations for parenteral administration include sterile solutions ready for injection, sterile dry soluble products, such as lyophilized powders, ready to be combined with a solvent just prior to use, including hypodermic tablets, sterile suspensions ready for injection, sterile dry insoluble products ready to be combined with a vehicle just prior to use and sterile emulsions. The solutions may be either aqueous or nonaqueous.

If administered intravenously, suitable carriers include physiological saline or phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents, such as glucose, polyethylene glycol, and polypropylene glycol and mixtures thereof.

Pharmaceutically acceptable carriers used in parenteral preparations include aqueous vehicles, nonaqueous vehicles, antimicrobial agents, isotonic agents, buffers, antioxidants, local anesthetics, suspending and dispersing agents, emulsifying agents, sequestering or chelating agents and other pharmaceutically acceptable substances.

Examples of aqueous vehicles include Sodium Chloride Injection, Ringers Injection, Isotonic Dextrose Injection, Sterile Water Injection, Dextrose and Lactated Ringers Injection. Nonaqueous parenteral vehicles include fixed oils of vegetable origin, cottonseed oil, corn oil, sesame oil and peanut oil. Antimicrobial agents in bacteriostatic or fungistatic concentrations can be added to parenteral preparations packaged in multiple-dose containers which include phenols or cresols, mercurials, benzyl alcohol, chlorobutanol, methyl and propyl p-hydroxybenzoic acid esters, thimerosal, benzalkonium chloride and benzethonium chloride. Isotonic agents include sodium chloride and dextrose. Buffers include phosphate and citrate. Antioxidants include sodium bisulfate. Local anesthetics include procaine hydrochloride. Suspending and dispersing agents include sodium carboxymethylcelluose, hydroxypropyl methylcellulose and polyvinylpyrrolidone. Emulsifying agents include Polysorbate 80 (TWEEN® 80). A sequestering or chelating agent of metal ions includes EDTA. Pharmaceutical carriers also include ethyl alcohol, polyethylene glycol and propylene glycol for water miscible vehicles; and sodium hydroxide, hydrochloric acid, citric acid or lactic acid for pH adjustment.

The concentration of the pharmaceutically active compound is adjusted so that an injection provides an effective amount to produce the desired pharmacological effect. The exact dose depends on the age, weight and condition of the patient or animal as is known in the art.

The unit-dose parenteral preparations can be packaged in an ampoule, a vial or a syringe with a needle. All preparations for parenteral administration can be sterile, as is known and practiced in the art.

Illustratively, intravenous or intraarterial infusion of a sterile aqueous solution containing an active compound is an effective mode of administration. Another embodiment is a sterile aqueous or oily solution or suspension containing an active material injected as necessary to produce the desired pharmacological effect.

Injectables are designed for local and systemic administration. In one embodiment, a therapeutically effective dosage is formulated to contain a concentration of at least about 0.1% w/w up to about 90% w/w or more, in certain embodiments more than 1% w/w of the active compound to the treated tissue(s).

The antibody can be suspended in micronized or other suitable form. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. The effective concentration is sufficient for ameliorating the symptoms of the condition and may be empirically determined.

In other embodiments, the pharmaceutical formulations are lyophilized powders, which can be reconstituted for administration as solutions, emulsions and other mixtures. They may also be reconstituted and formulated as solids or gels.

The lyophilized powder is prepared by dissolving an antibody provided herein, or a pharmaceutically acceptable derivative thereof, in a suitable solvent. In some embodiments, the lyophilized powder is sterile. The solvent may contain an excipient which improves the stability or other pharmacological component of the powder or reconstituted solution, prepared from the powder. Excipients that may be used include, but are not limited to, dextrose, sorbital, fructose, corn syrup, xylitol, glycerin, glucose, sucrose or other suitable agent. The solvent may also contain a buffer, such as citrate, sodium or potassium phosphate or other such buffer known to those of skill in the art at, in one embodiment, about neutral pH. Subsequent sterile filtration of the solution followed by lyophilization under standard conditions known to those of skill in the art provides the desired formulation. In one embodiment, the resulting solution will be apportioned into vials for lyophilization. Each vial will contain a single dosage

or multiple dosages of the compound. The lyophilized powder can be stored under appropriate conditions, such as at about 4 °C to room temperature.

Reconstitution of this lyophilized powder with water for injection provides a formulation for use in parenteral administration. For reconstitution, the lyophilized powder is added to sterile water or other suitable carrier. The precise amount depends upon the selected compound. Such amount can be empirically determined.

Topical mixtures are prepared as described for the local and systemic administration. The resulting mixture can be a solution, suspension, emulsions or the like and can be formulated as creams, gels, ointments, emulsions, solutions, elixirs, lotions, suspensions, tinctures, pastes, foams, aerosols, irrigations, sprays, suppositories, bandages, dermal patches or any other formulations suitable for topical administration.

The antibodies provided herein can be formulated as aerosols for topical application, such as by inhalation (see, *e.g.,* U.S. Patent Nos. 4,044,126, 4,414,209, and 4,364,923, which describe aerosols for delivery of a steroid useful for treatment of inflammatory diseases, particularly asthma). These formulations for administration to the respiratory tract can be in the form of an aerosol or solution for a nebulizer, or as a microfine powder for insufflations, alone or in combination with an inert carrier such as lactose. In such a case, the particles of the formulation will, in one embodiment, have diameters of less than 50 microns, in one embodiment less than 10 microns.

The compounds can be formulated for local or topical application, such as for topical application to the skin and mucous membranes, such as in the eye, in the form of gels, creams, and lotions and for application to the eye or for intracisternal or intraspinal application. Topical administration is contemplated for transdermal delivery and also for administration to the eyes or mucosa, or for inhalation therapies. Nasal solutions of the active compound alone or in combination with other pharmaceutically acceptable excipients can also be administered.

These solutions, particularly those intended for ophthalmic use, may be formulated as 0.01% - 10% isotonic solutions, pH about 5-7, with appropriate salts.

Other routes of administration, such as transdermal patches, including iontophoretic and electrophoretic devices, and rectal administration, are also contemplated herein.

Transdermal patches, including iotophoretic and electrophoretic devices, are well known to those of skill in the art. For example, such patches are disclosed in U.S. Patent Nos. 6,267,983, 6,261,595, 6,256,533, 6,167,301, 6,024,975, 6,010715, 5,985,317, 5,983,134, 5,948,433, and 5,860,957.

For example, pharmaceutical dosage forms for rectal administration are rectal suppositories, capsules and tablets for systemic effect. Rectal suppositories are used herein mean solid bodies for insertion into the rectum which melt or soften at body temperature releasing one or more pharmacologically or therapeutically active ingredients. Pharmaceutically acceptable substances utilized in rectal suppositories are bases or vehicles and agents to raise the melting point. Examples of bases include cocoa butter (theobroma oil), glycerin-gelatin, carbowax (polyoxyethylene glycol) and appropriate mixtures of mono-, di- and triglycerides of fatty acids. Combinations of the various bases may be used. Agents to raise the melting point of suppositories include spermaceti and wax. Rectal suppositories may be prepared either by the compressed method or by molding. The weight of a rectal suppository, in one embodiment, is about 2 to 3 gm.

Tablets and capsules for rectal administration can be manufactured using the same pharmaceutically acceptable substance and by the same methods as for formulations for oral administration.

The antibodies and other compositions provided herein may also be formulated to be targeted to a particular tissue, receptor, or other area of the body of the subject to be treated. Many such targeting methods are well known to those of skill in the art. All such targeting methods are contemplated herein for use in the instant compositions. For non-limiting examples of targeting methods, see, *e.g.*, U.S. Patent Nos. 6,316,652, 6,274,552, 6,271,359, 6,253,872, 6,139,865, 6,131,570, 6,120,751, 6,071,495, 6,060,082, 6,048,736, 6,039,975, 6,004,534, 5,985,307, 5,972,366, 5,900,252, 5,840,674, 5,759,542 and 5,709,874.

In one embodiment, liposomal suspensions, including tissue-targeted liposomes, such as tumor-targeted liposomes, may also be suitable as pharmaceutically

acceptable carriers. These can be prepared according to methods known to those skilled in the art. For example, liposome formulations can be prepared as described in U.S. Patent No. 4,522,811. Briefly, liposomes such as multilamellar vesicles (MLV's) may be formed by drying down egg phosphatidyl choline and brain phosphatidyl serine (7:3 molar ratio) on the inside of a flask. A solution of a compound provided herein in phosphate buffered saline lacking divalent cations (PBS) is added and the flask shaken until the lipid film is dispersed. The resulting vesicles are washed to remove unencapsulated compound, pelleted by centrifugation, and then resuspended in PBS.

METHODS OF ADMINISTRATION AND DOSING

Also provided herein are compositions comprising one or more antibodies provided herein for use in the prevention, treatment and/or alleviation of one or more symptom of a disease, such as a C10orf54-mediated disease.

In certain embodiments, provided herein are compositions comprising one or more antibodies provided herein for use in the management, prevention, or treatment of a C10orf54-mediated disease and/or the alleviation of one or more symptom of a C10orf54-mediated disease. Exemplary C10orf54-mediated diseases include a cell proliferative disorder, cancer, tumor, and graft-versus-host disease (GVHD), or a symptom thereof.

In certain embodiments, provided herein are compositions comprising one or more antibodies provided herein for use in the prevention, treatment and/or alleviation of one or more symptom of an C10orf54-mediated disease, such as a cell proliferative disorder. A cell proliferative disorder can include cancer or tumor formation, or a symptom thereof. In certain embodiments, the cell proliferative disorder is associated with increased expression and/or activity of C10orf54. For example, in certain embodiments, the cell proliferative disorder is associated with increased expression of C10orf54 on the surface of a cancer cell. Examples of cell proliferative disorders to be treated, prevented, or symptoms of which can be alleviated by the antibodies provided herein include, but are not limited to, bladder, breast, colon, connective tissue, rectal, gastric, esophageal, lung, laryx, kidney, oral, ovarian, or prostate cancers, or sarcomas, melanomas, gliomas, lymphomas or leukemias, or metatases

of any of these cancers. Exemplary cell proliferative disorders include, but are not limited to, a leukemia, either acute or chronic, a fibrosarcoma, and a bladder cancer.

Leukemias are cancers of the blood-forming tissues characterized by distorted proliferation and development of leukocytes and their precursors in the blood and bone marrow. Leukemias are typically classified as either chronic (slowly progressing) or acute (rapidly progressing). Leukemias can be further classified based upon the type of blood cell affected. For example, leukemia of lymphoid cells include lymphoid leukemia, lymphocytic leukemia or lymphoblastic leukemia, and leukemia of myeloid cells include myeloid leukemia, myelogenous leukemia, myeloblastic leukemia or granulocytic leukemia. The four of the main types of leukemias that can be treated, prevented or symptoms thereof alleviated by the methods provided herein include acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myelogenous leukemia (AML) and chronic myelobastic leukemia (CML).

In one aspect, provided herein are methods for preventing or treating a disease described herein by administering to a subject a therapeutically effective amount, respectively, of an anti-C10orf54 antibody described herein, or a composition thereof. In certain embodiments, a method for treating the disease comprises administering to subject a therapeutically effective amount of a pharmaceutical formulation comprising an anti-C10orf54 antibody and a pharmaceutically acceptable carrier or excipient. A method provided herein can also optionally include at least one additional therapeutic agent, such as those provided herein, either as a separate treatment or conjugated or recombinately fused to an anti-C10orf54 antibody provided herein.

In one embodiment, an anti-C10orf54 antibody provided herein can be used for targeting C10orf54 expressed by the cancer cells by contacting the antibody with C10orf54 to form an antibody-antigen complex such that a conjugated or recombinately fused agent described herein accesses the interior of the cell. In one embodiment, the bound antibody is internalized into the cancer cell expressing C10orf54.

In certain embodiments, provided herein are compositions comprising one or more antibodies provided herein for use in the prevention, treatment and/or alleviation of

one or more symptom of an C10orf54-mediated disease, such as GVHD, or a symptom thereof. GVHD generally occurs following allogeneic or matched unrelated bone marrow transplants (BMT).

In some embodiments, the GVHD is acute GVHD. The symptoms of acute GVHD can happen quickly and can be mild or severe. In certain instances, acute GVHD develops within about three months after transplant, such as when blood counts recover after transplant. It certain instances, the acute GVHD affects the skin, gastrointestinal (GI) tract and/or liver. For example, in some patients, acute skin GVHD begins with a rash, for example, on the palms of the patient's hands, soles of the feet, or shoulders. However, the rash can become widespread, and may be itchy and painful and/or might blister and peel. Acute liver GVHD may affect normal functions of the liver, such as liver enzymes, and may in turn, cause jaundice. Acute liver GVHD may also cause the patient's abdomen to become swollen and painful if the liver becomes enlarged. Finally, symptoms of acute gut GVHD (or GVHD of the digestive system) can include diarrhea, mucus or blood in the stool, cramping or abdominal pain, indigestion, nausea and/or loss of appetite. Other general symptoms of acute GVHD can include anemia, low grade fever, and/or being more prone to infections. Any combination of these symptoms of acute GVHD may be prevented, treated, and/or alleviated using the compositions and methods provided herein.

In other embodiments, the GVHD is chronic GVHD. Chronic GVHD can occur from about three months to about a year or longer after transplant. Chronic GVHD can be mild or severe, and generally includes symptoms similar to those of acute GVHD. Chronic GVHD can affect the skin and digestive system, including the liver but can also involve other organs and the immune system (*e.g.*, making the patient more prone to infections) and/or connective tissues. Symptoms of chronic skin GVHD include a rash, dry skin, tight skin, itchy skin, darkening of the color of the skin, thickening of the skin, and/or may affect hair (*e.g.*, hair loss, turning gray) or nails (*e.g.*, hard or brittle nails). Chronic gut GVHD can affect the digestive system, mouth, esophagus, lining of the stomach, and/or lining of the bowel, and symptoms can include diarrhea, dry or sore mouth, painful swallowing, low nutrient absorption by the stomach, bloating, stomach cramps,. Chronic liver GVHD can cause damage and scarring of the liver (cirrhosis). Chronic GVHD of the eyes can affect the glands that

make tears, causing eyes to become dry, burning and painful or difficult to tolerate bright light. Chronic lung GVHD can cause shortness of breath, wheezing, persistent cough, and/or being more prone to chest infections. Chronic GVHD affects tendons (*e.g.,* inflammation) that connect muscle to bone causing difficulty straightening or bending your arms and legs. Any combination of these symptoms of chronic GVHD may be prevented, treated, and/or alleviated using the compositions and methods provided herein.

In certain embodiments, an antibody provided herein may be used in, for example, *in vitro*, *ex vivo*, and *in vivo* therapeutic methods. In some embodiments, provided herein are methods for inhibiting cell growth or proliferation, either *in vivo* or *in vitro*, the method comprising contacting a cell with an effective amount of a composition or an anti-C10orf54 antibody provided herein. In some embodiments, an antibody provided herein may be used in a method for inducing cell death. The method can comprise contacting a cell with an effective amount of a composition or an anti-C10orf54 antibody provided herein. The methods can be performed under conditions permissive for binding of the antibody to a C10orf54 polypeptide, polypeptide fragment or epitope, such as, but not limited to when the C10orf54 polypeptide is expressed on the surface of a cell. For inhibiting the cell growth or proliferation of a cell, the inhibition can include decreasing a cell's growth or proliferation by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100%, and can include cell death. In certain embodiments, the cell is a cancer cell or a pre-cancerous cell. In certain embodiments, the cell is a bladder, breast, colon, connective tissue, rectal, gastric, esophageal, lung, laryx, kidney, oral, ovarian, or prostate cancer cell, or a sarcoma, melanoma, glioma, lymphoma or leukemia cell. In certain embodiments, the cell is an immune cell expressing a C10orf54 polypeptide, such as, but not limited to, a regulatory T cell (*i.e.* a suppressor T cell).

An anti-C10orf54 antibody can be administered to a human for therapeutic or prophylactic purposes. Moreover, an anti-C10orf54 antibody can be administered to a non-human mammal expressing C10orf54 with which the antibody cross-reacts (*e.g.,* a primate, pig, rat, or mouse) for veterinary purposes or as an animal model of human disease. Regarding the latter, such animal models may be useful for evaluating the therapeutic or prophylactic efficacy of antibodies or immunoconjugates provided herein (*e.g.,* testing of dosages and time courses of administration).

In certain embodiments, an antibody provided herein can be used in a method of modulating an immune response in a subject. Such methods can include administering an effective amount of the composition of comprising an antibody provided herein to a subject. In some aspects, the modulating can include (a) increasing T cell activation; (b) increasing T cell proliferation; and/or (c) increasing cytokine production. Methods for assaying the modulation of an immune response are well known to one of skill in the art, and it is understood that a skill artisian would be able to readily conduct such assays.

In a specific embodiment, a composition for use in the management, prevention, treatment and/or alleviation of one or more symptom of a C10orf54-mediated disease comprises an antibody as described herein. In another specific embodiment, a composition for use in the management, prevention, treatment and/or alleviation of one or more symptom of a C10orf54-mediated disease comprises an antigen-binding fragment, a fusion protein or an functional fragment of an antibody as described herein.

In another embodiment, a composition for use in the management, prevention, treatment and/or alleviation of one or more symptom of a C10orf54-mediated disease comprises one or more antibodies described herein.

As discussed in more detail elsewhere herein, a composition provided herein may be used either alone or in combination with other compounds or compositions. Moreover, the antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalently and non-covalently conjugations) to polypeptides or other compositions. For example, antibodies provided herein may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionucleotides, or toxins. See, *e.g.*, PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387.

Antibodies provided herein may be used, for example, to purify, detect, and target C10orf54 antigens, in both *in vitro* and *in vivo* diagnostic and therapeutic methods. For example, the modified antibodies have use in immunoassays for qualitatively and

quantitatively measuring levels of C10orf54 in biological samples. See, *e.g.,* Harlow *et al.*, Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988) (incorporated by reference herein in its entirety).

Also provided herein are methods of managing, treating, preventing and/or ameliorating one or more symptom of a C10orf54-mediated disease by administrating to a subject of an effective amount of an antibody, or pharmaceutical composition comprising an antibody provided herein. In one aspect, an antibody is substantially purified (*e.g.,* substantially free from substances that limit its effect or produce undesired side-effects). In specific embodiments, the antibody is a humanized monoclonal antibody. The subject administered a therapy can be a mammal such as non-primate (*e.g.,* cows, pigs, horses, cats, dogs, rats *etc.*) or a primate (*e.g.,* a monkey, such as a cynomolgous monkey, or a human). In a specific embodiment, the subject is a human. In another embodiment, the subject is a human with a C10orf54-mediated disease.

Various delivery systems are known and can be used to administer a prophylactic or therapeutic agent (*e.g.,* an antibody provided herein), including, but not limited to, encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the antibody, receptor-mediated endocytosis (see, *e.g.,* Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, *etc.* Methods of administering a prophylactic or therapeutic agent (*e.g.,* an antibody provided herein), or pharmaceutical composition include, but are not limited to, parenteral administration (*e.g.,* intradermal, intramuscular, intraperitoneal, intravenous and subcutaneous), epidural, and mucosal (*e.g.,* intranasal and oral routes). In a specific embodiment, a prophylactic or therapeutic agent (*e.g.,* an antibody provided herein), or a pharmaceutical composition is administered intranasally, intramuscularly, intravenously, or subcutaneously. The prophylactic or therapeutic agents, or compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (*e.g.,* oral mucosa, intranasal mucosa, rectal and intestinal mucosa, *etc.*) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, pulmonary administration can also be employed, *e.g.,* by use of an inhaler or nebulizer, and formulation with an aerosolizing agent. See, *e.g.,* U.S. Patent Nos. 6,019,968,

5,985,320, 5,985,309, 5,934,272, 5,874,064, 5,855,913, 5,290,540, and 4,880,078; and PCT Publication Nos. WO 92/19244, WO 97/32572, WO 97/44013, WO 98/31346, and WO 99/66903, each of which is incorporated herein by reference their entirety.

In a specific embodiment, it may be desirable to administer a prophylactic or therapeutic agent, or a pharmaceutical composition provided herein locally to the area in need of treatment. This may be achieved by, for example, and not by way of limitation, local infusion, by topical administration (*e.g.,* by intranasal spray), by injection, or by means of an implant, the implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In certain embodiments, when administering an antibody provided herein, care must be taken to use materials to which the antibody does not absorb.

In another embodiment, a therapeutic agent or composition provided herein can be delivered in a vesicle, in particular a liposome (see Langer, 1990, Science 249:1527-1533; Treat *et al.*, in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353- 365 (1989); Lopez-Berestein, ibid., pp. 317-327; see generally ibid.).

In another embodiment, a therapeutic agent or composition provided herein can be delivered in a controlled release or sustained release system. In one embodiment, a pump may be used to achieve controlled or sustained release (see Langer, *supra*; Sefton, 1987, CRC Crit. Ref. Biomed. Eng. 14:20; Buchwald *et al.*, 1980, Surgery 88:507; Saudek *et al.*, 1989, N. Engl. J. Med. 321:574). In another embodiment, polymeric materials can be used to achieve controlled or sustained release of a therapeutic agent (*e.g.,* an antibody provided herein) or a composition provided herein (see *e.g.,* Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, 1983, J., Macromol. Sci. Rev. Macromol. Chem. 23:61; see also Levy *et al.*, 1985, Science 228:190; During *et al.*, 1989, Ann. Neurol. 25:351; Howard *et al.*, 1989, J. Neurosurg. 7 1:105); U.S. Patent No. 5,679,377; U.S. Patent No. 5,916,597; U.S. Patent No. 5,912,015; U.S. Patent No. 5,989,463; U.S. Patent No. 5,128,326; PCT Publication No. WO 99/15154; and PCT Publication No. WO 99/20253.

Examples of polymers used in sustained release formulations include, but are not limited to, poly(2-hydroxy ethyl methacrylate), poly(methyl methacrylate), poly(acrylic acid), poly(ethylene-co-vinyl acetate), poly(methacrylic acid), polyglycolides (PLG), polyanhydrides, poly(N-vinyl pyrrolidone), poly(vinyl alcohol), polyacrylamide, poly(ethylene glycol), polylactides (PLA), poly(lactide-co-glycolides) (PLGA), and polyorthoesters. In a specific embodiment, the polymer used in a sustained release formulation is inert, free of leachable impurities, stable on storage, sterile, and biodegradable. In yet another embodiment, a controlled or sustained release system can be placed in proximity of the therapeutic target, *e.g.*, the nasal passages or lungs, thus requiring only a fraction of the systemic dose (see, *e.g.*, Goodson, in Medical Applications of Controlled Release, *supra*, vol. 2, pp. 115-138 (1984)). Controlled release systems are discussed in the review by Langer (1990, Science 249:1527-1533). Any technique known to one of skill in the art can be used to produce sustained release formulations comprising one or more antibodies provided herein. See, *e.g.*, U.S. Patent No. 4,526,938, PCT publication WO 91/05548, PCT publication WO 96/20698, Ning *et al.*, 1996, "Intratumoral Radioimmunotherapy of a Human Colon Cancer Xenograft Using a Sustained-Release Gel," Radiotherapy & Oncology 39:179- 189, Song *et al.*, 1995, "Antibody Mediated Lung Targeting of Long-Circulating Emulsions," PDA Journal of Pharmaceutical Science & Technology 50:372-397, Cleek *et al.*, 1997, "Biodegradable Polymeric Carriers for a bFGF Antibody for Cardiovascular Application," Pro. Int'l. Symp. Control. Rel. Bioact. Mater. 24:853-854, and Lam *et al.*, 1997, "Microencapsulation of Recombinant Humanized Monoclonal Antibody for Local Delivery," Proc. Int'l. Symp. Control Rel. Bioact. Mater. 24:759-760.

In a specific embodiment, where the composition provided herein is a nucleic acid encoding a prophylactic or therapeutic agent (*e.g.*, an antibody provided herein), the nucleic acid can be administered *in vivo* to promote expression of its encoded therapeutic agent, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, *e.g.*, by use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (*e.g.*, a gene gun; Biolistic, Dupont), or coating with lipids or cell surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (see, *e.g.*, Joliot *et al.*,

1991, Proc. Natl. Acad. Sci. USA 88:1864-1868), *etc.* Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression by homologous recombination.

In a specific embodiment, a composition comprises one, two or more antibodies provided herein. In another embodiment, a composition comprises one, two or more antibodies provided herein and a prophylactic or therapeutic agent other than an antibody provided herein. In certain embodiments, the agents are known to be useful for or have been or are currently used for the prevention, treatment and/or alleviation of one or more symptom of a C10orf54-mediated disease. In addition to prophylactic or therapeutic agents, the compositions provided herein may also comprise a carrier.

The compositions provided herein include bulk drug compositions useful in the manufacture of pharmaceutical compositions (*e.g.,* compositions that are suitable for administration to a subject or patient) that can be used in the preparation of unit dosage forms. In a specific embodiment, a composition provided herein is a pharmaceutical composition. Such compositions comprise a prophylactically or therapeutically effective amount of one or more prophylactic or therapeutic agents (*e.g.,* an antibody provided herein or other prophylactic or therapeutic agent), and a pharmaceutically acceptable carrier. In certain embodiments, the pharmaceutical compositions are formulated to be suitable for the route of administration to a subject.

In a specific embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocamne to ease pain at the site of the injection. Such compositions, however, may be administered by a route other than intravenous.

Generally, the ingredients of compositions provided herein are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing

sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

In certain embodiments, an antibody provided herein is packaged in a hermetically sealed container such as an ampoule or sachette indicating the quantity of antibody. In one embodiment, the antibody is supplied as a dry sterilized lyophilized powder or water free concentrate in a hermetically sealed container and can be reconstituted, *e.g.*, with water or saline to the appropriate concentration for administration to a subject. In certain embodiments, the antibody is supplied as a dry sterile lyophilized powder in a hermetically sealed container at a unit dosage of at least 0.1 mg, at least 0.5 mg, at least 1 mg, at least 2 mg, or at least 3 mg, such as at least 5 mg, at least 10 mg, at least 15 mg, at least 25 mg, at least 30 mg, at least 35 mg, at least 45 mg, at least 50 mg, at least 60 mg, at least 75 mg, at least 80 mg, at least 85 mg, at least 90 mg, at least 95 mg, or at least 100 mg. The lyophilized antibody can be stored at between 2 and 8° C in its original container and the antibody can be administered within 12 hours, such as within 6 hours, within 5 hours, within 3 hours, or within 1 hour after being reconstituted. In an alternative embodiment, an antibody is supplied in liquid form in a hermetically sealed container indicating the quantity and concentration of the antibody. In certain embodiments, the liquid form of the antibody is supplied in a hermetically sealed container at least 0.1 mg/ml, at least 0.5 mg/ml, or at least 1 mg/ml, such as at least 5 mg/ml, at least 10 mg/ml, at least 15 mg/ml, at least 25 mg/ml, at least 30 mg/ml, at least 40 mg/ml, at least 50 mg/ml, at least 60 mg/ml, at least 70 mg/ml, at least 80 mg/ml, at least 90 mg/ml, or at least 100 mg/ml.

The compositions provided herein can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, *etc.*, and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, *etc.*

The amount of a therapeutic agent (*e.g.*, an antibody provided herein) or a composition provided herein that will be effective in the prevention, treatment and/or

alleviation of one or more symptom of a C10orf54-mediated disease can be determined by standard clinical techniques.

Accordingly, a dosage of an antibody or a composition that results in a serum titer of from about 0.1 µg/ml to about 450 µg/ml, and in some embodiments at least 0.1 µg/ml, at least 0.2 µg/ml, at least 0.4 µg/ml, at least 0.5 µg/ml, at least 0.6 µg/ml, at least 0.8 µg/ml, at least 1 µg/ml, at least 1.5 µg/ml, such as at least 2 µg/ml, at least 5 µg/ml, at least 10 µg/ml, at least 15 µg/ml, at least 20 µg/ml, at least 25 µg/ml, at least 30 µg/ml, at least 35 µg/ml, at least 40 µg/ml, at least 50 µg/ml, at least 75 µg/ml, at least 100 µg/ml, at least 125 µg/ml, at least 150 µg/ml, at least 200 µg/ml, at least 250 µg/ml, at least 300 µg/ml, at least 350 µg/ml, at least 400 µg/ml, or at least 450 µg/ml can be administered to a human for the prevention, treatment and/or alleviation of one or more symptom of a C10orf54-mediated disease. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of a C10orf54-mediated disease, and should be decided according to the judgment of the practitioner and each patient's circumstances.

Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

For the antibodies provided herein, the dosage administered to a patient can be, in certain embodiments, 0.1 mg/kg to 100 mg/kg of the patient's body weight. In some embodiments, the dosage administered to the patient is about 1 mg/kg to about 75 mg/kg of the patient's body weight. In certain embodiments, the dosage administered to a patient is between 1 mg/kg and 20 mg/kg of the patient's body weight, such as 1 mg/kg to 5 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of the antibodies provided herein may be reduced by enhancing uptake and tissue penetration of the antibodies by modifications such as, for example, lipidation.

In one embodiment, approximately 100 mg/kg or less, approximately 75 mg/kg or less, approximately 50 mg/kg or less, approximately 25 mg/kg or less, approximately 10 mg/kg or less, approximately 5 mg/kg or less, approximately 1 mg/kg or less, approximately 0.5 mg/kg or less, or approximately 0.1 mg/kg or less of an antibody provided herein is administered 5 times, 4 times, 3 times, 2 times or 1 time to prevent, treat or alleviate one or more symptom of a C10orf54-mediated disease. In some embodiments, an antibody provided herein is administered about 1-12 times, wherein the doses may be administered as necessary, *e.g.*, weekly, biweekly, monthly, bimonthly, trimonthly, *etc.*, as determined by a physician. In some embodiments, a lower dose (*e.g.*, 1-15 mg/kg) can be administered more frequently (*e.g.*, 3-6 times). In other embodiments, a higher dose (*e.g.*, 25-100 mg/kg) can be administered less frequently (*e.g.*, 1-3 times). However, as will be apparent to those in the art, other dosing amounts and schedules are easily determinable and within the scope of the invention.

In a specific embodiment, approximately 100 mg/kg, approximately 75 mg/kg or less, approximately 50 mg/kg or less, approximately 25 mg/kg or less, approximately 10 mg/kg or less, approximately 5 mg/kg or less, approximately 1 mg/kg or less, approximately 0.5 mg/kg or less, approximately 0.1 mg/kg or less of an antibody provided herein in a sustained release formulation is administered to a subject, such as a human, to prevent, treat and/or alleviate one or more symptom of a C10orf54-mediated disease. In another specific embodiment, an approximately 100 mg/kg, approximately 75 mg/kg or less, approximately 50 mg/kg or less, approximately 25 mg/kg or less, approximately 10 mg/kg or less, approximately 5 mg/kg or less, approximately 1 mg/kg or less, approximately 0.5 mg/kg or less, or approximately 0.1 mg/kg or less bolus of an antibody provided herein not in a sustained release formulation is administered to a subject, such as a human, to prevent, treat and/or alleviate one or more symptom of a C10orf54-mediated disease, and after a certain period of time, approximately 100 mg/kg, approximately 75 mg/kg or less, approximately 50 mg/kg or less, approximately 25 mg/kg or less, approximately 10 mg/kg or less, approximately 5 mg/kg or less, approximately 1 mg/kg or less, approximately 0.5 mg/kg or less, or approximately 5 mg/kg or less of an antibody provided herein in a sustained release is administered to the subject (*e.g.*, intranasally or intramuscularly) one, two, three or four times. In accordance with this

embodiment, a certain period of time can be 1 to 5 days, a week, two weeks, or a month.

In some embodiments, a single dose of an antibody provided herein is administered to a patient to prevent, treat and/or alleviate one or more symptom of a C10orf54-mediated disease two, three, four, five, six, seven, eight, nine, ten, eleven, twelve times, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, nineteen, twenty, twenty-one, twenty-two, twenty-three, twenty-four, twenty five, or twenty six at bi-weekly (*e.g.,* about 14 day) intervals over the course of a year, wherein the dose is selected from the group consisting of about 0.1 mg/kg, about 0.5 mg/kg, about 1 mg/kg, about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 55 mg/kg, about 60 mg/kg, about 65 mg/kg, about 70 mg/kg, about 75 mg/kg, about 80 mg/kg, about 85 mg/kg, about 90 mg/kg, about 95 mg/kg, about 100 mg/kg, or a combination thereof (*e.g.,* each dose monthly dose may or may not be identical).

In another embodiment, a single dose of an antibody provided herein is administered to patient to prevent, treat and/or alleviate one or more symptom of a C10orf54-mediated disease two, three, four, five, six, seven, eight, nine, ten, eleven, or twelve times at about monthly (*e.g.,* about 30 day) intervals over the course of a year, wherein the dose is selected from the group consisting of about 0.1 mg/kg, about 0.5 mg/kg, about 1 mg/kg, about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 55 mg/kg, about 60 mg/kg, about 65 mg/kg, about 70 mg/kg, about 75 mg/kg, about 80 mg/kg, about 85 mg/kg, about 90 mg/kg, about 95 mg/kg, about 100 mg/kg, or a combination thereof (*e.g.,* each dose monthly dose may or may not be identical).

In one embodiment, a single dose of an antibody provided herein is administered to a patient to treat, prevent and/or alleviate a symptom of a C10orf54-mediated disease two, three, four, five, or six times at about bi-monthly (*e.g.,* about 60 day) intervals over the course of a year, wherein the dose is selected from the group consisting of about 0.1 mg/kg, about 0.5 mg/kg, about 1 mg/kg, about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg,

about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 55 mg/kg, about 60 mg/kg, about 65 mg/kg, about 70 mg/kg, about 75 mg/kg, about 80 mg/kg, about 85 mg/kg, about 90 mg/kg, about 95 mg/kg, about 100 mg/kg, or a combination thereof (*e.g.*, each bi-monthly dose may or may not be identical).

In some embodiments, a single dose of an antibody provided herein is administered to a patient to treat, prevent and/or alleviate one or more symptom of a C10orf54-mediated disease two, three, or four times at about tri-monthly (*e.g.*, about 120 day) intervals over the course of a year, wherein the dose is selected from the group consisting of about 0.1 mg/kg, about 0.5 mg/kg, about 1 mg/kg, about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 55 mg/kg, about 60 mg/kg, about 65 mg/kg, about 70 mg/kg, about 75 mg/kg, about 80 mg/kg, about 85 mg/kg, about 90 mg/kg, about 95 mg/kg, about 100 mg/kg, or a combination thereof (*e.g.*, each tri-monthly dose may or may not be identical).

In certain embodiments, the route of administration for a dose of an antibody provided herein to a patient is intranasal, intramuscular, intravenous, or a combination thereof, but other routes described herein are also acceptable. Each dose may or may not be administered by an identical route of administration. In some embodiments, an antibody provided herein may be administered via multiple routes of administration simultaneously or subsequently to other doses of the same or a different antibody provided herein.

In certain embodiments, antibodies provided herein are administered prophylactically or therapeutically to a subject. Antibodies can be prophylactically or therapeutically administered to a subject so as to prevent, lessen or alleviate a C10orf54-mediated disease or symptom thereof.

DIAGNOSTIC USE OF ANTIBODIES

Labeled antibodies provided herein and derivatives and analogs thereof, which bind to a C10orf54 antigen can be used for diagnostic purposes to detect, diagnose, or monitor a C10orf54-mediated disease. Also provided herein are methods for the detection of a C10orf54-mediated disease comprising: (a) assaying the expression of a C10orf54 antigen in cells or a tissue sample of a subject using one or more

antibodies provided herein that bind to the C10orf54 antigen; and (b) comparing the level of the C10orf54 antigen with a control level, *e.g.*, levels in normal tissue samples (*e.g.*, from a patient not having a C10orf54-mediated disease, or from the same patient before disease onset), whereby an increase in the assayed level of C10orf54 antigen compared to the control level of the C10orf54 antigen is indicative of a C10orf54-mediated disease.

Also provided herein is a diagnostic assay for diagnosing a C10orf54-mediated disease comprising: (a) assaying for the level of a C10orf54 antigen in cells or a tissue sample of an individual using one or more antibodies provided herein that bind to a C10orf54 antigen; and (b) comparing the level of the C10orf54 antigen with a control level, *e.g.*, levels in normal tissue samples, whereby an increase in the assayed C10orf54 antigen level compared to the control level of the C10orf54 antigen is indicative of a C10orf54-mediated disease. A more definitive diagnosis of a C10orf54-mediated disease may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the C10orf54-mediated disease.

Antibodies provided herein can be used to assay C10orf54 antigen levels in a biological sample using classical immunohistological methods as described herein or as known to those of skill in the art (*e.g.*, see Jalkanen *et al.*, 1985, J. Cell. Biol. 101:976-985; and Jalkanen *et al.*, 1987, J. Cell . Biol. 105:3087-3096). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (^{125}I, ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^{3}H), indium (^{121}In), and technetium (^{99}Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

One aspect provided herein is the detection and diagnosis of a C10orf54-mediated disease in a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled antibody that binds to a C10orf54 antigen; b) waiting for a time interval following the administering for permitting the labeled antibody to preferentially

concentrate at sites in the subject where the C10orf54 antigen is expressed (and for unbound labeled molecule to be cleared to background level); c) determining background level; and d) detecting the labeled antibody in the subject, such that detection of labeled antibody above the background level indicates that the subject has a C10orf54-mediated disease. Background level can be determined by various methods including, comparing the amount of labeled molecule detected to a standard value previously determined for a particular system.

It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of ^{99}Tc. The labeled antibody will then preferentially accumulate at the location of cells which contain the specific protein. *In vivo* tumor imaging is described in S.W. Burchiel *et al.*, "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B.A. Rhodes, eds., Masson Publishing Inc. (1982).

Depending on several variables, including the type of label used and the mode of administration, the time interval following the administration for permitting the labeled antibody to preferentially concentrate at sites in the subject and for unbound labeled antibody to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5 to 20 days or 5 to 10 days.

In one embodiment, monitoring of a C10orf54-mediated disease is carried out by repeating the method for diagnosing the a C10orf54-mediated disease, for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, *etc.*

Presence of the labeled molecule can be detected in the subject using methods known in the art for *in vivo* scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods provided herein include, but are not limited to, computed tomography (CT), whole

body scan such as position emission tomography (PET), magnetic resonance imaging (MRI), and sonography.

In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston *et al.*, U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patient using positron emission-tomography. In yet another embodiment, the molecule is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

METHODS OF PRODUCING ANTIBODIES

Antibodies provided herein that bind to an antigen can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or by recombinant expression techniques. The practice of the invention employs, unless otherwise indicated, conventional techniques in molecular biology, microbiology, genetic analysis, recombinant DNA, organic chemistry, biochemistry, PCR, oligonucleotide synthesis and modification, nucleic acid hybridization, and related fields within the skill of the art. These techniques are described in the references cited herein and are fully explained in the literature. See, *e.g.*,, Maniatis *et al.* (1982) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press; Sambrook *et al.* (1989), Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press; Sambrook *et al.* (2001) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY; Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons (1987 and annual updates); Current Protocols in Immunology, John Wiley & Sons (1987 and annual updates) Gait (ed.) (1984) Oligonucleotide Synthesis: A Practical Approach, IRL Press; Eckstein (ed.) (1991) Oligonucleotides and Analogues: A Practical Approach, IRL Press; Birren *et al.* (eds.) (1999) Genome Analysis: A Laboratory Manual, Cold Spring Harbor Laboratory Press.

Polyclonal antibodies that bind to an antigen can be produced by various procedures well-known in the art. For example, a human antigen can be administered to various

host animals including, but not limited to, rabbits, mice, rats, *etc.* to induce the production of sera containing polyclonal antibodies specific for the human antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow *et al.*, Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling *et al.*, in: Monoclonal Antibodies and T-Cell Hybridomas 563 681 (Elsevier, N.Y., 1981) (the references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. Other exemplary methods of producing monoclonal antibodies are discussed elsewhere herein, such as *e.g.,* use of the KM mouse™. Additional exemplary methods of producing monoclonal antibodies are provided in the Examples herein.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art. Briefly, mice can be immunized with a C10orf54 antigen and once an immune response is detected, *e.g.,* antibodies specific for C10orf54 antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution.

Additionally, a RIMMS (repetitive immunization multiple sites) technique can be used to immunize an animal (Kilptrack *et al.*, 1997 Hybridoma 16:381-9, incorporated by reference in its entirety). The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a given polypeptide.

Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

Accordingly, also provided herein are methods of generating antibodies by culturing a hybridoma cell secreting a modified antibody provided herein wherein, in certain embodiments, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with a C10orf54 antigen with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind to a C10orf54 antigen.

Antibody fragments which recognize specific C10orf54 antigens may be generated by any technique known to those of skill in the art. For example, Fab and $F(ab')_2$ fragments provided herein may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce $F(ab')_2$ fragments). $F(ab')_2$ fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain. Further, the antibodies provided herein can also be generated using various phage display methods known in the art.

For example, antibodies can also be generated using various phage display methods. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In particular, DNA sequences encoding VH and VL domains are amplified from animal cDNA libraries (*e.g.,* human or murine cDNA libraries of affected tissues). The DNA encoding the VH and VL domains are recombined together with an scFv linker by PCR and cloned into a phagemid vector. The vector is electroporated in *E. coli* and the *E. coli* is infected with helper phage. Phage used in these methods are typically filamentous phage including fd and M13 and the VH and VL domains are usually recombinantly fused to either the phage gene III or gene VIII. Phage expressing an antigen binding domain that binds to a particular antigen can be selected or identified with antigen, *e.g.,* using labeled antigen or antigen bound or captured to a solid surface or bead. Examples of phage display methods that can be used to make the antibodies provided herein include those disclosed in Brinkman *et al.*, 1995, J. Immunol. Methods 182:41-50; Ames *et al.*, 1995, J. Immunol. Methods 184:177-186; Kettleborough *et al.*, 1994, Eur. J. Immunol. 24:952-958; Persic *et al.*, 1997, Gene

187:9-18; Burton *et al.*, 1994, Advances in Immunology 57:191-280; PCT Application No. PCT/GB91/O1 134; International Publication Nos. WO 90/02809, WO 91/10737, WO 92/01047, WO 92/18619, WO 93/1 1236, WO 95/15982, WO 95/20401, and WO97/13844; and U.S. Patent Nos. 5,698,426, 5,223,409, 5,403,484, 5,580,717, 5,427,908, 5,750,753, 5,821,047, 5,571,698, 5,427,908, 5,516,637, 5,780,225, 5,658,727, 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, *e.g.,* as described below. Techniques to recombinantly produce Fab, Fab' and $F(ab')_2$ fragments can also be employed using methods known in the art such as those disclosed in PCT publication No. WO 92/22324; Mullinax *et al.*, 1992, BioTechniques 12(6):864-869; Sawai *et al.*, 1995, AJRI 34:26-34; and Better *et al.*, 1988, Science 240:1041-1043 (the references incorporated by reference in their entireties).

To generate whole antibodies, PCR primers including VH or VL nucleotide sequences, a restriction site, and a flanking sequence to protect the restriction site can be used to amplify the VH or VL sequences in scFv clones. Utilizing cloning techniques known to those of skill in the art, the PCR amplified VH domains can be cloned into vectors expressing a VH constant region, *e.g.,* the human gamma 4 constant region, and the PCR amplified VL domains can be cloned into vectors expressing a VL constant region, *e.g.,* human kappa or lambda constant regions. The VH and VL domains may also cloned into one vector expressing the necessary constant regions. The heavy chain conversion vectors and light chain conversion vectors are then co-transfected into cell lines to generate stable or transient cell lines that express full-length antibodies, *e.g.,* IgG, using techniques known to those of skill in the art.

For some uses, including *in vivo* use of antibodies in humans and *in vitro* detection assays, human or chimeric antibodies can be used. Completely human antibodies are particularly desirable for therapeutic treatment of human subjects. Human

antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also U.S. Patent Nos. 4,444,887 and 4,716,111; and International Publication Nos. WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

In specific embodiments, human antibodies are produced. Human antibodies and/or fully human antibodies can be produced using any method known in the art, including the Examples provided herein. For example, transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the J_H region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, *e.g.,* all or a portion of the polypeptide. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, Int. Rev. Immunol. 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, *e.g.,* PCT publication Nos. WO 98/24893, WO 96/34096, and WO 96/33735; and U.S. Patent Nos. 5,413,923, 5,625,126, 5,633,425, 5,569,825,

5,661,016, 5,545,806, 5,814,318, and 5,939,598, which are incorporated by reference herein in their entirety. Other methods are detailed in the Examples herein. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

A chimeric antibody is a molecule in which different portions of the antibody are derived from different immunoglobulin molecules. Methods for producing chimeric antibodies are known in the art. See, *e.g.,* Morrison, 1985, Science 229:1202; Oi *et al.*, 1986, BioTechniques 4:214; Gillies *et al.*, 1989, J. Immunol. Methods 125:191-202; and U.S. Patent Nos. 5,807,715, 4,816,567, 4,816,397, and 6,331,415, which are incorporated herein by reference in their entirety.

A humanized antibody is an antibody or its variant or fragment thereof which is capable of binding to a predetermined antigen and which comprises a framework region having substantially the amino acid sequence of a human immunoglobulin and a CDR having substantially the amino acid sequence of a non-human immunoglobulin. A humanized antibody comprises substantially all of at least one, and typically two, variable domains (Fab, Fab', $F(ab')_2$, Fabc, Fv) in which all or substantially all of the CDR regions correspond to those of a non human immunoglobulin (*e.g.,* donor antibody) and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. In certain embodiments, a humanized antibody also comprises at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. Ordinarily, the antibody will contain both the light chain as well as at least the variable domain of a heavy chain. The antibody also may include the CH1, hinge, CH2, CH3, and CH4 regions of the heavy chain. The humanized antibody can be selected from any class of immunoglobulins, including IgM, IgG, IgD, IgA and IgE, and any isotype, including IgG1, IgG2, IgG3 and IgG4. Usually the constant domain is a complement fixing constant domain where it is desired that the humanized antibody exhibit cytotoxic activity, and the class is typically IgG1. Where such cytotoxic activity is not desirable, the constant domain may be of the IgG2 class. Examples of VL and VH constant domains that can be used in certain embodiments include, but are not limited to, C-kappa and C-gamma-1 (nG1m) described in Johnson *et al.* (1997) *J. Infect. Dis.* 176, 1215-1224 and those described in U.S. Patent No. 5,824,307. The

humanized antibody may comprise sequences from more than one class or isotype, and selecting particular constant domains to optimize desired effector functions is within the ordinary skill in the art. The framework and CDR regions of a humanized antibody need not correspond precisely to the parental sequences, *e.g.*, the donor CDR or the consensus framework may be mutagenized by substitution, insertion or deletion of at least one residue so that the CDR or framework residue at that site does not correspond to either the consensus or the import antibody. Such mutations, however, will not be extensive. Usually, at least 75% of the humanized antibody residues will correspond to those of the parental FR and CDR sequences, more often 90%, or greater than 95%. Humanized antibodies can be produced using variety of techniques known in the art, including but not limited to, CDR-grafting (European Patent No. EP 239,400; International publication No. WO 91/09967; and U.S. Patent Nos. 5,225,539, 5,530,101, and 5,585,089), veneering or resurfacing (European Patent Nos. EP 592,106 and EP 519,596; Padlan, 1991, Molecular Immunology 28(4/5):489-498; Studnicka *et al.*, 1994, Protein Engineering 7(6):805-814; and Roguska *et al.*, 1994, PNAS 91:969-973), chain shuffling (U.S. Patent No. 5,565,332), and techniques disclosed in, *e.g.*, U.S. Pat. No. 6,407,213, U.S. Pat. No. 5,766,886, WO 9317105, Tan *et al.*, J. Immunol. 169:1119 25 (2002), Caldas *et al.*, Protein Eng. 13(5):353-60 (2000), Morea *et al.*, Methods 20(3):267 79 (2000), Baca *et al.*, J. Biol. Chem. 272(16):10678-84 (1997), Roguska *et al.*, Protein Eng. 9(10):895 904 (1996), Couto *et al.*, Cancer Res. 55 (23 Supp):5973s- 5977s (1995), Couto *et al.*, Cancer Res. 55(8):1717-22 (1995), Sandhu JS, Gene 150(2):409-10 (1994), and Pedersen *et al.*, J. Mol. Biol. 235(3):959-73 (1994). See also U.S. Patent Pub. No. US 2005/0042664 A1 (Feb. 24, 2005), which is incorporated by reference herein in its entirety. Often, framework residues in the framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter (*e.g.*, improve) antigen binding. These framework substitutions are identified by methods well known in the art, *e.g.*, by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, *e.g.*, Queen *et al.*, U.S. Patent No. 5,585,089; and Reichmann *et al.*, 1988, Nature 332:323, which are incorporated herein by reference in their entireties.)

Single domain antibodies, for example, antibodies lacking the light chains, can be produced by methods well-known in the art. See Riechmann *et al.*, 1999, J. Immunol. 231:25-38; Nuttall *et al.*, 2000, Curr. Pharm. Biotechnol. 1(3):253-263; Muylderman, 2001, J. Biotechnol. 74(4):277302; U.S. Patent No. 6,005,079; and International Publication Nos. WO 94/04678, WO 94/25591, and WO 01/44301, each of which is incorporated herein by reference in its entirety.

Further, the antibodies that bind to a C10orf54 antigen can, in turn, be utilized to generate anti-idiotype antibodies that "mimic" an antigen using techniques well known to those skilled in the art. (See, *e.g.,* Greenspan & Bona, 1989, FASEB J. 7(5):437-444; and Nissinoff, 1991, J. Immunol. 147(8):2429-2438).

POLYNUCLEOTIDES ENCODING AN ANTIBODY

Also provided herein are polynucleotides comprising a nucleotide sequence encoding an antibody provided herein that binds to C10orf54 (*e.g.*, C10orf54 polypeptide, C10orf54 polypeptide fragment, C10orf54 epitope). Also provided herein are polynucleotides that hybridize under high stringency, intermediate or lower stringency hybridization conditions, *e.g.,* as defined *supra*, to polynucleotides that encode a antibody or modified antibody provided herein.

In certain embodiments, nucleic acid molecules provided herein comprise or consist of a nucleic acid sequence encoding a VH and/or VL amino acid sequence disclosed herein, or any combination thereof (*e.g.,* as a nucleotide sequence encoding an antibody provided herein, such as a full-length antibody, heavy and/or light chain of an antibody, or a single chain antibody provided herein).

RECOMBINANT EXPRESSION OF AN ANTIBODY

Recombinant expression of an antibody provided herein (*e.g.,* a full-length antibody, heavy and/or light chain of an antibody, or a single chain antibody provided herein) that binds to a C10orf54 antigen requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule, heavy or light chain of an antibody, or fragment thereof (such as that containing the heavy and/or light chain variable domain) has been obtained, the vector for the production of the antibody molecule may be

produced by recombinant DNA technology using techniques well-known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Thus, also provided herein are replicable vectors comprising a nucleotide sequence encoding an antibody molecule provided herein, a heavy or light chain of an antibody, a heavy or light chain variable domain of an antibody or a fragment thereof, or a heavy or light chain CDR, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, *e.g.,* International Publication Nos. WO 86/05807 and WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy, the entire light chain, or both the entire heavy and light chains.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody provided herein. Thus, also provided herein are host cells containing a polynucleotide encoding an antibody provided herein or fragments thereof, or a heavy or light chain thereof, or fragment thereof, or a single chain antibody provided herein, operably linked to a heterologous promoter. In certain embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibodies provided herein (see, *e.g.,* U.S. Patent No. 5,807,715). Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody provided herein *in situ.* These include but are not limited to microorganisms such as bacteria (*e.g., E. coli* and *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors

containing antibody coding sequences; yeast (*e.g., Saccharomyces Pichia*) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (*e.g.*, baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (*e.g.*, Ti plasmid) containing antibody coding sequences; or mammalian cell systems (*e.g.*, COS, CHO, BHK, 293, NS0, and 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (*e.g.*, metallothionein promoter) or from mammalian viruses (*e.g.*, the adenovirus late promoter; the vaccinia virus 7.5K promoter). In certain embodiments, bacterial cells, such as *Escherichia coli*, or eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking *et al.*, 1986, Gene 45:101; and Cockett *et al.*, 1990, Bio/Technology 8:2). In specific embodiments, antibodies provided herein are produced in CHO cells. In a specific embodiment, the expression of nucleotide sequences encoding antibodies provided herein which bind to a C10orf54 antigen is regulated by a constitutive promoter, inducible promoter or tissue specific promoter.

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such an antibody is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited to, the *E. coli* expression vector pUR278 (Ruther *et al.*, 1983, EMBO 12:1791), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, 1985, Nucleic Acids Res. 13:3101-3109; Van Heeke & Schuster, 1989, J. Biol. Chem. 24:5503-5509); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione 5-transferase (GST). In

general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, *e.g.*, the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by *in vitro* or *in vivo* recombination. Insertion in a non-essential region of the viral genome (*e.g.*, region El or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts (*e.g.*, see Logan & Shenk, 1984, Proc. Natl. Acad. Sci. USA 8 1:355-359). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, *etc.* (see, *e.g.*, Bittner *et al.*, 1987, Methods in Enzymol. 153:51-544).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (*e.g.*, glycosylation) and processing (*e.g.*, cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-

translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, W138, BT483, Hs578T, HTB2, BT2O and T47D, NS0 (a murine myeloma cell line that does not endogenously produce any immunoglobulin chains), CRL7O3O and HsS78Bst cells. In specific embodiments, fully human, monoclonal anti-C10orf54 antibodies provided herein are produced in mammalian cells, such as CHO cells.

For long-term, high-yield production of recombinant proteins, stable expression is useful, but not mandatory. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (*e.g.*, promoter, enhancer, sequences, transcription terminators, polyadenylation sites, *etc.*), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compositions that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to, the herpes simplex virus thymidine kinase (Wigler *et al.*, 1977, Cell 11:223), hypoxanthineguanine phosphoribosyltransferase (Szybalska & Szybalski, 1992, Proc. Natl. Acad. Sci. USA 48:202), and adenine phosphoribosyltransferase (Lowy *et al.*, 1980, Cell 22:8-17) genes can be employed in tk-, hgprt- or aprt-cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: *dhfr*, which confers resistance to methotrexate (Wigler *et al.*, 1980, Natl. Acad. Sci. USA 77:357; O'Hare *et al.*, 1981, Proc. Natl. Acad. Sci. USA 78:1527); *gpt*,

which confers resistance to mycophenolic acid (Mulligan & Berg, 1981, Proc. Natl. Acad. Sci. USA 78:2072); neo, which confers resistance to the aminoglycoside G-418 (Wu and Wu, 1991, Biotherapy 3:87-95; Tolstoshev, 1993, Ann. Rev. Pharmacol. Toxicol. 32:573-596; Mulligan, 1993, Science 260:926-932; and Morgan and Anderson, 1993, Ann. Rev. Biochem. 62:191-217; May, 1993, TIB TECH 11(5):I55-215); and *hygro*, which confers resistance to hygromycin (Santerre *et al.*, 1984, Gene 30:147). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel *et al.* (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli *et al.* (eds.), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin *et al.*, 1981, J. Mol. Biol. 150:1, which are incorporated by reference herein in their entireties.

The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol. 3 (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse *et al.*, 1983, Mol. Cell. Biol. 3:257).

The host cell may be co-transfected with two expression vectors provided herein, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, 1986, Nature 322:52; and Kohler, 1980, Proc. Natl. Acad. Sci. USA 77:2197-2199). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

Once an antibody has been produced by recombinant expression, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (*e.g.,* ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. Further, the antibodies provided herein may be fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification.

KITS

Also provided herein is a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions provided herein, such as one or more antibodies provided herein. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In some embodiments, the kit comprises a package insert. The term "package insert" is used to refer to instructions customarily included in commercial packages of therapeutic products, that contain information about the indications, usage, dosage, administration, contraindications and/or warnings concerning the use of such therapeutic products, as well as instructions for use.

Also provided herein are kits that can be used in the above methods. In one embodiment, a kit comprises an antibody provided herein, such as an isolated antibody, in one or more containers. In a specific embodiment, the kits provided herein contain a substantially isolated C10orf54 antigen as a control. In certain embodiments, the kits provided herein further comprise a control antibody which does not react with the C10orf54 antigen. In another specific embodiment, the kits provided herein contain a means for detecting the binding of a modified antibody to a C10orf54 antigen (*e.g.,* the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate). In specific embodiments, the kit may include a recombinantly produced or chemically synthesized C10orf54 antigen. The

C10orf54 antigen provided in the kit may also be attached to a solid support. In a more specific embodiment the detecting means of the above described kit includes a solid support to which C10orf54 antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the C10orf54 antigen can be detected by binding of the the reporter-labeled antibody.

The following examples are offered by way of illustration, and not by way of limitation.

EXAMPLES

EXAMPLE 1 – IDENTIFICATION OF C10ORF54 ON THE SURFACE OF ACUTE MYELOGENOUS LEUKEMIA (AML) TUMOR CELLS

A total of 14 fresh bone marrow mononuclear cells (BMMCs) from patients with AML were obtained from AllCells and additional 16 frozen patient samples were from Fred Hutchinson Cancer Research Center (FHCRC). As a control, 16 fresh BMMC samples from healthy donors were analyzed. To monitor the quality of individual AML samples, hematoxylin and eosin staining of AML blasts were performed or AML marker expression was monitored using flow cytometry/FACS analysis. Sample handling was optimized so as to maximally maintain cell viability during sample isolation. Optimal labeling times for AML samples were determined to allow for efficient labeling without compromise of cellular integrity.

Surface tagged antigen profiling (sTAg) was used to identify and quantitatively profile the repertoire of surface proteins on cells in the samples. The extracellular domains of proteins associated with the cell membranes of intact primary AML tumor cells were chemically tagged and then chromatographically enriched for tagged proteins using a solid-phase affinity resin. Eluted proteins were stored at -80°C prior to mass spectrometry analysis as described below.

Proteins enriched by the sTAg method were identified and quantified using high-resolution, shotgun liquid chromatography tandem mass spectrometry (MS). A hybrid ThermoFisher LTQ-ORBITRAP VELOS mass spectrometer, which combines the sensitivity of a linear ion trap with the high-resolution and mass accuracy afforded by the revolutionary orbitrap mass analyzer (Olsen *et al.*, Mol. Cell Proteomics 8:2759-

2769, 2009) coupled to a nanoflow liquid chromatography apparatus was employed for shotgun-based, bottoms-up proteomics to determine the identities and quantitative abundance measurements of proteins in the AML cell surface enrichment fractions (Yates *et al.*, Annu. Rev. Biomed. Eng. 11:49-79, 2009). Tryptic digests from enriched surface proteins were separated by hydrophobicity via online, nanoflow liquid chromatography as peptide masses and fragmentation patterns were recorded dynamically by the mass spectrometer. To determine peptide and protein identities, the raw MS data were processed using the SEQUEST algorithm executed on a fast-processing Sorcerer 2 platform (Lundgren *et al.*, Curr. Protoc. Bioinformatics, Chapter 13: Unit 13.3, 2009), to determine best-fit matches between experimental fragmentation patterns and those determined *in-silico* from the human proteome. Resulting matches were statistically validated using the PEPTIDEPROPHET (Keller *et al.*, Anal. Chem. 74:5383-5392, 2002) and PROTEINPROPHET (Nesvizhskii *et al.*, Anal. Chem. 75: 4646-4658, 2003) algorithms as implemented in SCAFFOLD Software (Proteome Software) to ensure the lowest possible false discovery rates (FDR) and thus inclusion of only robustly identified proteins in the candidate pool.

The relative quantitative levels of identified proteins in the sTAg samples were determined using the spectral counting method (reviewed in Neilson *et al.*, Proteomics 11:535-553, 2011). Spectral counting is based on the empirical demonstration that the number of assigned (positively identified) spectra associated with peptides from each protein correlates strongly with that protein's relative abundance in the original mixture (Liu *et al.*, Anal. Chem. 76:4193-4201, 2004). Spectral counts of identified peptides were obtained from the SCAFFOLD Software program that displays, sorts and filters the results of SEQUEST-searched mass spectrometry data. Raw spectral counts were transformed to percent Normalized Spectral Abundance Factor (%NSAF) values (Zybailov et al., J. Proteome Res. 5:2339-2347, 2006) to account for differences in protein length and variability in total protein concentration. Selected monoclonal antibodies were used to validate the proteomic measurements using quantitative FACS analysis as an independent, external confirmatory measure of the sTAg mass spectrometry-based proteomic profiling of the primary tumor cell surface expression (see, *e.g.,* Example 2).

Using sTAg analysis, C10orf54 having the amino acid sequence of SEQ ID NO:1080 was identified as being present on the surface of AML tumor cells. As shown in **FIG.**

1A, the sTAg method identified C10orf54 in 7 of 30 primary AML samples with a median %NSAF of 0.06. In contrast, C10orf54 was not detected in any 16 BMMC samples from healthy donors. The AML benchmark, CD33, was identified in 11 of 30 AML samples with a median %NSAF of 0.07, and four of 16 normal BMMC samples with a median %NSAF of 0.05. **FIG. 1B**, shows a subset of the sTAg samplesshwon in **FIG. 1A**. Based on this analysis, C10orf54 appears to be comparably expressed to CD33 in patient-derived AML specimens and expressed on a significant portion of AML patients relative to relevant normal controls.

EXAMPLE 2 – EXPRESSION OF C10ORF54 IN AML

Flow cytometry studies were conducted with 23 primary and 3 normal BM-MNC samples obtained as described in Example 1 using anti-C10orf54 antibodies to analyze the expression profile of C10orf54 in AML. Antibodies were labeled with AF647 or AF488 fluorochromes. Cells were counted and used at 500000 cells/stain, resuspended in FACS buffer: RPMI, 4% HIFBS, 0.02%NaN3. Antibodies were incubated for 15 minutes, at room temperature in the dark and then analyzed on a MACSQuant (Miltenyl Biotec, Auburn, CA) instrument. Data analysis was performed using the FLOWJO (TreeStar, Ashland, OR) software. Results of FACS analysis using anti-C10orf54 antibody 76E1 are shown in **FIG. 2**.

EXAMPLE 3 – PREPARATION OF MONOCLONAL ANTIBODIES TO C10ORF54

Antibodies to C10orf54 were generated using the iTAb platform. In this system, a mouse tumor cell line is transduced to stably express the human protein and then implanted subcutaneously in syngeneic mice. The mice are treated with anti-CD8 antibody to remove the cell mediated rejection pathway while leaving the humoral immune response intact. Following this immunization, spenocytes are harvested, and are fused to an immortalized partner cell to generate hybridomas. Antibodies from these hybridomas are screened in multiple assays designed to identify a diverse panel of antibodies with good binding properties. The selected antibodies are then produced for *in vivo* testing as follows.

Murine sarcoma cell lines that express C10orf54 were prepared by virus infection of sarcoma cell lines. A PCR-amplified C10orf54 gene was cloned into a murine stem cell virus expression vector with a neomycin resistance gene and sequenced to

confirm the identity. To prepare virus particles, HEK 293t cells with retroviral packaging proteins were transfected, in the presence of transfection reagent FUGENE HD (Roche), with the retroviral expression vector containing C10orf54. The virus particles collected from the supernatant of the culture media 48 hours after transfection were used to infect the sarcoma cells. After G418 selection, stable transfectants were pooled and then cloned by limiting dilution. Clones were then picked and expanded in the presence of antibiotics. Clones with the highest expression level of C10orf54 as measured by flow cytometry were expanded and banked. These cell lines were then used to immunize the syngeneic mice for antibody production and in the binding assays for antibody selection as follows.

For immunization, the mouse sarcoma cell line that expresses C10orf54 was implanted subcutaneously in 129s6/SvEv mice, which are syngeneic with the sarcoma line. Mice were boosted with the cell line three days prior to spleen harvest. Splenocytes were isolated as single cells and fused with SP2-MIL6 cells using PEG1500. Resulting hybridomas were plated in 384-well plates and allowed to grow for ten days.

Antibodies against C10orf54 were initially selected using a cell-based enzyme-linked immunosorbant assay (ELISA) to detect binding to C10orf54. For this assay, the C10orf54 expressing sarcoma cells were plated in 384-well plates one day prior to assay. Cells were then treated with hybridoma supernatants. Following incubation and wash, the presence of bound antibody was detected using a peroxidase-conjugated goat anti-mouse IgG antibody (Jackson ImmunResearch Laboratories) followed by a chemiluminescent substrate (ThermoScientific SuperSignal ELISA Pico Substrate). Hybridomas identified as positive in the initial screen were transferred to the wells of a 96-well plate. After growth, the supernatants were tested in a similar assay for confirmation.

The isotype of the antibodies was identified by ELISA by using isotype specific goat anti-mouse Fc antibodies. For this assay, C10orf54 expressing cells were plated in 384-well plates one day prior to assay. Cells were then treated with hybridoma supernatants. Following incubation and wash, cells were incubated with peroxidase-conjugated goat antibody specific for mouse IgG1 or IgG2a (Jackson

ImmunResearch Laboratories), followed by a chemiluminescent substrate (ThermoScientific SuperSignal ELISA Pico Substrate).

Concentration of antibody in supernatants found to be positive for binding to the C10orf54 expressing cells was measured by ELISA. Supernatants were tested at four dilutions. For each antibody, the dilution that generated a value within the linear range of the standard curve was used to calculate the concentration of the antibody in the supernatant. Antibody concentration in the supernatants ranged in concentration from <1µg/ml to >500 µg/ml, with approximately 300 supernatants >10µg/ml. Twenty-two monoclonal antibodies were selected for their binding to C10orf54 and further analyzed in vitro and in vivo as described herein.

EXAMPLE 4 – PREPARATION OF HUMANIZED ANTIBODIES

Murine antibodies prepared as described in Example 3 were selected for sequencing. The selected monoclonal antibodies designated 76E1, 141A and 175A were humanized by two methods as follows. The results of humanization are shown in **FIGS. 3-8**.

In a first humanization method, most amino acids in each complementarity-determining region (CDR), as previously identified, in the variable heavy (VH) and variable light (VL) domain sequence were converted to alanine. The resulting sequence for VH and for VL as shown in **FIG. 9** was used as input to the human subgroup identification algorithm on the website of Dr. Andrew C. R. Martin www.bioinf.org.uk/abs/; this method is a derivation of Deret, S. et al SUBIM: a Program for Analysing the Kabat Database and Determining the Variability Subgroup of a new Immunoglobulin Sequence Comput Appl Biosci 11:435-439 (1995). Antibody 76E1 VH, 141A VH and 175A VH were closest to human VH subgroup I, 76E1 VL and 175A VL were closest to human VL kappa subgroup II, and 141A VL was closest to human VL kappa subgroup III. For each murine 76E1, 141A and 175A VH and VL sequence, a single human VH or VL germline acceptor sequence was chosen from the corresponding human subgroup germline sequences and all human joining region sequences compiled at IMGT® the international ImMunoGeneTics information system® www.imgt.org (founder and director: Marie-Paule Lefranc, Montpellier, France).

In a second humanization method (Carter *et al., Proc Natl Acad Sci USA* 89:4285-4289 (1992)), human VH subgroup III germline was used as acceptor for the murine VH sequences of 76E1 VH, 141A VH and 175A VH; human VL subgroup kappa I was used as acceptor for 76E1 VL, 141A VL and 175A VL.

Alteration of human germline framework (*e.g.*, non-CDR residues in VH and VL) positions to corresponding parental murine 76E1, 141A or 175A sequence might be required to optimize binding of the humanized antibody. Potential changes for each humanized sequence are noted in **FIGS. 3-8**. Potential changes in the CDR sequences of the humanized antibodies in order to alleviate complications due to deamidation of solvent-exposed asparagines, oxidation of solvent-exposed methionines, and formation of isoaspartic acid are also noted in **FIGS. 3-8.**

Computer-graphics models of murine 76E1, 141A and 175A VH and VL domains were generated to aid in selection of CDR and framework residues that might require alteration. The Swiss-PdB Viewer program was used (Guex, N and Peitsch, MC SWISS-MODEL and the Swiss-PdBViewer: An environment for comparative protein modeling. Electrophoresis 18:2714-2723 (1997) Expasy website. Crystal structures of antibodies were taken from the Protein Data Bank website (Berman, HM; Westbrook, J; Feng, Z; Gilliland, G; Bhat, TN; Weissig, H; Shindyalov, IN; Bourne PE, The Protein Data Bank Nucleic Acids Research 28:235-242 (2000). The sequences of humanized 76E1, 141A and 175A VH and VL domains are shown in **FIGS. 3-8.**

EXAMPLE 5 – ANTI-TUMOR ACTIVITY

Anti-C10orf54 antibodies were tested for their anti-tumor activity in an animal tumor model. For these studies, the cell line Kasumi-3 (acute myeloid leukemia), was obtained from ATCC (CRL-2725) and cultured according to the suppliers' protocols. Animals were obtained from Taconic (Hudson, NY). Studies were conducted with anti-C10orf54 antibodies in an animal tumor model.

In these experiments, 4-6 week-old immunodeficient NOD-SCID female mice were used for the Kasumi-3 tumor model. Mice were subcutaneously injected on the right flank with $1.2x10^6$ viable cells (Kasumi-3) in a mixture of PBS (without magnesium or calcium) and BD Matrigel (BD Biosciences) at a 1:1 ratio. The injected total volume per mouse was 200µl with 50% being Matrigel (BD Biosciences). Once the tumor

reached a size between 65-200mm^3 mice were randomized. Antibodies were administered weekly at 15mg/kg for four weeks, bodyweights and tumors measured once and twice weekly, respectively. Tumor volume was calculated as described (van der Horst et al., 2009, Neoplasia 11(4):355-364). Experiments were performed on groups of at least 8 animals per experimental point.

Statistical significance between treatment and control groups was calculated using the Graphpad Prism software package and applying Student's two-tailed t-test. A p-value of less than 0.05 was considered significant. The results of three exemplary experiments are shown in Table 11. For Experiment 1, tumor volumes at which treatment was initiated were 114.7 mm3 (day 96). For Experiment 2, tumor volumes at which treatment was initiated were 114.5 mm3 (day 103). For Experiment 3, tumor volumes at which treatment was initiated were 133 mm3 (day 34).

TABLE 11

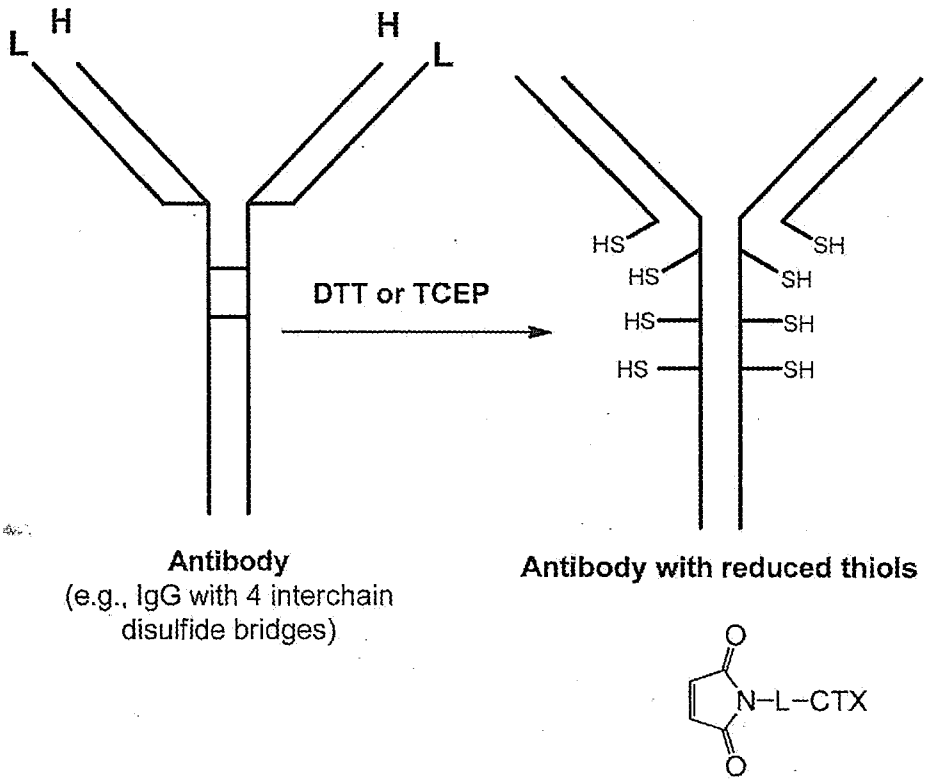
EXPERIMENT 1			
Treatment	Volume±SD [mm^3]	TGI [%]	P-value
CTRL IgG	3255±1704	-	-
175A	833±429	-77	0.0088
124A	1305±674	-62	0.0363
33A	1514±1156	-55	0.0447
51A	1668±638	-51	0.0507
46A	1925±791	-42	0.0937
26A	1982±997	-41	0.1154
39A	2039±1102	-39	0.1370
EXPERIMENT 2			
Treatment	Volume±SD [mm^3]	TGI [%]	P-value
CTRL IgG	2689±866	-	-
141A	1271±962	-55	0.0079
164A	1638±553	-41	0.0136

128A	2119±1340	-22	0.3585
321D	2588±1371	-4	0.8638
EXPERIMENT 3			
Treatment	Volume±SD [mm^3]	TGI [%]	P-value
CTRL IgG	1961±1060	-	-
175A	344±841	-81	0.0342

As shown in **FIG. 10** (see also, Table 11, Experiment 1), anti-C10orf54 antibody treatment induced strong tumor growth inhibition in established Kasumi-3 tumors. None of the antibody treatments had significant effect on body-weight, which indicates that the antibody treatment was not toxic. As shown in **FIG. 11** (see also, Table 11, Experiment 3), antibody treatment again with antibody 175A induces strong tumor growth inhibition in established Kasumi-3 tumors.

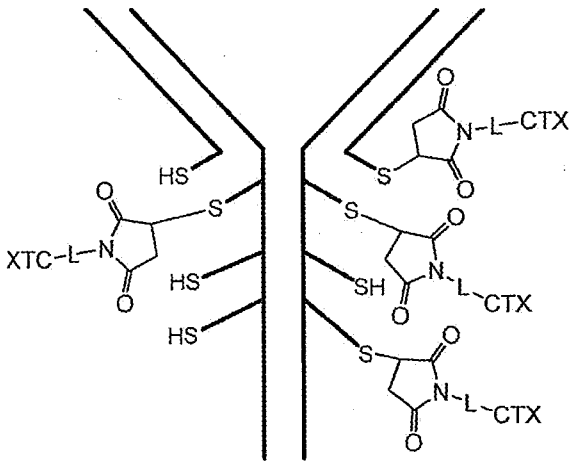
EXAMPLE 6 – PREPARATION AND USE OF ANTIBODY-DRUG CONJUGATES

Antibody-drug conjugates (ADCs) were prepared and used in secondary ADC assays and direct ADC assays with antibodies to C10orf54, as illustrated in the following exemplary generic Scheme A:



Scheme A: ADCs with conventional maleimide linker-drug conjugates

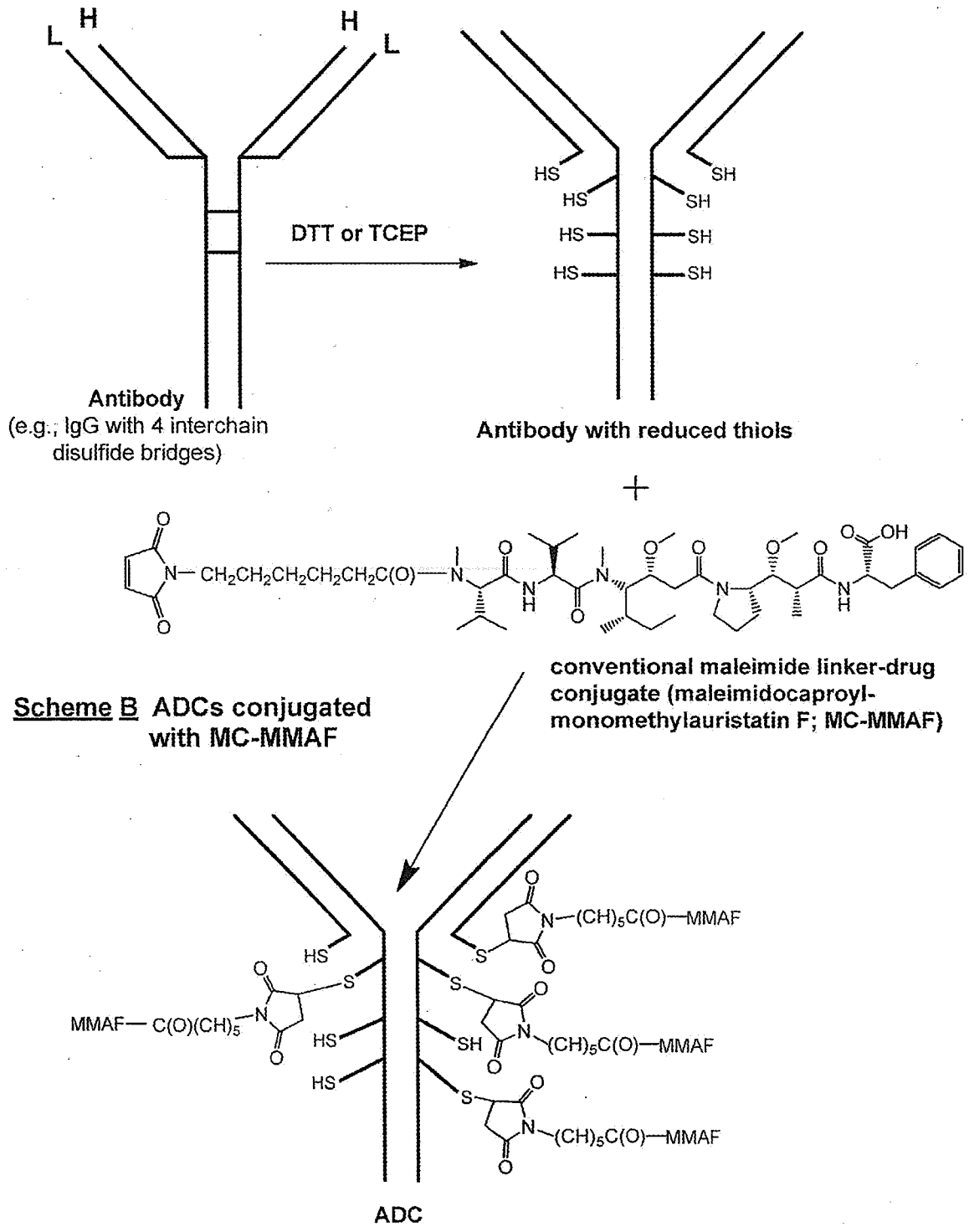
conventional maleimide linker-drug conjugate



ADC

where the depicted bonds of the maleimide linker-drug conjugate indicates possible sites of attachment to the antibody.

Exemplary antibody-drug conjugates were prepared using maleimidocaproyl–monomethylauristatin F (MC-MMAF), as illustrated in the following exemplary Scheme B:



where the depicted bonds of the MC-MMAF linker-drug conjugate indicates possible sites of attachment to the antibody.

An exemplary synthetic scheme is as follows. In a sterile 1.7ml eppendorf tube, 20 mg of antibody at 20 mg/ml concentration in phosphate buffered saline (PBS) pH 7.4 (Gibco, Mg and Ca free) was reacted with 1mM diethylene triamine pentaacetic acid (DTPA) as the chelator. Then 2.75 eq. of tris(2-carboxyethyl)phosphine hydrochloride solution (TCEP HCl) (Sigma ampule 0.5M concentration) or 50 µL of 100 mM dithiothreitol (DTT) was added for an average drug-antibody ratio (DAR) of 4 drugs per antibody and incubated at 37°C for 1 hour. Dithiobisnitro-benzoate (DTNB; Ellman's reagent) colorimetric assay was used to assess free thiols available for conjugation (Ellman et al., *Biochemical Pharmacology* 7:88-95 (1961)). The reduced antibody solution was cooled in an ice-bath at ~ 0°C for 15 minutes. Then 60 µL of MC-MMAF from a 10mM stock solution in DMSO (9.74 mg in 1.074 ml of DMSO for 10 mM) was added and incubated on a roller-plate in a refrigerator at 4°C overnight (or alternatively at 37°C for 2 hours). The DTNB assay was repeated to demonstrate no free thiols remaining (clear means no free thiol and a yellow color indicates remaining free thiols and incomplete conjugation of payload). The concentration of the ADC was obtained via the NanoDrop spectrophotometer. The ADC was stored at 4°C.

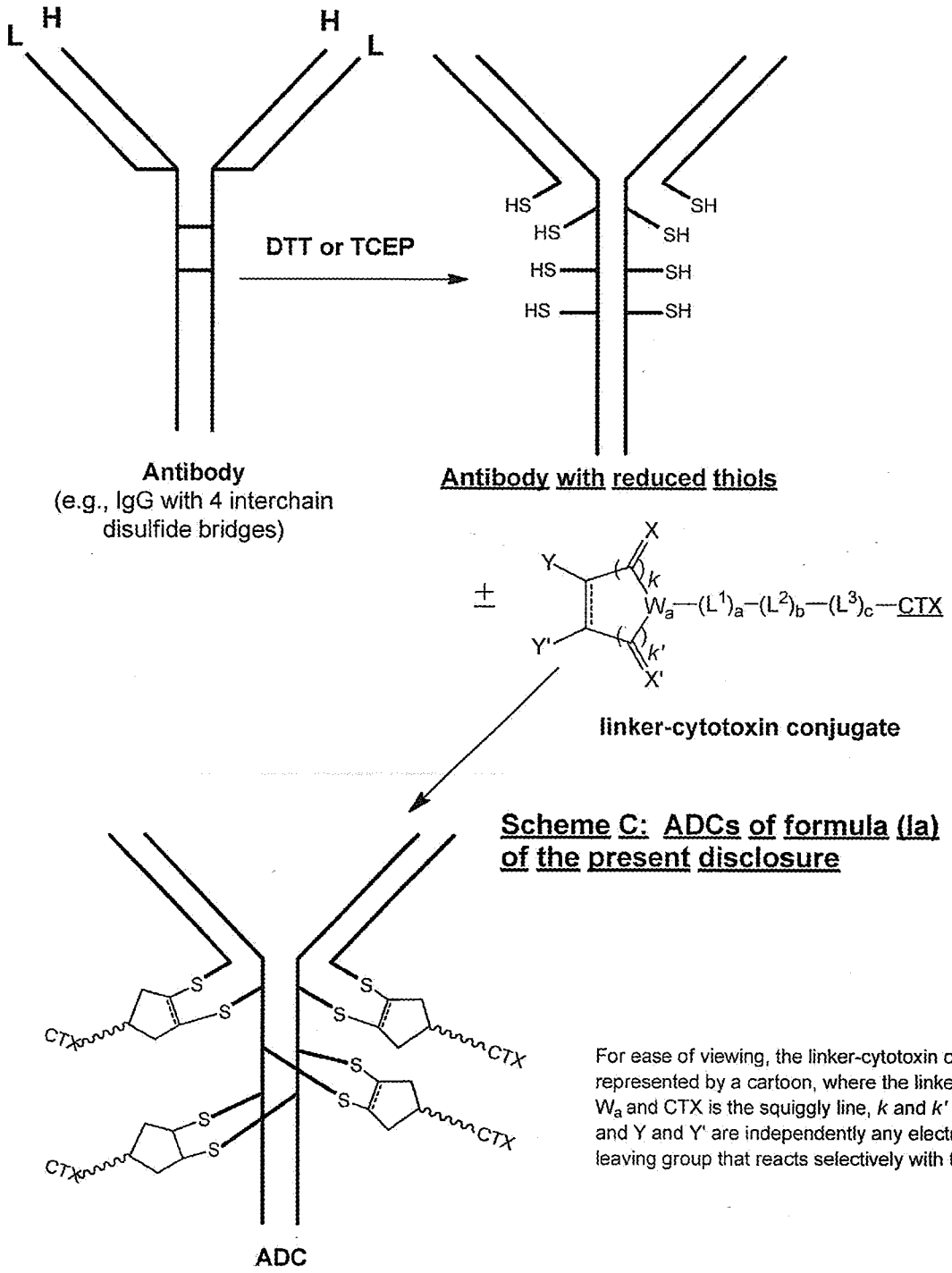
FIG. 12 shows the results of a secondary ADC assay using anti-C10orf54 antibodies in a cell viability assay using a C10orf54 expressing sarcoma line. Anti-C10orf54 antibodies were incubated at a 2:1 ratio with a secondary goat anti mouse antibody conjugated with MMAF. Cells were plated at 1000 cells/well and incubated in the presence of antibodies for 72 hours. The C10orf54 expressing sarcoma cells were killed by the anti-C10orf54 antibodies tested in a concentration-dependent manner.

FIGS. 13-14 show the activity of unconjugated and anti-C10orf54 antibodies directly conjugated with MMAE in cell viability assays using C10orf54 expressing sarcoma lines. For these assays, cells may be plated in varying numbers in the wells and are incubated for various times in the presence or absence of anti- C10orf54 antibodies and ADCs. For example, for the assays shown in **FIG. 13**, cells were plated at 1000 cells/well and incubated in the presence of antibodies for 72 hours. In these *in vitro* cell-based assays, the MMAF conjugated anti-C10orf54 antibodies killed the sarcoma cells in a concentration-dependent manner.

FIG. 15 shows results of treatment with anti-C10orf54 antibodies and ADCs (*e.g.*, unconjugated and MMAF conjugated anti-C10orf54 antibodies) in an animal tumor (*e.g.*, xenograft) model, with C10orf54-expressing and parental sarcoma lines.

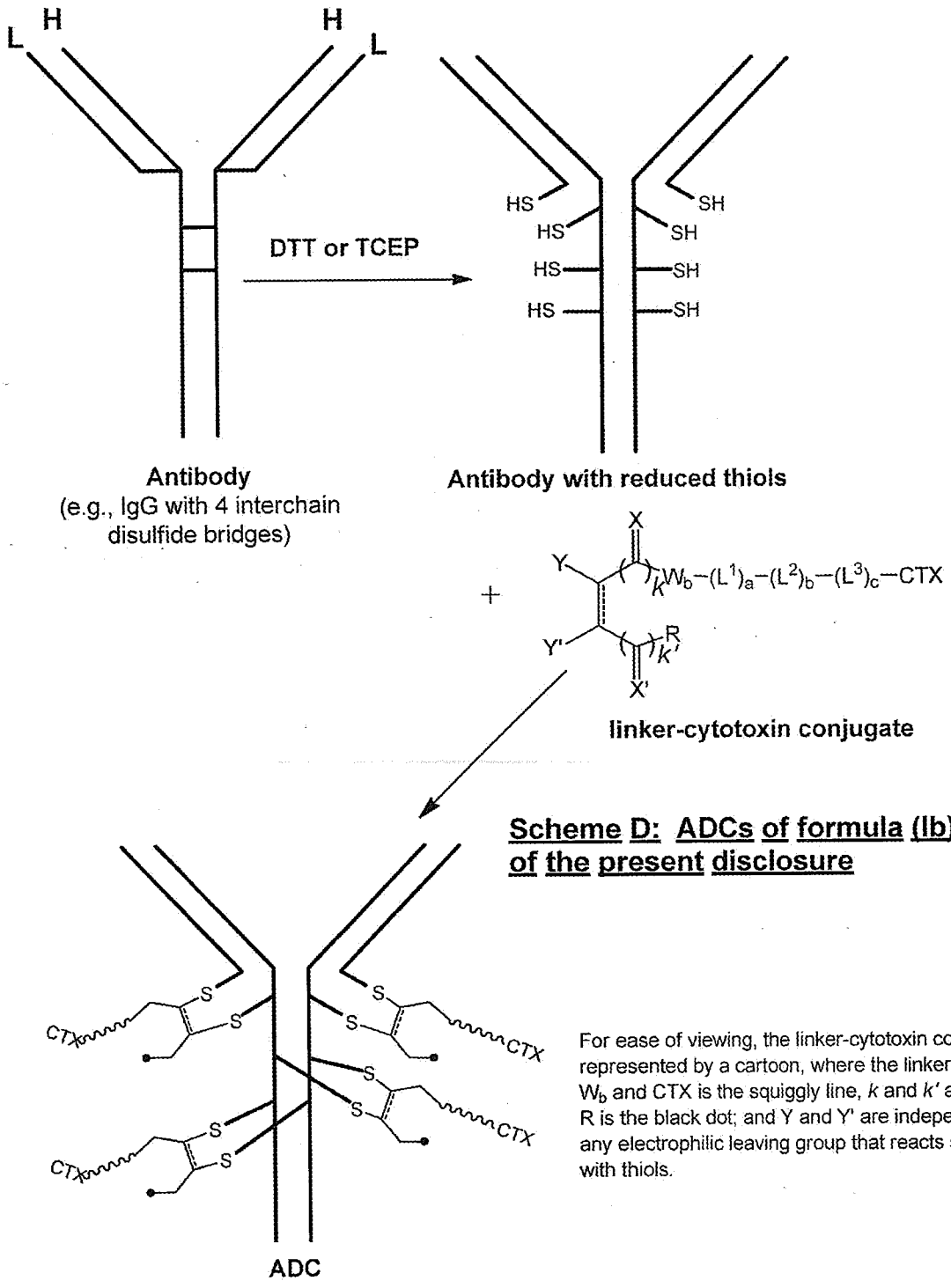
EXAMPLE 7 – METHODS OF SYNTHESIZING ADDITIONAL ANTI-C10ORF54 ANTIBODY-DRUG CONJUGATES

Alternatively, antibody-drug conjugates of formulas (Ia) and (Ib) of the present disclosure may be prepared using, as illustrated in the following Scheme C and D, respectively:



Scheme C: ADCs of formula (Ia) of the present disclosure

For ease of viewing, the linker-cytotoxin conjug represented by a cartoon, where the linker bet W_a and CTX is the squiggly line, *k* and *k'* are b and Y and Y' are independently any electrophil leaving group that reacts selectively with thiols.



Scheme D: ADCs of formula (Ib) of the present disclosure

For ease of viewing, the linker-cytotoxin conjugate is represented by a cartoon, where the linker between W_b and CTX is the squiggly line, *k* and *k'* are both 0, R is the black dot; and Y and Y' are independently any electrophilic leaving group that reacts selectively with thiols.

In Schemes C and D, the depicted bonds of the linker-drug conjugate indicates possible sites of attachment to the antibody.

Antibody-drug conjugates of Schemes C and D may be prepared using, for example, the exemplary synthetic scheme of Example 6, where maleimidocaproyl–

monomethylauristatin F (MC-MMAF) is substituted with the linker-cytotoxin conjugates depicted in the schemes.

Antibody-drug conjugates, as described in this example and herein, are prepared wherein one or more interchain disulfide bonds of the antibody (*e.g.*, four interchain disulfide bonds as depicted in exemplary Schemes C and D above) are conjugated. Antibody-drug conjugates, wherein one or more of the intrachain disulfide bonds of the antibody are conjugated, as described herein, have a preferred antibody-to-drug ratio of four.

The embodiments of the present invention described above are intended to be merely exemplary, and those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, numerous equivalents to the specific procedures described herein. All such equivalents are considered to be within the scope of the present invention and are covered by the following claims. Furthermore, as used in this specification and claims, the singular forms "a," "an" and "the" include plural forms unless the content clearly dictates otherwise. Thus, for example, reference to "an antibody" includes a mixture of two or more such antibodies, and the like. Additionally, ordinarily skilled artisans will recognize that operational sequences must be set forth in some specific order for the purpose of explanation and claiming, but the present invention contemplates various changes beyond such specific order.

The contents of all references described herein are hereby incorporated by reference.

Other embodiments are within the following claims.

WHAT IS CLAIMED:

1 An isolated antibody that binds to C10orf54, said antibody being selected from:

a. an antibody comprising:

i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 36, SEQ ID NO. 37, and SEQ ID NO. 38, and

ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 46, and SEQ ID NO. 47;

b. an antibody comprising:

i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 30, SEQ ID NO. 31, and SEQ ID NO. 32, and

ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 40, and SEQ ID NO. 41; and

c. an antibody comprising:

i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 33, SEQ ID NO. 34, and SEQ ID NO. 35, and

ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 42, SEQ ID NO. 43, and SEQ ID NO. 44.

2 The antibody of claim 1, wherein the antibody is a humanised antibody, a monoclonal antibody, a recombinant antibody, a fusion protein, an antigen binding fragment, a Fab Fragment, F(ab')2 fragment, single chain Fv (sFv), diabody, triabody, or minibody.

3 The antibody of any one of claims 1 or 2 which is a monoclonal antibody.

4 The antibody of any one of claims 1 to 3, wherein the antibody is selected from:

a. an antibody comprising:

i. a VH region having the amino acid sequence SEQ ID NO. 3, and
ii. a VL region having the amino acid sequence SEQ ID NO. 6;

b. an antibody comprising:

i. a VH region having the amino acid sequence SEQ ID NO. 1, and
ii. a VL region having the amino acid sequence SEQ ID NO. 4; and

c. an antibody comprising:

i. a VH region having the amino acid sequence SEQ ID NO. 2, and
ii. a VL region having the amino acid sequence SEQ ID NO. 5.

5 The antibody of any one of claims 1 to 3, wherein the antibody is humanised.

6 The antibody of claim 5, wherein the antibody is selected from:

a. an antibody comprising:

i. a VH region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 20, 21, 22, and 23, and
ii. a VL region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 28 and 29;

b. an antibody comprising:

i. a VH region having an amino acid sequence selected from the group consisting of SEQ ID NOs. NO. 12, 13, 14, 15, and
ii. a VL region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 24 and 25; and

c. an antibody comprising:

i. a VH region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 16, 17, 18, 19, and
ii. a VL region having an amino acid sequence selected from the group consisting of SEQ ID NOs.26 and 27.

7 An antibody of any one of claims 1 to 6, wherein the antibody is conjugated or recombinantly fused to a diagnostic agent, detectable agent or therapeutic agent.

8 An isolated nucleic acid molecule encoding an antibody according to any one of claims 1 to 6, said nucleic acid molecule comprising or consisting of a nucleic acid sequence that encodes the VH region and/or VL region of said antibody.

9 A vector comprising the nucleic acid molecule of claim 8.

10 A host cell comprising the vector of claim 9.

11 A method of producing an antibody comprising 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 claims 1 to 6 and a pharmaceutically-acceptable excipient.

13 The antibody of any one of claims 1 to 6 or the composition of claim 12 for use as a medicament.

14 Use of the antibody of any one of claims 1 to 6 or the composition of claim 12 in the manufacture of a medicament for treating or alleviating one or more symptoms of a disease, wherein the disease is a cancer or graft-versus-host disease.

15 The use of claim 14, wherein the cancer is a leukemia, a bladder cancer or a fibrosarcoma.

16 The antibody of any one of claims 1 to 6 or the composition of claim 12 for use in treating or alleviating one or more symptoms of a cancer by stimulating an immune response in a subject.

17 Use of the anti-C10orf54 antibody of any one of claims 1 to 6 or the antibody-drug conjugate of claim 7, in the manufacture of a medicament for treating cancer.

18 Use of the anti-C10orf54 antibody of any one of claims 1 to 6 or the antibody-drug conjugate of claim 7, in the manufacture of a medicament for killing a tumor cell.

ANTI-C10ORF54 ANTIBODIES AND USES THEREOF

ABSTRACT

The present disclosure relates generally to anti-C10orf54 antibodies, including antibody-drug conjugates comprising the antibodies, and methods of their use.

FIG. 1A