

CLAIMS

1. An antibody that binds to CD3 and CD19, wherein the antibody comprises
 - (a) a first antigen binding domain that binds to CD3, comprising a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 2,
5 a HCDR 2 of SEQ ID NO: 3, and a HCDR 3 of SEQ ID NO: 5, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 8, a LCDR 2 of SEQ ID NO: 9 and a LCDR 3 of SEQ ID NO: 10; and
 - (b) a second and optionally a third antigen binding domain that binds to CD19.
2. The antibody of claim 1, wherein the VH of the first antigen binding domain comprises an amino
10 acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 7, and/or the VL of the first antigen binding domain comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 11.
3. An antibody that binds to CD3 and CD19, wherein the antibody comprises
 - 15 (a) a first antigen binding domain that binds to CD3 comprising a VH sequence of SEQ ID NO: 7 and a VL sequence of SEQ ID NO: 11; and
 - (b) a second and optionally a third antigen binding domain that binds to CD19.
4. The antibody of any one of claims 1-3, wherein the first, the second and/or, where present, the third antigen binding domain is a Fab molecule.
- 20 5. The antibody of any one of claims 1-4, comprising an Fc domain composed of a first and a second subunit.
6. The antibody of any one of claims 1-5, wherein the first antigen binding domain is a Fab molecule wherein the variable domains VL and VH or the constant domains CL and CH1, particularly the variable domains VL and VH, of the Fab light chain and the Fab heavy chain are
25 replaced by each other.
7. The antibody of any one of claims 1-6, wherein the second and, where present, the third antigen binding domain is a conventional Fab molecule.
8. The antibody of any one of claims 1-7, wherein the second and, where present, the third antigen binding domain is a Fab molecule wherein in the constant domain CL the amino acid at position
30 124 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat) and the amino acid at position 123 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat), and in the constant domain CH1 the amino acid at position 147 is substituted independently by glutamic acid (E), or aspartic acid (D)

(numbering according to Kabat EU index) and the amino acid at position 213 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index).

9. The antibody of any one of claims 1-8, wherein the first and the second antigen binding domain are fused to each other, optionally via a peptide linker.

5 10. The antibody of any one of claims 1-9, wherein the first and the second antigen binding domain are each a Fab molecule and either (i) the second antigen binding domain is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the first antigen binding domain, or (ii) the first antigen binding domain is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the second antigen binding domain.

10 11. The antibody of any one of claims 1-10, wherein the first, the second and, where present, the third antigen binding domain are each a Fab molecule and the antibody comprises an Fc domain composed of a first and a second subunit; and wherein either (i) the second antigen binding domain is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the first antigen binding domain and the first antigen binding domain is fused at the C-terminus of the
15 Fab heavy chain to the N-terminus of the first subunit of the Fc domain, or (ii) the first antigen binding domain is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the second antigen binding domain and the second antigen binding domain is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain; and the third antigen binding domain, where present, is fused at the C-terminus of the Fab heavy
20 chain to the N-terminus of the second subunit of the Fc domain.

12. The antibody of any one of claims 5-11, wherein the Fc domain is an IgG, particularly an IgG₁, Fc domain.

13. The antibody of any one of claims 5-12, wherein the Fc domain is a human Fc domain.

14. The antibody of any one of claims 5-13, wherein the Fc comprises a modification promoting
25 the association of the first and the second subunit of the Fc domain.

15. The antibody of any one of claims 5-14, wherein the Fc domain comprises one or more amino acid substitution that reduces binding to an Fc receptor and/or effector function.

16. The antibody of any one of claims 1-15, wherein the second and, where present, the third antigen binding domain comprises

30 (i) a VH comprising a HCDR 1 of SEQ ID NO: 15, a HCDR 2 of SEQ ID NO: 16, and a HCDR 3 of SEQ ID NO: 17, and a VL comprising a LCDR 1 of SEQ ID NO: 19, a LCDR 2 of SEQ ID NO: 20 and a LCDR 3 of SEQ ID NO: 21; or

(ii) a VH comprising a HCDR 1 of SEQ ID NO: 28, a HCDR 2 of SEQ ID NO: 29, and a HCDR 3 of SEQ ID NO: 30, and a VL comprising a LCDR 1 of SEQ ID NO: 32, a LCDR 2 of SEQ ID NO: 33 and a LCDR 3 of SEQ ID NO: 34.

5 17. The antibody of any one of claims 1-16, wherein the second and, where present, the third antigen binding domain comprises

(i) a VH comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 18, and/or a VL comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 22; or

10 (ii) a VH comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 31, and/or a VL comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 35.

18. An isolated polynucleotide encoding the antibody of any one of claims 1-17.

15 19. A host cell comprising the isolated polynucleotide of claim 18.

20. A method of producing an antibody that binds to CD3 and CD19, comprising the steps of (a) culturing the host cell of claim 19 under conditions suitable for the expression of the antibody and optionally (b) recovering the antibody.

21. An antibody that binds to CD3 and CD19 produced by the method of claim 20.

20 22. A pharmaceutical composition comprising the antibody of any one of claims 1-17 or 21 and a pharmaceutically acceptable carrier.

23. The antibody of any one of claims 1-17 or 21 or the pharmaceutical composition of claim 22 for use as a medicament.

25 24. The antibody of any one of claims 1-17 or 21 or the pharmaceutical composition of claim 22 for use in the treatment of a disease.

25. The antibody for use of claim 24, wherein the disease is cancer or an autoimmune disease.

26. Use of the antibody of any one of claims 1-17 or 21 or the pharmaceutical composition of claim 22 in the manufacture of a medicament.

30 27. Use of the antibody of any one of claims 1-17 or 21 or the pharmaceutical composition of claim 22 in the manufacture of a medicament for the treatment of a disease.

28. The use of claim 27, wherein the disease is cancer or an autoimmune disease.

29. A method of treating a disease in an individual, comprising administering to said individual an effective amount of the antibody of any one of claims 1-17 or 21 or the pharmaceutical composition of claim 22.

30. The method of claim 29, wherein the disease is cancer or an autoimmune disease.