

CLAIMS

1. An isolated antibody having a binding specificity for human CD137, which comprises an HCDR1, HCDR2, HCDR3 sequences of SEQ ID NOs: 1, 2 and 3, respectively, and an LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NOs: 18, 19 and 20,
5 respectively.
2. The antibody of claim 1, wherein the antibody comprises a heavy chain variable region (VH), wherein said VH is VH3 or VH4, preferably VH3.
- 10 3. The antibody of claim 1 or claim 2, wherein the antibody comprises a light chain variable region (VL), wherein said VL comprises V κ frameworks FR1, FR2 and FR3, particularly V κ 1 or V κ 3 FR1 to FR3, preferably V κ 1 FR1 to FR3, and a framework FR4, which is selected from a V κ FR4, particularly V κ 1 FR4, V κ 3 FR4, and V λ FR4, particularly V λ FR4 comprising the amino acid sequence having at least 60, 70, 80, 90
15 percent identity to an amino acid sequence selected from any of SEQ ID NO: 62 to SEQ ID NO: 68, preferably V λ FR4 as set forth in any of SEQ ID NO: 62 to SEQ ID NO: 68, preferably V λ FR4 as set forth in SEQ ID NO: 62 or 63, more preferably V λ FR4 as set forth in SEQ ID NO: 62.
- 20 4. The antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 90 percent identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 15, 16 and 17, preferably SEQ ID NO: 14 and 17, more preferably SEQ ID NO: 17; and a light chain variable region comprising an amino acid sequence
25 that is at least 90 percent identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 27, 28, 29 and 30, preferably SEQ ID NO: 27 and 30, more preferably SEQ ID NO: 30.
- 30 5. The antibody of claim 4, comprising: (a) a VH sequence of SEQ ID NO: 14 and a VL sequence of SEQ ID NO: 27; (b) a VH sequence of SEQ ID NO: 15 and a VL sequence of SEQ ID NO: 28; (c) a VH sequence of SEQ ID NO: 16 and a VL sequence of SEQ ID NO: 29; or (d) a VH sequence of SEQ ID NO: 17 and a VL

sequence of SEQ ID NO: 30.

6. The antibody of any one of the preceding claims, wherein said antibody:

- 5 (i) binds to human CD137 with a dissociation constant (KD) of less than 10 nM, particularly less than 5 nM, particularly less than 1 nM, in particular as measured by surface plasmon resonance (SPR), particularly wherein said antibody is an scFv;
- 10 (ii) binds to human CD137 with a K_{off} rate of 10^{-3} s^{-1} or less, or 10^{-4} s^{-1} or less, or 10^{-5} s^{-1} or less as measured by SPR, particularly wherein said antibody is an scFv;
- (iii) binds to human CD137 with a K_{on} rate of at least $10^4 \text{ M}^{-1} \text{ s}^{-1}$ or greater, at least $10^5 \text{ M}^{-1} \text{ s}^{-1}$ or greater, at least $10^6 \text{ M}^{-1} \text{ s}^{-1}$ or greater, as measured by SPR, particularly wherein said antibody is an scFv;
- 15 (iv) is cross-reactive with *Macaca fascicularis* (Cynomolgus) CD137, in particular binds to Cynomolgus PDL1 with a KD of less than 15 nM, particularly less than 10 nM, particularly less than 5 nM as measured by SPR, particularly wherein said antibody is an scFv; and/or
- (v) does not bind to human CD40 and/or human OX40, in particular as measured by SPR.

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7. The antibody of any one of the preceding items, wherein said antibody:

- 25 (i) when in scFv format, has a melting temperature (T_m), determined by differential scanning fluorimetry, of at least 50°C , preferably of at least 55°C , more preferably at least 60°C , in particular wherein said antibody is formulated in 50 mM phosphate-citrate buffer at pH 6.4, 150 mM NaCl;
- (ii) when in scFv format, has a loss in monomer content, after storage for at least two weeks, particularly for at least four weeks, at 4°C , of less than 5%, e.g. less than 4%, less than 3%, less than 2%, preferably less than 1%, when the antibody of the invention is at a starting concentration of 10 mg/ml, and in particular wherein the antibody is formulated in 50 mM phosphate citrate buffer with 150 mM NaCl at pH 6.4; and/or
- 30 (iii) when in scFv format, has a loss in monomer content, after storage for at least two weeks, particularly for at least four weeks, at 40°C , of less than 5%, e.g.

less than 4%, less than 3%, less than 2%, preferably less than 1%, when the antibody of the invention is at a starting concentration of 10 mg/ml, and in particular wherein the antibody is formulated in 50 mM phosphate citrate buffer with 150 mM NaCl at pH 6.4.

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8. The antibody of any one of the previous claims, wherein the isolated antibody is selected from the group consisting of: a monoclonal antibody, a chimeric antibody, a Fab, an Fv, an scFv, dsFv, a scAb, STAB, and binding domains based on alternative scaffolds including but limited to ankyrin-based domains, fynomers, avimers, anticalins, fibronectins, and binding sites being built into constant regions of antibodies (e.g. F-star's Modular Antibody TechnologyTM), preferably Fv or scFv.
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9. The antibody of claim 8, wherein said scFv has the amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34 and SEQ ID NO: 35, preferably SEQ ID NO: 32 and SEQ ID NO: 35, more preferably SEQ ID NO: 35.
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10. The antibody of any one of claims 1 to 7, wherein said antibody is a multispecific molecule, in particular wherein said multispecific molecule comprises at least a second functional molecule.
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11. A pharmaceutical composition comprising the antibody of any one of claims 1-10, and a pharmaceutically acceptable carrier.
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12. The antibody of any one of claims 1 to 10, or the composition of claim 11 for use as a medicament.
13. The antibody of any one of claims 1 to 10, or the composition of claim 11 for use in the treatment of a cancer.
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14. A nucleic acid encoding the antibody of any one of claims 1-10.

15. A method of producing the antibody of any one of claims 1-10, the method comprising the step of culturing a host cell comprising the nucleic acid of claims 1-8.