

## CLAIMS

1. A CD19 binding molecule that specifically binds to human CD19 and comprises sequences selected from the group consisting of
  - a) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:14, SEQ ID NO:15, and SEQ ID NO:16;
  - b) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:17, SEQ ID NO:18, and SEQ ID NO:19;
  - c) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:20, SEQ ID NO:21, and SEQ ID NO:22; or
  - d) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:23, SEQ ID NO:24, and SEQ ID NO:25.
2. The CD19 binding molecule of claim 1, which comprises a VH having the amino acid sequence of SEQ ID NO:13 and/or which comprises a VL having the amino acid sequence of SEQ ID NO:26.
3. The CD19 binding molecule of any one of claims 1 to 2, which is a trispecific binding molecule (TBM) comprising:
  - (a) an antigen-binding module 1 (ABM1) that binds specifically to CD19; and
  - (b) an antigen-binding module 2 (ABM2), in which ABM2 binds specifically to a component of a human T-cell receptor (TCR) complex and
  - (c) an antigen-binding module 3 (ABM3), in which ABM3 binds specifically to human CD2.

4. The CD19 binding molecule of claim 3, which is trivalent and has the configuration referred to as T2 in Section 7.6.1.
5. The CD19 binding molecule of any one of claims 3 or 4, in which ABM1 is capable of binding CD19 at the same time as ABM2 is bound to its target molecule.
6. The CD19 binding molecule of claim 5, in which ABM1 is capable of binding CD19 at the same time ABM3 is bound to its target molecule.
7. The CD19 binding molecule of any one of claims 3 to 6, wherein ABM1 is a Fab.
8. The CD19 binding molecule of any one of claims 3 to 7, wherein ABM2 is an scFv.
9. The CD19 binding molecule of any one of claims 3 to 8, wherein the component of the TCR complex is CD3.
10. The CD19 binding molecule of claim 9, wherein ABM2 is an anti-CD3 antibody or an antigen-binding domain thereof and comprises the CDR sequences of any of CD3-1 to CD3-130.
11. The CD19 binding molecule of any one of claims 3 to 10, wherein ABM3 is a CD58 moiety.
12. The CD19-binding molecule of claim 11, wherein the CD58 moiety comprises sequences selected from the group consisting of
  - the amino acid sequence of CD58-1 as set forth in Table 15,
  - the amino acid sequence of CD58-2 as set forth in Table 15,
  - the amino acid sequence of CD58-3 as set forth in Table 15,
  - the amino acid sequence of CD58-4 as set forth in Table 15,

the amino acid sequence of CD58-5 as set forth in Table 15,

the amino acid sequence of CD58-6 as set forth in Table 15,

the amino acid sequence of CD58-7 as set forth in Table 15,

the amino acid sequence of CD58-8 as set forth in Table 15,

the amino acid sequence of CD58-9 as set forth in Table 15,

the amino acid sequence of CD58-10 as set forth in Table 15,

the amino acid sequence of CD58-11 as set forth in Table 15 and

the amino acid sequence of CD58-12 as set forth in Table 15.

13. The CD19-binding molecule of claim 12, wherein the CD58 moiety comprises the amino acid sequence of CD58-6 as set forth in Table 15.

14. A pharmaceutical composition comprising (a) the CD19 binding molecule of any one of claims 1 to 13 and (b) an excipient.

15. The CD19 binding molecule of any one of claims 1 to 13, or the pharmaceutical composition of claim 14 for use in a method of treating a subject with a CD19-associated disease or disorder, wherein an effective amount of the CD19 binding molecule, or the pharmaceutical composition is to be administered to the subject.

16. The CD19 binding molecule or the pharmaceutical composition for use of claim 15, wherein the CD19-associated disease or disorder is cancer.

17. The CD19 binding molecule or the pharmaceutical composition for use of claim 16, wherein the disease or disorder is a B cell malignancy that expresses cell surface CD19.

18. The CD19 binding molecule or the pharmaceutical composition for use of any of claims 15 to 17, further comprising at least one further agent to be administered the subject.
19. A nucleic acid or plurality of nucleic acids encoding the CD19-binding molecule of any one of claims 1 to 13.
20. A cell engineered to express the CD19 binding molecule of any one claims 1 to 13.
21. A method of producing a CD19 binding molecule, comprising:
- (a) culturing the cell of claim 20 in conditions under which the CD19 binding molecule is expressed; and
  - (b) recovering the CD19-binding molecule from the cell culture.
22. A CD19 binding molecule which is a trispecific binding molecule (TBM) comprising:
- (a) an antigen-binding module 1 (ABM1) that binds specifically to CD19 and comprises CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:17, SEQ ID NO:18, and SEQ ID NO:19;
  - (b) an antigen-binding module 2 (ABM2) that binds specifically to a component of a human T-cell receptor (TCR) complex; and
  - (c) an antigen-binding module 3 (ABM3) that binds specifically to human CD2.
23. The CD19 binding molecule of claim 22, in which ABM1 is a Fab.
24. The CD19 binding molecule of any one of claims 22 or 23, in which the Fab comprises a VH having the amino acid sequence of SEQ ID NO:13 and a VL having the amino acid sequence of SEQ ID NO:26.

25. The CD19 binding molecule of any one of claims 22 to 24, wherein the component of the TCR complex is CD3.

26. The CD19 binding molecule of claim 25, wherein ABM2 is an anti-CD3 antibody or an antigen-binding domain thereof and wherein ABM2 comprises the heavy and light chain variable sequences of CD3-21, as set forth in Table 12A.

27. The CD19 binding molecule of claim 26, wherein the anti-CD3 antibody or antigen-binding domain thereof is in the form of a scFv.

28. The CD19 binding molecule of any one of claims 22 to 27, wherein ABM3 comprises the amino acid sequence of CD58-6 as set forth in Table 15.

29. The CD19 binding molecule of any one of claims 22 to 28, which comprises an Fc domain.

30. The CD19 binding molecule of any one of claims 22 to 29, which comprises a first variant Fc region and a second variant Fc region that together form an Fc heterodimer.

31. The CD19 binding molecule of any one of claims 29 to 30, wherein the Fc domain is a human IgG1 Fc domain which comprises:

- (a) a first CH3 domain comprising the modification T366W; and
- (b) a second CH3 domain that heterodimerizes with the first CH3 domain and comprises the modifications T366S, L368A and Y407V.

32. The CD19 binding molecule of any one of claims 29 to 31, wherein the Fc domain comprises a human IgG1 sequence of SEQ ID NO:1109 with a mutation at 1, 2, 3, 4, 5 or 6 positions of positions 233, 234, 235, 236, 237, 239, 265, 266, 267, 268, 269, 297, 299, 322, 327, 328, 329, 330, 331 and 332 (EU numbering).

33. The CD19 binding molecule of any one of claims 29 to 32, wherein the Fc domain comprises a human IgG1 Fc domain modified by substituting the aspartate residue

at position 265 with an alanine residue, the asparagine residue at position 297 with an alanine residue and the proline residue at position 329 with an alanine residue (D265A/N297A/P329A).

34. A CD19 binding molecule comprising:

- (a) first half antibody heavy chain whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:758 and a Fc sequence;
- (b) a first half antibody light chain whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:759;
- (c) a second half antibody whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:760 and a Fc sequence.

35. A CD19 binding molecule comprising:

- (a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1077;
- (b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:759; and
- (c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1078 or SEQ ID NO:1086.

36. A CD19 binding molecule comprising:

- (a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1077;
- (b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:759; and
- (c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1086.

37. A combination comprising the CD19 binding molecule of any one of claims 22 to 36 and at least one additional therapeutic agent.

38. A pharmaceutical composition comprising (a) the CD19 binding molecule of any one of claims 22 to 36 or the combination of claim 37 and (b) a pharmaceutically acceptable excipient.