

CLAIMS

1. A CD19 antibody or antigen-binding fragment thereof comprising:
(a) a heavy chain variable complementarity determining region (CDR) sequences of SYGMH (SEQ ID NO: 1) (HCDR1), LIWYDGSNKYYADSVKG (SEQ ID NO: 2) (HCDR2) and PVEGLLRGFDY (SEQ ID NO: 3) (HCDR3); and
- ~~2. The CD19 antibody or antigen-binding fragment thereof of claim 1, further comprising:~~
(b) a light chain variable region with complementarity determining region (CDR) sequences of :
i. RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGAVPIT (SEQ ID NO: 12) (LCDR3); or
- ~~3. The CD19 antibody or antigen-binding fragment thereof of claim 1, further comprising:~~
~~a light chain variable region with complementarity determining region (CDR) sequences of~~ ii. RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQVDSLHPFT (SEQ ID NO: 13) (LCDR3); or
- ~~4. The CD19 antibody or antigen-binding fragment thereof of claim 1, further comprising:~~
~~a light chain variable region with complementarity determining region (CDR) sequences of~~ iii. RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGGVPLT (SEQ ID NO: 14) (LCDR3); or
- ~~5. The CD19 antibody or antigen-binding fragment thereof of claim 1, further comprising:~~
~~a light chain variable region with complementarity determining region (CDR) sequences of~~ iv. RASQSVSSSYLA (SEQ ID NO: 8) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQLFDSPYT (SEQ ID NO: 15) (LCDR3); or
- ~~6. The CD19 antibody or antigen-binding fragment thereof of claim 1, further comprising:~~

~~a light chain variable region with complementarity determining region (CDR) sequences
of fv. RASQSVRSSYLA (SEQ ID NO: 8) (LCDR1), GASSRAT (SEQ ID NO: 9)
(LCDR2), and QQAGVPPLT (SEQ ID NO: 16) (LCDR3); or:~~

~~7. The CD19 antibody or antigen-binding fragment thereof of claim 1, further
comprising:~~

~~a light chain variable region with complementarity determining region (CDR) sequences
of vi. RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9)
(LCDR2), and QQAGGVPPFT (SEQ ID NO: 17) (LCDR3); or:~~

~~8. The CD19 antibody or antigen-binding fragment thereof of claim 1, further
comprising:~~

~~a light chain variable region with complementarity determining region (CDR)
sequences of vii. RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASNRAT
(SEQ ID NO: 10) (LCDR2), and QQAGVFPFT (SEQ ID NO: 18) (LCDR3); or:~~

~~9. The CD19 antibody or antigen-binding fragment thereof of claim 1, further
comprising:~~

~~a light chain variable region with complementarity determining region (CDR) sequences
of viii. RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASRRAT (SEQ ID NO: 11)
(LCDR2), and QQAGIPPYT (SEQ ID NO: 19) (LCDR3).~~

~~2.10.~~ The CD19 antibody or antigen-binding fragment thereof of claim 1, comprising
an immunoglobulin light chain variable (V_L) region comprising an amino acid
sequence that is at least 90% identical to SEQ ID NO: 20-27; and
an immunoglobulin heavy chain variable (V_H) region comprising an amino
acid sequence that is at least 90% identical to SEQ ID NO: 5.

~~11. A CD19 antibody or antigen-binding fragment thereof comprising:~~

~~an immunoglobulin light chain variable (V_L) region comprising an amino acid
sequence that is at least 90% identical to SEQ ID NOs: 20-27; and
an immunoglobulin heavy chain variable (V_H) region comprising an amino
acid sequence that is at least 90% identical to SEQ ID NO: 5.~~

~~312.~~ The CD19 antibody or antigen-binding fragment thereof of claims 1 ~~or 2-41~~, wherein the V_L region comprises an amino acid sequence that is at least 95% identical to SEQ ID NOs: 20-27, optionally wherein the amino acid sequence that is identical to one of SEQ ID NOs: 20-27.

~~13.~~ ~~The CD19 antibody or antigen-binding fragment thereof of claim 12, wherein the V_L region comprises an amino acid sequence that is identical to SEQ ID NOs: 20-27.~~

~~414.~~ The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the V_H region comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 5, optionally wherein the amino acid sequence that is identical to SEQ ID NO: 5.

~~15.~~ ~~The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the V_H region comprises an amino acid sequence that is identical to SEQ ID NO: 5.~~

~~516.~~ The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the V_L region comprises an amino acid sequence ~~that~~ is identical to one of SEQ ID NOs:20-27 and the V_H region is identical to SEQ ID NO: 5.

~~617.~~ The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the CD19 antibody or fragment thereof is selected from the group consisting of an IgA antibody, IgG antibody, IgE antibody, IgM antibody, bi- or multi-specific antibody, Fab fragment, Fab' fragment, F(ab')₂ fragment, Fd' fragment, Fd fragment, isolated CDRs or sets thereof; single-chain variable fragment (scFv), polypeptide-Fc fusion, single domain antibody, cameloid antibody; masked antibody, Small Modular ImmunoPharmaceutical ("SMIPsTM"), single chain, Tandem diabody, VHHs, Anticalin, Nanobody, minibodies, BiTE, ankyrin repeat protein, DARPIN, Avimer, DART, TCR-like antibody, Adnectin, Affilin, Transbody; Affibody, TrimerX, MicroProtein, Fynomer, Centyrin; and KALBITOR.

- ~~718.~~ The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the CD19 antibody or fragment thereof is
- ~~(i) _____ a monoclonal antibody; or~~
 - ~~(ii) _____ an antibody comprising an IgG constant region single-chain variable fragment (scFv).~~
- ~~19.~~ ~~The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the CD19 antibody or fragment thereof is an antibody comprising an IgG constant region.~~
- ~~820.~~ The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the CD19 antibody or fragment thereof is a single-chain variable fragment (scFv), optionally wherein the scFv comprises linker sequence comprising SEQ ID Nos: 36-39, optionally wherein the scFv comprises a signal peptide selected from SEQ ID NOs: 40 or 41.
- ~~21.~~ ~~The CD19 antibody or antigen-binding fragment thereof of claim 20, wherein the CD19-scFv comprises linker sequence comprising SEQ ID Nos: 36-39.~~
- ~~22.~~ ~~The CD19 antibody or antigen-binding fragment thereof of claim 20 or 21, wherein the CD19-scFv comprises a signal peptide selected from SEQ ID NOs: 40 or 41.~~
- ~~923.~~ The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the antibody or fragment thereof binds CD19
- ~~(i) _____ with a K_D between about 8 nanomolar (nM) and about 242 nM; and/or~~
 - ~~(ii) _____ with an EC_{50} between about 0.1 nM and about 2.7 nM on target cells.~~
- ~~24.~~ ~~The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the antibody or fragment thereof binds CD19 on target cells with an EC_{50} between about 0.1 nM and about 2.7 nM.~~
- ~~1025.~~ ~~A method of treating a cancer comprising administering t~~The CD19 antibody or antigen-binding fragment thereof for use in treating a cancer in a to a subject in need of treatment.

1126. The CD19 antibody or antigen-binding fragment thereof of any one of the preceding claims for use according to claim 10~~method of claim 25~~, wherein the cancer is selected from leukemia, lymphoma, or myeloma.

1227. A pharmaceutical composition comprising a CD19 antibody or antigen-binding fragment thereof of anyone of claims 1-9 and a pharmaceutically acceptable carrier,
~~wherein the CD19 antibody or fragment thereof comprises:~~
~~a heavy chain variable region with complementarity determining region (CDR) sequences of SYGMH (SEQ ID NO: 1) (HCDR1), LIWYDGSNKYYADSVKG (SEQ ID NO: 2) (HCDR2) and PVEGLLRGFDY (SEQ ID NO: 3) (HCDR3).~~

28. ~~The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGAVPIT (SEQ ID NO: 12) (LCDR3).~~

29. ~~The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQVDSLHPFT (SEQ ID NO: 13) (LCDR3).~~

30. ~~The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGGVPPLT (SEQ ID NO: 14) (LCDR3).~~

31. ~~The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVRSSSYLA (SEQ ID NO: 8) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQLFDSPYT (SEQ ID NO: 15) (LCDR3).~~

- ~~32.—The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
- ~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVRSSYLA (SEQ ID NO: 8) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGVPPLT (SEQ ID NO: 16) (LCDR3).~~
- ~~33.—The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
- ~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGGVPPFT (SEQ ID NO: 17) (LCDR3).~~
- ~~34.—The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
- ~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASNRAT (SEQ ID NO: 10) (LCDR2), and QQAGVFPFT (SEQ ID NO: 18) (LCDR3).~~
- ~~35.—The pharmaceutical composition of claim 27, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~
- ~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASRRAT (SEQ ID NO: 11) (LCDR2), and QQAGIPPYT (SEQ ID NO: 19) (LCDR3).~~
- ~~36.—A method of treating a cancer comprising administering an CD19 antibody or antigen-binding fragment thereof to a subject in need of treatment, wherein the CD19 antibody or fragment thereof comprises:~~
- ~~a heavy chain variable region with complementarity determining region (CDR) sequences of SYGMH (SEQ ID NO: 1) (HCDR1), LIWYDGSNKYYADSVKG (SEQ ID NO: 2) (HCDR2) and PVEGLLRGFDY (SEQ ID NO: 3) (HCDR3).~~
- ~~37.—The method of claim 36, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGAVPIT (SEQ ID NO: 12) (LCDR3).~~

38. ~~The method of claim 36, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQVDSLHPFT (SEQ ID NO: 13) (LCDR3).~~

39. ~~The method of claim 36, wherein the CD19 antibody or fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGGVPLT (SEQ ID NO: 14) (LCDR3).~~

40. ~~The method of claim 36, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVRSSSYLA (SEQ ID NO: 8) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQLFDSPTYT (SEQ ID NO: 15) (LCDR3).~~

41. ~~The method of claim 36, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVRSSSYLA (SEQ ID NO: 8) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGVPPLT (SEQ ID NO: 16) (LCDR3).~~

42. ~~The method of claim 36, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASSRAT (SEQ ID NO: 9) (LCDR2), and QQAGGVPPFT (SEQ ID NO: 17) (LCDR3).~~

43. ~~The method of claim 36, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASNRAT (SEQ ID NO: 10) (LCDR2), and QQAGVFPFT (SEQ ID NO: 18) (LCDR3).~~

~~44. The method of claim 36, wherein the CD19 antibody or antigen-binding fragment thereof further comprises~~

~~a light chain variable region with complementarity determining region (CDR) sequences of RASQSVSSSYLA (SEQ ID NO: 7) (LCDR1), GASRRAT (SEQ ID NO: 11) (LCDR2), and QQAGIPPYT (SEQ ID NO: 19) (LCDR3).~~

1345. A nucleic acid encoding

(i) the heavy chain variable region of the CD19 antibody or antigen-binding fragment thereof of claim 1; and/or

(ii) the light chain variable region of the CD19 antibody or antigen-binding fragment thereof of claim 1.~~an amino acid sequence that is at least 90% identical to SEQ ID NO: 5.~~

~~46. A nucleic acid encoding an amino acid sequence that is at least 90% identical to any one of SEQ ID NOs:20-27.~~

1447. A vector comprising the ~~isolated~~ nucleic acid ~~sequence of claim 13~~any claims 45 or 46.

1548. An isolated cell comprising the vector of claim 1447.