

CLAIMS

What is claimed is:

- ~~1.—An isolated antibody or an antigen binding fragment thereof, comprising one or more heavy chain complementarity determining region (CDR) sequences selected from the group consisting of: SEQ ID NOs: 1, 2, 3, 7, 8, 9, 13, 14, 15, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 43, 44, 45, 136, 140, and 141, and/or one or more kappa light chain CDR sequences selected from the group consisting of: SEQ ID NOs: 4, 5, 6, 10, 11, 12, 16, 17, 18, 40, 41, 42, 137, 138, and 139.~~
- ~~2.—The antibody or an antigen binding fragment thereof of claim 1, comprising a heavy chain variable region selected from the group consisting of:~~
 - ~~a)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3;~~
 - ~~b)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9;~~
 - ~~c)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15;~~
 - ~~d)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 19, SEQ ID NO: 20, and SEQ ID NO: 21;~~
 - ~~e)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24;~~
 - ~~f)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27;~~
 - ~~g)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 28, SEQ ID NO: 29, and SEQ ID NO: 30;~~
 - ~~h)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 31, SEQ ID NO: 32, and SEQ ID NO: 33;~~
 - ~~i)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 34, SEQ ID NO: 35, and SEQ ID NO: 36;~~
 - ~~j)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39;~~
 - ~~k)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 43, SEQ ID NO: 44, and SEQ ID NO: 45;~~
 - ~~l)—a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 136, SEQ ID NO: 2, and SEQ ID NO: 3;~~

- m) ~~a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 7, SEQ ID NO: 140, and SEQ ID NO: 9; and~~
 - n) ~~a heavy chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 13, SEQ ID NO: 141, and SEQ ID NO: 15.~~
3. ~~The antibody or an antigen binding fragment thereof of any of the preceding claims, comprising a kappa light chain variable region selected from the group consisting of:~~
- a) ~~a kappa light chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6;~~
 - b) ~~a kappa light chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12;~~
 - c) ~~a kappa light chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18;~~
 - d) ~~a kappa light chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 40, SEQ ID NO: 41, and SEQ ID NO: 42; and~~
 - e) ~~a kappa light chain variable region comprising 1, 2, or 3 CDR sequences selected from SEQ ID NO: 137, SEQ ID NO: 138, and SEQ ID NO: 139.~~
- 4.1. The An isolated anti-CD19 antibody or an antigen binding fragment thereof ~~of any of the preceding claims~~, comprising:
- a) ~~a heavy chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected fromof~~ SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3, respectively; and ~~a kappa light chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
 - b) ~~a heavy chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected fromof~~ SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9, respectively; and ~~a kappa light chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected fromof~~ SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, respectively;
 - c) ~~a heavy chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected fromof~~ SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15, respectively; and ~~a kappa light chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected fromof~~ SEQ ID NO: 16, SEQ ID NO: 17, and SEQ ID NO: 18, respectively;
 - d) ~~a heavy chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected fromof~~ SEQ ID NO: 19, SEQ ID NO: 20, and SEQ ID NO: 21, respectively; and ~~a kappa light chain variable region comprising 1, 2, or 3 CDRs 1-3 sequences selected~~

- ~~fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
- e) ~~a-heavy chain-variable-region-comprising 1, 2, or 3 CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3 CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
- f) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
- g) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 28, SEQ ID NO: 29, and SEQ ID NO: 30, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
- h) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 31, SEQ ID NO: 32, and SEQ ID NO: 33, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
- i) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 34, SEQ ID NO: 35, and SEQ ID NO: 36, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
- j) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 40, SEQ ID NO: 41, and SEQ ID NO: 42, respectively;
- k) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 43, SEQ ID NO: 44, and SEQ ID NO: 45, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively;
- l) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 136, SEQ ID NO: 2, and SEQ ID NO: 3, respectively; and a
kappa light chain ~~variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~
~~fromof~~ SEQ ID NO: 137, SEQ ID NO: 138, and SEQ ID NO: 139, respectively;
- m) ~~a-heavy chain variable-region-comprising 1, 2, or 3-CDRs 1-3 sequences-selected~~

- ~~from~~ SEQ ID NO: 7, SEQ ID NO: 140, and SEQ ID NO: 9, respectively; and a kappa light ~~chain-variable-region comprising 1, 2, or 3 CDRs 1-3 sequences selected from~~ SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, respectively; or
- n) ~~a heavy chain-variable-region comprising 1, 2, or 3 CDRs 1-3 sequences selected from~~ SEQ ID NO: 13, SEQ ID NO: 141, and SEQ ID NO: 15, respectively; and ~~a kappa light chain-variable-region comprising 1, 2, or 3 CDRs 1-3 sequences selected from~~ SEQ ID NO: 16, SEQ ID NO: 17, and SEQ ID NO: 18, respectively.
5. ~~The antibody or an antigen binding fragment thereof of any of the preceding claims, comprising:~~
- a) ~~a heavy chain CDR1 sequence selected from SEQ ID NO: 1, SEQ ID NO: 7, SEQ ID NO: 13, SEQ ID NO: 19, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 28, SEQ ID NO: 31, SEQ ID NO: 34, SEQ ID NO: 37, SEQ ID NO: 43, and SEQ ID NO: 136;~~
- b) ~~a heavy chain CDR2 sequence selected from SEQ ID NO: 2, SEQ ID NO: 8, SEQ ID NO: 14, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 26, SEQ ID NO: 29, SEQ ID NO: 32, SEQ ID NO: 35, SEQ ID NO: 38, SEQ ID NO: 44, SEQ ID NO: 140, and SEQ ID NO: 141 and~~
- c) ~~a heavy chain CDR3 sequence selected from SEQ ID NO: 3, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 21, SEQ ID NO: 24, SEQ ID NO: 27, SEQ ID NO: 30, SEQ ID NO: 33, SEQ ID NO: 36, SEQ ID NO: 39, and SEQ ID NO: 45.~~
6. ~~The antibody or an antigen binding fragment thereof of any of the preceding claims, comprising:~~
- a) ~~a light chain CDR1 sequence selected from SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 40, and SEQ ID NO: 137;~~
- b) ~~a light chain CDR2 sequence selected from SEQ ID NO: 5, SEQ ID NO: 11, SEQ ID NO: 17, SEQ ID NO: 41, and SEQ ID NO: 138; and~~
- c) ~~a light chain CDR3 sequence selected from SEQ ID NO: 6, SEQ ID NO: 12, SEQ ID NO: 18, SEQ ID NO: 42, and SEQ ID NO: 139.~~
7. ~~The antibody or an antigen binding fragment thereof of any of the preceding claims, comprising:~~
- a) ~~a heavy chain CDR1 sequence selected from SEQ ID NO: 1, SEQ ID NO: 7, SEQ ID NO: 13, SEQ ID NO: 19, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 28, SEQ ID NO: 31, SEQ ID NO: 34, SEQ ID NO: 37, SEQ ID NO: 43, and SEQ ID NO: 136;~~
- b) ~~a heavy chain CDR2 sequence selected from SEQ ID NO: 2, SEQ ID NO: 8, SEQ ID~~

~~NO: 14, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 26, SEQ ID NO: 29, SEQ ID NO: 32, SEQ ID NO: 35, SEQ ID NO: 38, SEQ ID NO: 44, SEQ ID NO: 140, and SEQ ID NO: 141~~

- ~~e) a heavy chain CDR3 sequence selected from SEQ ID NO: 3, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 21, SEQ ID NO: 24, SEQ ID NO: 27, SEQ ID NO: 30, SEQ ID NO: 33, SEQ ID NO: 36, SEQ ID NO: 39, and SEQ ID NO: 45;~~
 - ~~d) a light chain CDR1 sequence selected from SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 40, and SEQ ID NO: 137;~~
 - ~~e) a light chain CDR2 sequence selected from SEQ ID NO: 5, SEQ ID NO: 11, SEQ ID NO: 17, SEQ ID NO: 41, and SEQ ID NO: 138; and~~
 - ~~f) a light chain CDR3 sequence selected from SEQ ID NO: 6, SEQ ID NO: 12, SEQ ID NO: 18, SEQ ID NO: 42, and SEQ ID NO: 139.~~
- ~~8. The antibody or an antigen binding fragment thereof of any of the preceding claims, further comprising one or more heavy chain framework region (FR) sequences selected from the group consisting of: SEQ ID NO: 54, 55, 56, 57, 70, 71, 72, 73, 86, 87, 88, and 89, and/or one or more kappa light chain framework region (FR) sequences selected from SEQ ID NO: 58, 59, 60, 61, 74, 75, 76, 77, 90, 91, 92, and 93.~~
- ~~9. The antibody or an antigen binding fragment thereof of any of the preceding claims, further comprising a heavy chain FR1 sequence selected from SEQ ID NO: 54, 70 and 86; a heavy chain FR2 sequence selected from SEQ ID NO: 55, 71 and 87; a heavy chain FR3 sequence selected from SEQ ID NO: 56, 72 and 88; and a heavy chain FR4 sequence selected from SEQ ID NO: 57, 73 and 89.~~
- ~~10. The antibody or an antigen binding fragment thereof of any of the preceding claims, further comprising a light chain FR1 sequence selected from SEQ ID NO: 58, 74 and 90; a light chain FR2 sequence selected from SEQ ID NO: 59, 75 and 91; a light chain FR3 sequence selected from SEQ ID NO: 60, 76 and 92; and a light chain FR4 sequence selected from SEQ ID NO: 61, 77 and 93.~~
- ~~11. The antibody or an antigen binding fragment thereof of any of the preceding claims, comprising a heavy chain variable region selected from the group consisting of: SEQ ID NO: 94, SEQ ID NO: 98, SEQ ID NO: 102, SEQ ID NO: 106, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 118, SEQ ID NO: 122, SEQ ID NO: 124, SEQ ID NO: 128, SEQ ID NO: 132 and a homologue sequence thereof having at least 80% sequence identity.~~
- ~~12. The antibody or an antigen binding fragment thereof of any of the preceding claims,~~

~~comprising a kappa light chain variable region selected from the group consisting of: SEQ ID NO: 96, SEQ ID NO: 100, SEQ ID NO: 104, SEQ ID NO: 120, SEQ ID NO: 126, SEQ ID NO: 130, SEQ ID NO: 134 and a homologue sequence thereof having at least 80% sequence identity.~~

13.2. The antibody or an antigen binding fragment thereof of ~~any of the preceding~~ claims 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.

- ~~14. The antibody or antigen-binding fragment thereof of any of the preceding claims, further comprising one or more amino acid residue substitutions yet retains specific binding affinity to CD19.~~
- ~~15. The antibody or antigen-binding fragment thereof of claim 14, wherein the substitution is in one or more CDR sequences, and/or in one or more FR sequences, in one or both variable region sequences, and/or in Fc region.~~
- ~~16. The antibody or antigen-binding fragment thereof of claim 14 or 15, wherein the substitution confers one or more desirable properties selected from:~~
- ~~a) improving binding affinity to CD19;~~
 - ~~b) introducing or removing a glycosylation site;~~
 - ~~c) introducing a free cysteine residue;~~
 - ~~d) enhancing or reducing ADCC or CDC;~~
 - ~~e) increasing serum half life; and~~
 - ~~f) increasing FcRn binding.~~
- 17.3. The antibody or antigen-binding fragment thereof of ~~any of the preceding~~ claims 1, further comprising an immunoglobulin constant region, optionally a constant region of IgG, optionally a constant region of human IgG1.
- 18.4. The antibody or an antigen binding fragment thereof ~~of any of the preceding~~ claims 1, which is a humanized antibody.
- 19.5. The antibody or antigen-binding fragment thereof of ~~any of the preceding~~ claims 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.
- ~~20. The antibody or an antigen-binding fragment thereof of any of the preceding claims, which is bispecific.~~
- 21.6. The antibody or antigen-binding fragment thereof of ~~any of the preceding~~ claims 1 linked to one or more conjugates.
- ~~22. The antibody or antigen-binding fragment thereof of claim 21, wherein the conjugate comprises a chemotherapeutic agent, a toxin, a radioactive isotope, a lanthanide, a luminescent label, a fluorescent label, or an enzyme-substrate label.~~
- ~~23. The antibody or an antigen binding fragment thereof any of the preceding claims, capable of specifically binding to CD19, optionally CD19 derived from human, or monkey.~~

- ~~24. The antibody or an antigen binding fragment thereof of any of the preceding claims, capable of specifically binding to human CD19 expressed on a cell at a K_D value of no more than 5×10^{-9} M as measured by flow cytometry assay.~~
- ~~25. The antibody or an antigen binding fragment thereof of any of the preceding claims, capable of specifically binding to human CD19 expressed on a cell at an EC_{50} of no more than 0.9 nM, or no more than 1 nM by flow cytometry assay.~~
- ~~26. The antibody or an antigen binding fragment thereof of any of the preceding claims, capable of specifically binding to Cynomolgus monkey CD19 expressed on a cell at an EC_{50} of no more than 3 nM by flow cytometry assay.~~
- ~~27. The antibody or an antigen binding fragment thereof of any of the preceding claims, capable of being internalized by a CD19-expressing cell at an EC_{50} of no more than 50pM by Fab-Zap assay.~~
- ~~28. An antibody or an antigen binding fragment thereof, which competes for the same epitope with W7011-4.155.8.~~
- 29.7. An isolated polynucleotide sequence encoding the antibody or an antigen binding fragment thereof of ~~any of the preceding claims~~ 1.
- ~~30. The isolated polynucleotide sequence of claim 29, which comprises a nucleotide sequence selecting from a group consisting of SEQ ID NO: 95, 99, 103, 107, 109, 111, 113, 115, 117, 119, 123, 125, 129 and 133, and/or a nucleotide sequence selecting from a group consisting of SEQ ID NO: 97, 101, 105, 121, 127, 131 and 135, or a homologue sequence thereof having at least 80% sequence identity but encoding the same protein sequence.~~
- 31.8. A vector comprising the isolated polynucleotide of claim ~~29 or 30~~ 7.
- 32.9. A host cell comprising the vector of claim ~~31~~ 8.
- 33.10. A method of expressing the antibody or antigen-binding fragment thereof of ~~any of claims 1-28, comprising culturing the~~ a host cell comprising a ~~claim 32 under the condition at which the~~ vector ~~of claim 31 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.
- 34.11. An antibody-drug conjugate comprising one or more drug moieties covalently attached to the antibody or antigen-binding fragment of ~~any of claims 1-28~~ either directly or via a linker, wherein the drug moiety is a cytotoxin or a radioactive isotope.
- ~~35. The antibody drug conjugate of claim 34, wherein the linker is a hydrazone linker, a~~

~~disulfide linker, a bifunctional linker, dipeptide linker, glucuronide linker, a thioether linker, optionally the linker is SMCC.~~

~~36. The antibody drug conjugate of claim 34 or 35, wherein at least one drug moiety is attached to a specific site of the antibody or antigen-binding fragment thereof, optionally the specific site is a cysteine residue.~~

~~37. The antibody drug conjugate of claim 36, wherein the drug moiety is a cytotoxin or a radioactive isotope.~~

~~38. The antibody or antigen-binding fragment thereof of claim 21, wherein the conjugate is a toxin, optionally a cytotoxin, a DNA-alkylators, a topoisomerase inhibitor, a tubulin binders, or other anticancer drugs, optionally a maytansinoid cytotoxic agent, optionally the toxin is DM1.~~

~~39.12.~~ A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of ~~any of~~ claims 1-28 or ~~the an~~ antibody-drug conjugate comprising one or more drug moieties covalently attached to the antibody or antigen-binding fragment thereof of ~~any of~~ claims 34-37, and a pharmaceutically acceptable carrier.

~~40.13.~~ A method of treating a CD19 related disease or condition in a subject, comprising administering a therapeutically effective amount of the Use of an antibody or antigen-binding fragment thereof of ~~any of~~ claims 1-28, ~~the or an~~ antibody-drug conjugate comprising one or more drug moieties covalently attached to the antibody or antigen-binding fragment thereof of ~~any of~~ claims 34-37, or the pharmaceutical composition of claim 39 to the subject in the manufacture of a medicament for the treatment of CD19 related disease or condition in a subject.

~~41. The method of claim 40, wherein the disease or condition is cancer.~~

~~42. The method of claim 41, wherein the cancer is lymphoma, lung cancer, liver cancer, cervical cancer, colon cancer, breast cancer, ovarian cancer, pancreatic cancer, melanoma, glioblastoma, prostate cancer, esophageal cancer or gastric cancer.~~

~~43. The method of claim 40, wherein the disease or condition is B-cell lymphoma, optionally Hodgkin lymphoma or non-Hodgkin lymphoma, wherein the non-Hodgkin lymphoma comprises: Diffuse large B-cell lymphoma (DLBCL), Follicular lymphoma, Marginal zone B-cell lymphoma (MZL), Mucosa Associated Lymphatic Tissue lymphoma (MALT), Small lymphocytic lymphoma (chronic lymphocytic leukemia, CLL), Mantle cell lymphoma (MCL), Acute Lymphoblastic Leukemia (ALL), or Waldenstrom's Macroglobulinemia (WM).~~

~~44. The method of claim 40, wherein the administration is via oral, nasal, intravenous,~~

~~subcutaneous, sublingual, or intramuscular administration.~~

~~45. The method of claim 40, wherein the subject is human.~~

~~46. A method of modulating CD19 activity in a CD19-expressing cell, comprising exposing the CD19-expressing cell to the antibody or antigen-binding fragment thereof of any of claims 1-28.~~

~~47. An in vivo or in vitro method of killing a CD19-expressing cell, comprising contacting the CD19-expressing cell with the antibody-drug conjugate of any of claims 34-37.~~

~~48. A method of detecting presence or amount of CD19 in a sample, comprising contacting the sample with the antibody or antigen-binding fragment thereof of any of claims 1-28, and determining the presence or the amount of CD19 in the sample.~~

~~49. A method of diagnosing a CD19-related disease or condition in a subject, comprising:
a) obtaining a sample from the subject; b) contacting the sample with the antibody or antigen-binding fragment thereof of any of claims 1-28; c) determining presence or amount of CD19 in the sample; d) correlating the presence or amount of CD19 to a disease or a condition in the subject.~~

~~50. Use of the antibody or antigen-binding fragment thereof of any of claims 1-28, the antibody-drug conjugate of any of claims 34-37, or the pharmaceutical composition of claim 39 in the manufacture of a medicament for treating a disease or condition in a subject in need thereof, wherein the treating comprising: administering a therapeutically effective amount of the antibody or antigen-binding fragment thereof to the subject.~~

~~51. Use of the antibody or antigen-binding fragment thereof of any of claims 1-28 in the manufacture of a diagnostic reagent for diagnosing CD19-related disease or condition.~~

~~52.14.~~ A chimeric antigen receptor (CAR) comprising the antigen binding fragment of ~~any of claims 1-28~~ 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.

~~53. The chimeric antigen receptor (CAR) of claim 52, wherein the antigen binding fragment is a scFv.~~

~~54.15.~~ A nucleic acid sequence encoding the CAR of claim ~~52~~14.

~~55. The nucleic acid sequence of claim 54, comprising the polynucleotide sequence of claims 29 or 30 operably linked to a second polynucleotide sequence encoding a transmembrane domain of the T cell receptor and a signal transduction domain of the T cell receptor.~~

~~56.16.~~ A vector comprising the nucleic acid sequence of claim ~~54 or 55~~15.

57.17. An isolated T cell which expresses the CAR of claim 5214.

18. ~~A method for stimulating a T-cell mediated immune response to a CD19-expressing target in a subject, the method comprising administering to the subject an effective amount of the~~Use of a T cell of claim 5717 in the manufacture of a medicament for stimulating a T cell-mediated immune response to a CD19 expressing target in a subject.

58.19. 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.