

CLAIMS

1. An antibody that binds to HLA-A2/MAGE-A4, wherein the antibody comprises a first antigen binding domain, comprising
 - (i) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 25, a HCDR 2 of SEQ ID NO: 26, and a HCDR 3 of SEQ ID NO: 27, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 28, a LCDR 2 of SEQ ID NO: 29 and a LCDR 3 of SEQ ID NO: 30;
 - (ii) a VH comprising a HCDR 1 of SEQ ID NO: 1, a HCDR 2 of SEQ ID NO: 2, and a HCDR 3 of SEQ ID NO: 3, and a VL comprising a LCDR 1 of SEQ ID NO: 4, a LCDR 2 of SEQ ID NO: 5 and a LCDR 3 of SEQ ID NO: 6;
 - (iii) a VH comprising a HCDR 1 of SEQ ID NO: 41, a HCDR 2 of SEQ ID NO: 42, and a HCDR 3 of SEQ ID NO: 43, and a VL comprising a LCDR 1 of SEQ ID NO: 44, a LCDR 2 of SEQ ID NO: 45 and a LCDR 3 of SEQ ID NO: 46;
 - (iv) a VH comprising a HCDR 1 of SEQ ID NO: 9, a HCDR 2 of SEQ ID NO: 10, and a HCDR 3 of SEQ ID NO: 11, and a VL comprising a LCDR 1 of SEQ ID NO: 12, a LCDR 2 of SEQ ID NO: 13 and a LCDR 3 of SEQ ID NO: 14;
 - (v) a VH comprising a HCDR 1 of SEQ ID NO: 17, a HCDR 2 of SEQ ID NO: 18, and a HCDR 3 of SEQ ID NO: 19, and a VL comprising a LCDR 1 of SEQ ID NO: 20, a LCDR 2 of SEQ ID NO: 21 and a LCDR 3 of SEQ ID NO: 22; or
 - (vi) a VH comprising a HCDR 1 of SEQ ID NO: 33, a HCDR 2 of SEQ ID NO: 34, and a HCDR 3 of SEQ ID NO: 35, and a VL comprising a LCDR 1 of SEQ ID NO: 36, a LCDR 2 of SEQ ID NO: 37 and a LCDR 3 of SEQ ID NO: 38.
2. The antibody of claim 1, wherein the first 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: 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: 32;
 - (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: 7, 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: 8;

- (iii) 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: 47, 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: 48;
- 5 (iv) 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: 15, 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: 16;
- (v) a VH comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or
10 100% identical to the amino acid sequence of SEQ ID NO: 23, 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: 24; or
- (vi) a VH comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or
15 100% identical to the amino acid sequence of SEQ ID NO: 39, 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: 40.
3. An antibody that binds to HLA-A2/MAGE-A4, wherein the antibody comprises a first antigen binding domain comprising
- (i) a VH comprising the amino acid sequence of SEQ ID NO: 31, and/or a VL comprising the
20 amino acid sequence of SEQ ID NO: 32;
- (ii) a VH comprising the amino acid sequence of SEQ ID NO: 7, and/or a VL comprising the amino acid sequence of SEQ ID NO: 8;
- (iii) a VH comprising the amino acid sequence of SEQ ID NO: 47, and/or a VL comprising the amino acid sequence of SEQ ID NO: 48;
- 25 (iv) a VH comprising the amino acid sequence of SEQ ID NO: 15, and/or a VL comprising the amino acid sequence of SEQ ID NO: 16;
- (v) a VH comprising the amino acid sequence of SEQ ID NO: 23, and/or a VL comprising the amino acid sequence of SEQ ID NO: 24; or
- (vi) a VH comprising the amino acid sequence of SEQ ID NO: 39, and/or a VL comprising the
30 amino acid sequence of SEQ ID NO: 40.
4. The antibody of any one of the preceding claims, wherein the antibody is a multispecific, particularly a bispecific, antibody.

5. The antibody of any one of the preceding claims, wherein the antibody comprises a second antigen binding domain which binds to a second antigen.
6. The antibody of claim 5, wherein the second antigen is an activating T cell antigen, particularly CD3, most particularly CD3ε.
- 5 7. The antibody of claim 5 or 6, wherein the second antigen binding domain comprises
- (i) a VH comprising a HCDR 1 of SEQ ID NO: 59, a HCDR 2 of SEQ ID NO: 60, and a HCDR 3 of SEQ ID NO: 61, and a VL comprising a LCDR 1 of SEQ ID NO: 62, a LCDR 2 of SEQ ID NO: 63 and a LCDR 3 of SEQ ID NO: 64; or
- (ii) a VH comprising a HCDR 1 of SEQ ID NO: 51, a HCDR 2 of SEQ ID NO: 52, and a HCDR 3 of SEQ ID NO: 53, and a VL comprising a LCDR 1 of SEQ ID NO: 54, a LCDR 2 of SEQ ID NO: 55 and a LCDR 3 of SEQ ID NO: 56.
- 10 8. The antibody of any one of claims 5-7, wherein the second 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: 65, 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: 66; or
- 15 (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: 57, 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: 58.
- 20 9. The antibody of any one of claims 5-8, wherein the second antigen binding domain comprises
- (i) a VH comprising the amino acid sequence of SEQ ID NO: 65, and/or a VL comprising the amino acid sequence of SEQ ID NO: 66;
- (ii) a VH comprising the amino acid sequence of SEQ ID NO: 57, and/or a VL comprising the amino acid sequence of SEQ ID NO: 58.
- 25 10. The antibody of any one of the preceding claims, wherein the antibody comprises a third antigen binding domain.
11. The antibody of claim 10, wherein the third antigen domain binds to HLA-A2/MAGE-A4.
12. The antibody of claim 10 or 11, wherein the third antigen domain is identical to the first antigen binding domain.
- 30 13. The antibody of any one of the preceding claims, wherein the first, the second and/or the third antigen binding domain is a Fab molecule.

14. The antibody of any one of claims 5-13, wherein the second 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 replaced by each other.
- 5 15. The antibody of any one of the preceding claims, wherein the first and, where present, the third antigen binding domain is a conventional Fab molecule.
16. The antibody of any one of the preceding claims, wherein the first and, where present, the third antigen binding domain is a Fab molecule wherein in the constant domain CL the amino acid at position 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),
10 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).
- 15 17. The antibody of any one of claims 5-16, wherein the first and the second antigen binding domain are fused to each other, optionally via a peptide linker.
18. The antibody of any one of claims 5-17, wherein the first and the second antigen binding domain are each a Fab molecule and either (i) 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
20 binding domain, or (ii) 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.
19. The antibody of any one of the preceding claims, wherein the antibody comprises an Fc domain composed of a first and a second subunit.
20. The antibody of any one of claims 5-19, wherein the first, the second and, where present, the
25 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 either (i) 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, or (ii) the second antigen
30 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 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 chain to the N-terminus of the second subunit of the Fc domain.

21. The antibody of claims 19 or 20, wherein the Fc domain is an IgG, particularly an IgG₁, Fc domain.

5 22. The antibody of any one of claims 19-21, wherein the Fc domain is a human Fc domain.

23. The antibody of any one of claims 19-21, wherein the Fc comprises a modification promoting the association of the first and the second subunit of the Fc domain.

24. The antibody of any one of claims 19-23, wherein the Fc domain comprises one or more amino acid substitution that reduces binding to an Fc receptor and/or effector function.

10 25. An isolated polynucleotide encoding the antibody of any one of claims 1-24.

26. A host cell comprising the isolated polynucleotide of claim 25.

27. A method of producing an antibody that binds to HLA-A2/MAGE-A4, comprising the steps of (a) culturing the host cell of claim 26 under conditions suitable for the expression of the antibody and optionally (b) recovering the antibody.

15 28. An antibody that binds to HLA-A2/MAGE-A4, produced by the method of claim 27.

29. A pharmaceutical composition comprising the antibody of any one of claims 1-24 or 28 and a pharmaceutically acceptable carrier.

30. The antibody of any one of claims 1-24 or 28 or the pharmaceutical composition of claim 29 for use as a medicament.

20 31. The antibody of any one of claims 1-24 or 28 or the pharmaceutical composition of claim 29 for use in the treatment of a disease.

32. The antibody or the pharmaceutical composition for use of claim 31, wherein the disease is cancer.

25 33. Use of the antibody of any one of claims 1-24 or 28 or the pharmaceutical composition of claim 29 in the manufacture of a medicament.

34. Use of the antibody of any one of claims 1-24 or 28 or the pharmaceutical composition of claim 29 in the manufacture of a medicament for the treatment of a disease, particularly cancer.

30 35. 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 1-24 or 28 or the pharmaceutical composition of claim 29.

36. The method of claim 35, wherein the disease is cancer.

~~37. The invention as described hereinbefore.~~