

WHAT IS CLAIMED IS: CLAIMS

1. A CD19 binding molecule that specifically binds to human CD19 and comprises
 - (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; and
 - (b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.
2. A CD19 binding molecule that specifically binds to human CD19 and comprises
 - (a) 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; and
 - (b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.
3. A CD19 binding molecule that specifically binds to human CD19 and comprises
 - (a) 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; and

(b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

4. A CD19 binding molecule that specifically binds to human CD19 and comprises

(a) 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; and

(b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

5. The CD19 binding molecule of any one of claims 1 to 4, which comprises a VH having the amino acid sequence of SEQ ID NO:13.

6. The CD19 binding molecule of any one of claims 1 to 5, which comprises a VL having the amino acid sequence of SEQ ID NO:26.

7. A CD19 binding molecule that specifically binds to human CD19 and comprises

(a) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:27, SEQ ID NO:28, and SEQ ID NO:29, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:40, SEQ ID NO:41, and SEQ ID NO:42; and

(b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

8. A CD19 binding molecule that specifically binds to human CD19 and comprises

(a) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:30, SEQ ID NO:31, and SEQ ID NO:32, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45; and

(b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

9. A CD19 binding molecule that specifically binds to human CD19 and comprises

(a) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:33, SEQ ID NO:34, and SEQ ID NO:35, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:46, SEQ ID NO:47, and SEQ ID NO:48; and

(b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or

L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

10. A CD19 binding molecule that specifically binds to human CD19 and comprises

(a) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:36, SEQ ID NO:37, and SEQ ID NO:38, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:49, SEQ ID NO:50, and SEQ ID NO:51; and

(b) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

11. The CD19 binding molecule of any one of claims 7 to 10, which comprises a VH having the amino acid sequence of SEQ ID NO:39.

12. The CD19 binding molecule of any one of claims 7 to 11, which comprises a VL having the amino acid sequence of SEQ ID NO:52.

13. The CD19 binding molecule of any one of claims 1 to 12, which is a multispecific binding molecule (MBM) comprising:

(a) an antigen-binding module 1 (ABM1) that binds specifically to CD19; and

(b) an antigen-binding module 2 (ABM2) that binds specifically to a different target molecule, optionally wherein the target molecule is a component of a human T-cell receptor (TCR) complex.

14. The CD19 binding molecule of claim 13, in which ABM2 binds specifically to a component of a human T-cell receptor (TCR) complex.

15. The CD19 binding molecule of claim 13, which is a bispecific binding molecule (BBM).

16. The CD19 binding molecule of claim 15, in which ABM2 binds specifically to a component of a human T-cell receptor (TCR) complex.
17. The CD19 binding molecule of claim 15 or claim 16, which is bivalent.
18. The CD19 binding molecule of claim 15 or claim 16, which is trivalent.
19. The CD19 binding molecule of claim 18, which has the configuration referred to as T1 in Section 7.5.2.
20. The CD19 binding molecule of claim 18, which has the configuration referred to as T2 in Section 7.5.2.
21. The CD19 binding molecule of claim 18, which has the configuration referred to as T3 in Section 7.5.2.
22. The CD19 binding molecule of claim 18, which has the configuration referred to as T4 in Section 7.5.2.
23. The CD19 binding molecule of claim 18, which has the configuration referred to as T5 in Section 7.5.2.
24. The CD19 binding molecule of claim 18, which has the configuration referred to as T6 in Section 7.5.2.
25. The CD19 binding molecule of claim 15 or claim 16, which is tetravalent.
26. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv1 in Section 7.5.3.
27. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv2 in Section 7.5.3.
28. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv3 in Section 7.5.3.

29. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv4 in Section 7.5.3.

30. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv5 in Section 7.5.3.

31. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv6 in Section 7.5.3.

32. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv7 in Section 7.5.3.

33. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv8 in Section 7.5.3.

34. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv9 in Section 7.5.3.

35. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv10 in Section 7.5.3.

36. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv11 in Section 7.5.3.

37. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv12 in Section 7.5.3.

38. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv13 in Section 7.5.3.

39. The CD19 binding molecule of claim 25, which has the configuration referred to as Tv14 in Section 7.5.3.

40. The CD19 binding molecule of claim 13, which is a trispecific binding molecule (TBM) comprising an antigen-binding module 3 (ABM3) that binds specifically to a target molecule other than CD19.

41. The CD19 binding molecule of claim 40, in which ABM2 binds specifically to a component of a human T-cell receptor (TCR) complex and ABM3 binds specifically to (i) human CD2 or (ii) a tumor associated antigen (TAA).

42. The CD19 binding molecule of claim 40 or claim 41, which is trivalent.

43. The CD19 binding molecule of claim 42, which has the configuration referred to as T1 in Section 7.6.1.

44. The CD19 binding molecule of claim 42, which has the configuration referred to as T2 in Section 7.6.1.

45. The CD19 binding molecule of claim 42, which has the configuration referred to as T3 in Section 7.6.1.

46. The CD19 binding molecule of claim 42, which has the configuration referred to as T4 in Section 7.6.1.

47. The CD19 binding molecule of claim 42, which has the configuration referred to as T5 in Section 7.6.1.

48. The CD19 binding molecule of claim 42, which has the configuration referred to as T6 in Section 7.6.1.

49. The CD19 binding molecule of claim 40 or claim 41, which is tetravalent.

50. The CD19 binding molecule of claim 40 or claim 41, which is pentavalent.

51. The CD19 binding molecule of claim 40 or claim 41, which is hexavalent.

52. The CD19 binding molecule of any one of claims 13 to 51, in which ABM1 is capable of binding CD19 at the same time as ABM2 is bound to its target molecule.

53. The CD19 binding molecule of claim 52, in which ABM1 is capable of binding CD19 at the same time ABM3, if present, is bound to its target molecule.

54. The CD19 binding molecule of any one of claims 13 to 53, wherein ABM1 is an antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain.

55. The CD19 binding molecule of claim 54, wherein ABM1 is an scFv.

56. The CD19 binding molecule of claim 54, wherein ABM1 is a Fab.

57. The CD19 binding molecule of claim 54, wherein the Fab is a Fab heterodimer.

58. The CD19 binding molecule of claim 54, wherein ABM1 is an anti-CD19 antibody or an antigen-binding domain thereof.

59. The CD19 binding molecule of any one of claims 13 to 58, wherein ABM2 is an antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain.

60. The CD19 binding molecule of claim 59, wherein ABM2 is an scFv.

61. The CD19 binding molecule of claim 59, wherein ABM2 is a Fab.

62. The CD19 binding molecule of any one of claims 13 to 61, wherein the component of the TCR complex is CD3.

63. The CD19 binding molecule of claim 62, wherein ABM2 is an anti-CD3 antibody or an antigen-binding domain thereof.

64. The CD19 binding molecule of claim 63, wherein ABM2 comprises the CDR sequences of any of CD3-1 to CD3-130.

65. The CD19 binding molecule of any one of claims 13 to 61, wherein the component of the TCR complex is TCR- α , TCR- β , or a TCR- α/β dimer.

66. The CD19-binding molecule of claim 65, wherein ABM2 is an antibody or an antigen-binding domain thereof.

67. The CD19-binding molecule of claim 65, wherein ABM2 is a Fab.
68. The CD19 binding molecule of any one of claims 40 to 51 and claims 52 to 67 to the extent dependent from claims 40 to 51, in which ABM3 binds specifically to human CD2.
69. The CD19-binding molecule of claim 68, wherein ABM3 is a CD58 moiety.
70. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-1 as set forth in Table 15.
71. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-2 as set forth in Table 15.
72. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-3 as set forth in Table 15.
73. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-4 as set forth in Table 15.
74. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-5 as set forth in Table 15.
75. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-6 as set forth in Table 15.
76. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-7 as set forth in Table 15.
77. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-8 as set forth in Table 15.
78. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-9 as set forth in Table 15.
79. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-10 as set forth in Table 15.

80. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-11 as set forth in Table 15.

81. The CD19-binding molecule of claim 69, wherein the CD58 moiety comprises the amino acid sequence of CD58-12 as set forth in Table 15.

82. The CD19-binding molecule of claim 68, wherein ABM3 is an anti-CD2 antibody or an antigen-binding domain thereof.

83. The CD19 binding molecule of any one of claims 40 to 51 and claims 52 to 67 to the extent dependent from claims 40 to 51, in which ABM3 binds specifically to a human TAA.

84. The CD19 binding molecule of claim 83, wherein the TAA is a TAA expressed on cancerous B cells that are B cell-derived plasma cells.

85. The CD19 binding molecule of claim 83 or claim 84, wherein the TAA is a TAA expressed on cancerous B cells that are not plasma cells.

86. The CD19 binding molecule of any one of claims 83 to 85, wherein the TAA is selected from BCMA, CD20, CD22, CD123, CD33, CLL1, CD138, CS1, CD38, CD133, FLT3, CD52, TNFRSF13C, TNFRSF13B, CXCR4, PD-L1, LY9, CD200, FCGR2B, CD21, CD23, CD24, CD40L, CD72, CD79a, and CD79b.

87. The CD19 binding molecule of claim 86, wherein ABM3 comprises a binding sequence set forth in Table 16 or Table 17.

88. The CD19 binding molecule of claim 87, which has the heavy and / or light chain variable regions of any one of BCMA-1 to BCMA-40 as set forth in Table 17A.

89. The CD19 binding molecule of claim 87, which has the heavy and / or light chain CDR sequences (as defined by Kabat) of any one of BCMA-1 to BCMA-40 as set forth in Tables 17B and 17E.

90. The CD19 binding molecule of claim 87, which has the heavy and / or light chain CDR sequences (as defined by Chothia) of any one of BCMA-1 to BCMA-40 as set forth in Tables 17C and 17F.

91. The CD19 binding molecule of claim 87, which has the heavy and / or light chain CDR sequences (as defined by a combination of Kabat and Chothia sequences) of any one of BCMA-1 to BCMA-40 as set forth in Tables 17D and 17G.

92. A CD19 binding molecule which is 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;

(c) an antigen-binding module 3 (ABM3) that binds specifically to human CD2; and

(d) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

93. The CD19 binding molecule of claim 92 which is trivalent.

94. The CD19 binding molecule of claim 92 or claim 93, in which ABM1 is a Fab.

95. The CD19 binding molecule of any one of claims 92 to 94, 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.

96. The CD19 binding molecule of any one of claims 92 to 95, wherein the component of the TCR complex is CD3.

97. The CD19 binding molecule of claim 96, wherein ABM2 is an anti-CD3 antibody or an antigen-binding domain thereof.

98. The CD19 binding molecule of claim 97, wherein ABM2 comprises the CDR sequences of CD3-21.

99. The CD19 binding molecule of claim 97 or claim 98, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-21, as set forth in Table 12A.

100. The CD19 binding molecule of any one of claims 97 to 99, wherein the anti-CD3 antibody or antigen-binding domain thereof is in the form of a scFv.

101. The CD19 binding molecule of claim 100, wherein ABM2 comprises the amino acid sequence of the scFv designated as CD3-21 in Table 12A.

102. The CD19 binding molecule of any one of claims 92 to 101, wherein ABM3 is a CD58 moiety.

103. The CD19 binding molecule of any one of claims 92 to 102, wherein ABM3 comprises the amino acid sequence of CD58-6 as set forth in Table 15.

104. 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 which is a Fab comprising: (i) 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; or (ii) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:30, SEQ ID NO:31, and SEQ ID NO:32, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45;

(b) an antigen-binding module 2 (ABM2) that binds specifically to CD3 and which comprises the amino acid sequence of the scFv designated as CD3-21 in Table 12A;

(c) an antigen-binding module 3 (ABM3) that binds specifically to human CD2 and which comprises the amino acid sequence of CD58-6 as set forth in Table 15; and

(d) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc

regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

105. 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 which is a Fab comprising: (i) 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; or (ii) CDR-H1, CDR-H2, and CDR-H3 having the amino acid sequences of SEQ ID NO:30, SEQ ID NO:31, and SEQ ID NO:32, and CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45;

(b) an antigen-binding module 2 (ABM2) that binds specifically to CD3 and which comprises the amino acid sequence of the scFv designated as CD3-129 in Table 12A;

(c) an antigen-binding module 3 (ABM3) that binds specifically to human CD2 and which comprises the amino acid sequence of CD58-6 as set forth in Table 15; and

(d) a first variant human IgG1 Fc region and a second variant human IgG1 Fc region forming a Fc domain, wherein the first and second variant Fc regions comprise L234A, L235A, and G237A ("LALAGA") substitutions, L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, D265A, P329A, and S267K ("DAPASK") substitutions, G237A, D265A, and P329A ("GADAPA") substitutions, G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, L234A, L235A, and P329G ("LALAPG") substitutions, or L234A, L235A, and P329A ("LALAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

106. The CD19 binding molecule of claim 104 or claim 105, wherein ABM1 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.

107. The CD19 binding molecule of any one of claims 104 to 106, wherein ABM1 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.

108. The CD19 binding molecule of any one of claim 92 to 107, wherein the CD19 binding molecule has the configuration depicted in FIG. 2I and referred to as T2 in Section 7.6.1.

109. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and the second variant Fc region comprise L234A, L235A, and G237A ("LALAGA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

110. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and the second variant Fc region comprise L234A, L235A, S267K, and P329A ("LALASKPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

111. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and the second variant Fc region comprise D265A, P329A, and S267K ("DAPASK") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

112. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and the second variant Fc region comprise G237A, D265A, and P329A ("GADAPA") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

113. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and the second variant Fc region comprise G237A, D265A, P329A, and S267K ("GADAPASK") substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

114. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and the second variant Fc region comprise L234A, L235A, and P329G (“LALAPG”) substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

115. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and the second variant Fc region comprise L234A, L235A, and P329A (“LALAPA”) substitutions, wherein the amino acid residues are numbered according to the EU numbering system.

116. The CD19 binding molecule of any one of claims 1 to 108, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95% identity to FCV-1, FCV-2, FCV-3, FCV-4, FCV-5, FCV-6, or FCV-7.

117. The CD19 binding molecule of claim 116, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to FCV-1.

118. The CD19 binding molecule of claim 116, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to FCV-2.

119. The CD19 binding molecule of claim 116, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to FCV-3.

120. The CD19 binding molecule of claim 116, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to FCV-4.

121. The CD19 binding molecule of claim 116, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to FCV-5.

122. The CD19 binding molecule of claim 116, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to FCV-6.

123. The CD19 binding molecule of claim 116, wherein the first variant Fc region and/or the second variant Fc region comprises a sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to FCV-7.

124. The CD19 binding molecule of any one of claims 1 to 123, wherein the first variant Fc region and the second variant Fc region together form an Fc heterodimer.

125. The CD19 binding molecule of claim 124, wherein the first and second variant Fc regions comprise the amino acid substitutions T366W : T366S/L368A/Y407V.

126. The CD19 binding molecule of any one of claims 124 to 125, the first and second variant Fc regions comprise the amino acid substitutions S354C : Y349C.

127. A CD19 binding molecule comprising:

(a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1120;

(b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1122; and

(c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1110.

128. A CD19 binding molecule comprising:

(a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1127;

(b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1129; and

(c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1110.

129. A CD19 binding molecule comprising:

(a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1134;

(b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1135; and

(c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1110.

130. A CD19 binding molecule comprising:

- (a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1136;
- (b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1137; and
- (c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1110.

131. A CD19 binding molecule comprising:

- (a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1138;
- (b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1139; and
- (c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1110.

132. A CD19 binding molecule comprising:

- (a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1140;
- (b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1141; and
- (c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1110.

133. A CD19 binding molecule comprising:

- (a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1142;
- (b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1143; and
- (c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1110.

134. A CD19 binding molecule comprising:

- (a) a first polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1131;

(b) a second polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1132; and

(c) a third polypeptide whose amino acid sequence comprises the amino acid sequence of SEQ ID NO:1133.

135. A conjugate comprising (a) the CD19 binding molecule of any one of claims 1 to 134, and (b) an agent.

136. The conjugate of claim 135, wherein the agent is a therapeutic agent, a diagnostic agent, a masking moiety, a cleavable moiety, a stabilizing agent, or any combination thereof.

137. A pharmaceutical composition comprising (a) the CD19 binding molecule of any one of claims 1 to 134 or the conjugate of any one of claims 135 to 136 and (b) an excipient.

138. A nucleic acid or plurality of nucleic acids encoding the CD19-binding molecule of any one of claims 1 to 134.

139. A cell engineered to express the CD19 binding molecule of any one claims 1 to 134.

140. A method of producing a CD19 binding molecule, comprising:

(a) culturing the cell of claim 139 in conditions under which the CD19 binding molecule is expressed; and

(b) recovering the CD19-binding molecule from the cell culture.

141. A combination comprising the CD19 binding molecule of any one of claims 1 to 134 and at least one additional therapeutic agent.

142. The combination of claim 141, wherein the one or more additional therapeutic agents comprise an immunomodulatory imide drug (IMiD).

143. The combination of claim 142, wherein the immunomodulatory imide drug (IMiD) is lenalidomide, thalidomide, pomalidomide, or iberdomide.

144. The combination of claim 143, wherein the immunomodulatory imide drug (IMiD) is lenalidomide.

145. The CD19 binding molecule of any one of claims 1 to 134, the composition of claim 137 or combination of any one of claims 141 to 144 for use as a medicament.

146. The CD19 binding molecule of any one of claims 1 to 134, the composition of claim 137 or combination of any one of claims 141 to 144 for use in treating a CD19-associated disease or disorder.

147. Use of the antibody or antigen binding fragment thereof of any one of claims 1 to 134, the composition of claim 137 or combination of any one of claims 141 to 144 in the manufacture of a medicament to treat a CD19-associated disease or disorder.

~~148. A method of treating a subject with a CD19-associated disease or disorder, comprising administering to the subject an effective amount of the CD19 binding molecule of any one of claims 1 to 134, the composition of claim 137 or combination of any one of claims 141 to 144.~~

~~149.~~148. The CD19 binding molecule, combination or composition for use of claim 146, or use of claim 147 ~~or method of claim 148~~, wherein the CD19-associated disease or disorder is cancer.

~~150.~~149. The CD19 binding molecule, combination or composition for use of claim 146, or use of claim 147 ~~or method of claim 148~~, wherein the disease or disorder is a plasma cell neoplasm.

~~151.~~150. The CD19 binding molecule, combination or composition for use of claim 146, or use of claim 147 ~~or method of claim 148~~, wherein the disease or disorder is a B cell malignancy that expresses cell surface CD19.

~~152.~~151. The CD19 binding molecule, combination or composition for use of claim 146, or use of claim 147 ~~or method of claim 148~~, wherein the CD19-associated disease or disorder is non-Hodgkin's lymphoma.

~~153.~~152. The CD19 binding molecule, combination or composition for use of claim 146, or use of claim 147 ~~or method of claim 148~~, wherein the CD19-associated

disease or disorder is diffuse large B-cell lymphoma (DLBCL), optionally wherein the DLBCL is relapsed or refractory DLBCL.

~~454.153.~~ The CD19 binding molecule, combination or composition for use of claim 146, or use of claim 147 ~~or method of claim 148~~, wherein the CD19-associated disease or disorder is Burkitt's lymphoma.

~~455.154.~~ The CD19 binding molecule, combination or composition for use or use of any one of claims ~~152-151~~ to ~~153~~154, wherein the subject has failed at least one prior line of standard of care therapy.

~~456.155.~~ The CD19 binding molecule, combination or composition for use or use of claim ~~155~~154, wherein the subject has failed up to five prior lines of standard of care therapies.

~~457.156.~~ The CD19 binding molecule, combination or composition for use or use of claim ~~155~~ 154 or ~~156~~155, wherein the subject has failed one prior line of standard of care therapy.

~~458.157.~~ The CD19 binding molecule, combination or composition for use or use of claim 154 or ~~155~~ 155 ~~or 156~~, wherein the subject has failed two prior lines of standard of care therapy.

~~459.158.~~ The CD19 binding molecule, combination or composition for use or use of claim ~~155~~ 154 or ~~156~~155, wherein the subject has failed three prior lines of standard of care therapy.

~~460.159.~~ The CD19 binding molecule, combination or composition for use or use of claim 154 or ~~155~~ 155 ~~or 156~~, wherein the subject has failed four prior lines of standard of care therapy.

~~461.160.~~ The CD19 binding molecule, combination or composition for use or use of claim 154 or ~~155~~ 155 ~~or 156~~, wherein the subject has failed five prior lines of standard of care therapy.

~~462.161.~~ The CD19 binding molecule, combination or composition for use or use of any one of claims ~~154 to 160~~~~155 to 164~~, wherein the at least one prior line of standard of care therapies comprise an anti-CD20 therapy.

~~463.162.~~ The CD19 binding molecule, combination or composition for use or use of claim ~~462~~~~161~~, wherein the anti-CD20 therapy is rituximab.

~~464.163.~~ The CD19 binding molecule, combination or composition for use or use of any one of claims ~~154 to 162~~~~155 to 163~~, wherein the subject is intolerant to or ineligible for one or more other approved therapies.

~~465.164.~~ The CD19 binding molecule, combination or composition for use or use of claim ~~464~~~~163~~, wherein the one or more other approved therapies comprise an autologous stem cell transplant (ASCT).

~~466.165.~~ The CD19 binding molecule, combination or composition for use or use of any one of claims ~~455-154~~ to ~~465~~~~164~~, wherein the subject is a non-responder to a CAR composition.

~~467.166.~~ The CD19 binding molecule, combination or composition for use or use of claim ~~466~~~~165~~, wherein the CAR composition is an anti-CD19 CAR composition.

~~468.167.~~ The CD19 binding molecule, combination or composition for use or use of claim ~~466-165~~ or claim ~~467~~~~166~~, wherein the CAR composition comprises CTL019, tisagenlecleucel, axicabtagene ciloleucel, brexucabtagene autoleucel or lisocabtagene maraleucel.