

Claims

1. An antibody molecule that binds to CD137 and OX40, comprising:

(a) a complementarity determining region (CDR)-based antigen-binding site for CD137; and

(b) an OX40 antigen-binding site located in a CH3 domain of the antibody molecule; wherein the CDR-based antigen-binding site comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, defined according to the ImMunoGeneTics (IMGT) numbering scheme, set forth in:

(i) SEQ ID Nos: **1, 2, 3, 4, 5** and **6**, respectively [**FS30-10-16**];

(ii) SEQ ID Nos: **1, 2, 16, 4, 5** and **6**, respectively [**FS30-10-3**];

(iii) SEQ ID Nos: **1, 2, 21, 4, 5** and **6**, respectively [**FS30-10-12**];

(iv) SEQ ID Nos: **25, 26, 27, 4, 5** and **28**, respectively [**FS30-35-14**]; or

(v) SEQ ID Nos: **33, 34, 35, 4, 5** and **36**, respectively [**FS30-5-37**]; or

wherein the CDR-based antigen-binding site comprises the VH CDR1, VH CDR2,

VH CDR3, VL CDR1, VL CDR2, and VL CDR3, defined according to the Kabat numbering scheme, set forth in:

(vi) SEQ ID NOS: **7, 8, 9, 10, 11** and **6**, respectively [**FS30-10-16**];

(vii) SEQ ID NOS: **7, 8, 17, 10, 11** and **6**, respectively [**FS30-10-3**];

(viii) SEQ ID NOS: **7, 8, 22, 10, 11** and **6**, respectively [**FS30-10-12**];

(ix) SEQ ID NOS: **29, 30, 31, 10, 11** and **28**, respectively [**FS30-35-14**]; or

(x) SEQ ID NOS: **37, 38, 39, 10, 11** and **36**, respectively [**FS30-5-37**]; and

wherein the OX40 antigen-binding site comprises a first sequence, a second sequence, and a third sequence located in the AB, CD and EF structural loops of the CH3 domain, respectively, wherein the first, second and third sequence have the sequence set forth in

SEQ ID NOS: **51, 52** and **53**, respectively [**FS20-22-49**].

2. The antibody molecule according to claim 1, wherein:

(i) the first sequence is located at positions 14 to 18 of the CH3 domain of the antibody molecule;

(ii) the second sequence is located at positions 45.1 to 77 of the CH3 domain of the antibody molecule; and/or

(iii) the third sequence is located at positions 93 to 101 of the CH3 domain of the antibody molecule; and

wherein the amino acid residue numbering is according to the IMGT numbering scheme.

3. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule comprises the CH3 domain sequence set forth in SEQ ID NO: **54** [**FS20-22-49**].
- 5 4. The antibody molecule according to claim 3, wherein the CH3 domain sequence further comprises a lysine residue (K) at the immediate C-terminus of the CH3 domain sequence.
- 10 5. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule comprises the VH domain and VL domain set forth in:
- (i) SEQ ID NOs: **12** and **14**, respectively [**FS30-10-16**];
 - (ii) SEQ ID NOs: **18** and **14**, respectively [**FS30-10-3**];
 - (iii) SEQ ID NOs: **23** and **14**, respectively [**FS30-10-12**];
 - 15 (iv) SEQ ID NOs: **170** and **172**, respectively [**FS30-35-14**]; or
 - (v) SEQ ID NOs: **40** and **42**, respectively [**FS30-5-37**].
6. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule comprises the heavy chain and light chain of antibody:
- 20 (i) **FS20-22-49AA/FS30-10-16** set forth in SEQ ID NOs: **95** and **97**, respectively;
- (ii) **FS20-22-49AA/FS30-10-3** set forth in SEQ ID NOs: **99** and **97**, respectively;
- (iii) **FS20-22-49AA/FS30-10-12** set forth in SEQ ID NOs: **103** and **97**, respectively;
- (iv) **FS20-22-49AA/FS30-35-14** set forth in SEQ ID NOs: **105** and **107**, respectively; or
- (v) **FS20-22-49AA/FS30-5-37** set forth in SEQ ID NOs: **109** and **111**, respectively.
- 25 7. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule comprises:
- (i) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, defined according to the IMGT numbering scheme, set forth in SEQ ID NOs: **1**, **2**, **3**, **4**, **5** and **6**,
30 respectively [**FS30-10-16**];
 - (ii) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3, defined according to the Kabat numbering scheme, set forth in SEQ ID NOs: **7**, **8**, **9**, **10**, **11** and **6**, respectively [**FS30-10-16**];
 - (iii) the VH domain and VL domain set forth in SEQ ID NOs: **12** and **14**, respectively
35 [**FS30-10-16**]; and/or
 - (iv) the heavy chain and light chain set forth in SEQ ID NOs: **95** and **97**, respectively [**FS20-22-49AA/FS30-10-16**].

8. The antibody molecule according to claim 7, wherein the antibody molecule comprises the heavy chain and light chain set forth in SEQ ID NOs: **95** and **97**, respectively [FS20-22-49AA/FS30-10-16].

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9. The antibody molecule according to claim 8, wherein the CH3 domain in the heavy chain sequence comprises a lysine residue (K) at the immediate C-terminus of the CH3 domain sequence.

10 10. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule binds human CD137 and human OX40, wherein the antibody molecule is optionally capable of binding to human CD137 and human OX40 concurrently.

11. The antibody molecule according to any one of the preceding claims, wherein:

15 (i) the antibody molecule is capable of activating the OX40 on an immune cell in the presence of cell surface-expressed CD137, and/or the antibody molecule is capable of activating CD137 on an immune cell in the presence of cell surface expressed OX40;

(ii) binding of the antibody molecule to OX40 on an immune cell and to CD137 causes clustering of OX40 on the immune cell, and/or wherein binding of the antibody molecule to CD137 on the immune cell and to OX40 causes clustering of CD137 on the immune cell; and/or

(iii) the antibody molecule has been modified to reduce or abrogate binding of the CH2 domain of the antibody molecule to one or more Fc γ receptors.

25 12. A nucleic acid molecule or molecules encoding the antibody molecule according to any one of the preceding claims.

13. A vector or vectors comprising the nucleic acid molecule or molecules according to claim 12.

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14. A recombinant host cell comprising the nucleic acid molecule(s) according to claim 12, or the vector(s) according to claim 13.

15. A method of producing the antibody molecule according to any one of claims 1 to 11 comprising culturing the recombinant host cell of claim 14 under conditions for production of

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the antibody molecule, optionally further comprising isolating and/or purifying the antibody molecule.

16. A pharmaceutical composition comprising the antibody molecule according to any
5 one of claims 1 to 11 and a pharmaceutically acceptable excipient.

17. A pharmaceutical composition for the treatment of cancer or an infectious disease in an individual, comprising the antibody molecule according to any one of claims 1 to 11.

10 18. The pharmaceutical composition for the treatment of cancer according to claim 17, further comprising a second therapeutic.

19. The pharmaceutical composition according to claim 18, wherein the second
therapeutic is an antibody that binds PD-1 or PD-L1.

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