CLAIMS

What is claimed is:

1. An isolated anti-CD19 antibody or an antigen binding fragment thereof, comprising:
    a) heavy chain CDRs 1-3 of SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
    b) heavy chain CDRs 1-3 of SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, respectively;
    c) heavy chain CDRs 1-3 of SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 16, SEQ ID NO: 17, and SEQ ID NO: 18, respectively;
    d) heavy chain CDRs 1-3 of SEQ ID NO: 19, SEQ ID NO: 20, and SEQ ID NO: 21, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
    e) heavy chain CDRs 1-3 of SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
    f) heavy chain CDRs 1-3 of SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
    g) heavy chain CDRs 1-3 of SEQ ID NO: 28, SEQ ID NO: 29, and SEQ ID NO: 30, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
    h) heavy chain CDRs 1-3 of SEQ ID NO: 31, SEQ ID NO: 32, and SEQ ID NO: 33, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
    i) heavy chain CDRs 1-3 of SEQ ID NO: 34, SEQ ID NO: 35, and SEQ ID NO: 36, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
    j) heavy chain CDRs 1-3 of SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 40, SEQ ID NO: 41, and SEQ ID NO: 42, respectively;
    k) heavy chain CDRs 1-3 of SEQ ID NO: 43, SEQ ID NO: 44, and SEQ ID NO: 45,

respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;

l) heavy chain CDRs 1-3 of SEQ ID NO: 136, SEQ ID NO: 2, and SEQ ID NO: 3, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 137, SEQ ID NO: 138, and SEQ ID NO: 139, respectively;

m) heavy chain CDRs 1-3 of SEQ ID NO: 7, SEQ ID NO: 140，and SEQ ID NO: 9, respectively; and kappa light CDRs 1-3 of SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, respectively; or

n) heavy chain CDRs 1-3 of SEQ ID NO: 13, SEQ ID NO: 141, and SEQ ID NO: 15, respectively; and kappa light chain CDRs 1-3 of SEQ ID NO: 16, SEQ ID NO: 17, and SEQ ID NO: 18, respectively.

2. The antibody or an antigen binding fragment thereof of claim 1, comprising:

a) a heavy chain variable region comprising SEQ ID NO: 94 and a kappa light chain variable region comprising SEQ ID NO: 96;

b) a heavy chain variable region comprising SEQ ID NO: 98 and a kappa light chain variable region comprising SEQ ID NO: 100;

c) a heavy chain variable region comprising SEQ ID NO: 102 and a kappa light chain variable region comprising SEQ ID NO: 104;

d) a heavy chain variable region comprising SEQ ID NO: 106 and a kappa light chain variable region comprising SEQ ID NO: 96;

e) a heavy chain variable region comprising SEQ ID NO: 108 and a kappa light chain variable region comprising SEQ ID NO: 96;

f) a heavy chain variable region comprising SEQ ID NO: 110 and a kappa light chain variable region comprising SEQ ID NO: 96;

g) a heavy chain variable region comprising SEQ ID NO: 112 and a kappa light chain variable region comprising SEQ ID NO: 96;

h) a heavy chain variable region comprising SEQ ID NO: 114 and a kappa light chain variable region comprising SEQ ID NO: 96;

i) a heavy chain variable region comprising SEQ ID NO: 116 and a kappa light chain variable region comprising SEQ ID NO: 96;

j) a heavy chain variable region comprising SEQ ID NO: 118 and a kappa light chain variable region comprising SEQ ID NO: 120;

k) a heavy chain variable region comprising SEQ ID NO: 122 and a kappa light chain

variable region comprising SEQ ID NO: 96;

l) a heavy chain variable region comprising SEQ ID NO: 124 and a kappa light chain variable region comprising SEQ ID NO: 126;

m) a heavy chain variable region comprising SEQ ID NO: 128 and a kappa light chain variable region comprising SEQ ID NO: 130; or

n) a heavy chain variable region comprising SEQ ID NO: 132 and a kappa light chain variable region comprising SEQ ID NO: 134.

3. The antibody or antigen-binding fragment thereof of claim 1, further comprising an immunoglobulin constant region, optionally a constant region of IgG, optionally a constant region of human IgG1.
4. The antibody or an antigen binding fragment thereof of claim 1, which is a humanized antibody.
5. The antibody or antigen-binding fragment thereof of claim 1, which is a bispecific antibody, a camelized single domain antibody, a diabody, a scFv, an scFv dimer, a BsFv, a dsFv, a (dsFv)2, a dsFv-dsFv', an Fv fragment, a Fab, a Fab', a F(ab')2, a ds diabody, a nanobody, a domain antibody, or a bivalent domain antibody.
6. The antibody or antigen-binding fragment thereof of claim 1 linked to one or more conjugates.
7. An isolated polynucleotide sequence encoding the antibody or an antigen binding fragment thereof of claim 1.
8. A vector comprising the isolated polynucleotide of claim 7.
9. A host cell comprising the vector of claim 8.
10. A method of expressing the antibody or antigen-binding fragment thereof of claim 1, comprising culturing a host cell comprising a vector comprising an isolated polynucleotide sequence encoding the antibody or antigen binding fragment thereof of claim 4 under the condition at which the vector is expressed.
11. An antibody-drug conjugate comprising one or more drug moieties covalently attached to the antibody or antigen-binding fragment of claim 1 either directly or via a linker, wherein the drug moiety is a cytotoxin or a radioactive isotope.
12. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of claim 1 or an antibody-drug conjugate comprising one or more drug moieties covalently attached to the antibody or antigen-binding fragment thereof of claim 4, and a pharmaceutically acceptable carrier.
13. Use of an antibody or antigen-binding fragment thereof of claim 1, or an antibody-drug

conjugate comprising one or more drug moieties covalently attached to the antibody or antigen-binding fragment thereof of claim 4, in the manufacture of a medicament for the treatment of CD19 related disease or condition in a subject.

14. A chimeric antigen receptor (CAR) comprising the antigen binding fragment of claim 1 and a T-cell activation moiety, wherein the T-cell activation moiety comprises a transmembrane domain of a T cell receptor and an intracellular signal transduction domain of a T cell receptor.
15. A nucleic acid sequence encoding the CAR of claim 14.
16. A vector comprising the nucleic acid sequence of claim 15.
17. An isolated T cell which expresses the CAR of claim 14.
18. Use of a T cell of claim 17 in the manufacture of a medicament for stimulating a T cell-mediated immune response to a CD19 expressing target in a subject.
19. A kit comprising the antibody or antigen-binding fragment thereof of claim 1, useful in detecting presence or amount of CD19 in a sample, or useful in diagnosing a CD19 related disease or condition in a subject.