

Claims

1. An antibody molecule that binds to mesothelin (MSLN) and CD137, comprising
- (a) a complementarity determining region (CDR)-based antigen-binding site for MSLN; and
- (b) a CD137 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 set forth in:

- (i) SEQ ID NOs **42, 33, 44, 20, 22, and 80, respectively [FS28-256-271];**
- (ii) SEQ ID NOs **14, 16, 27, 20, 22 and 24, respectively [FS28-024-052];**
- (iii) SEQ ID NOs **42, 33, 44, 20, 22, and 40, respectively [FS28-256-021];**
- (iv) SEQ ID NOs **42, 33, 44, 20, 22, and 37, respectively [FS28-256-012];**
- (v) SEQ ID NOs **50, 33, 52, 20, 22 and 40, respectively [FS28-256-023];**
- (vi) SEQ ID NOs **42, 33, 44, 20, 22 and 41, respectively [FS28-256-024];**
- (vii) SEQ ID NOs **50, 33, 52, 20, 22 and 41, respectively [FS28-256-026];**
- (viii) SEQ ID NOs **42, 33, 44, 20, 22, and 80, respectively [FS28-256-027];**
- (ix) SEQ ID NOs **38, 33, 35, 20, 22, and 40, respectively [FS28-256-001];**
- (x) SEQ ID NOs **38, 33, 35, 20, 22, and 41 respectively [FS28-256-005];**
- (xi) SEQ ID NOs **46, 33, 48, 20, 22 and 37, respectively [FS28-256-014];**
- (xii) SEQ ID NOs **50, 33, 52, 20, 22 and 37, respectively [FS28-256-018];**
- (xiii) SEQ ID NOs **31, 33, 35, 20, 22 and 37, respectively [FS28-256];**
- (xiv) SEQ ID NOs **14, 16, 25, 20, 22 and 24, respectively [FS28-024-051];**
- (xv) SEQ ID NOs **14, 16, 29, 20, 22 and 24, respectively [FS28-024-053];** or
- (xvi) SEQ ID NOs **14, 16, 18, 20, 22 and 24, respectively [FS28-024];** and

wherein the CD137 antigen-binding site comprises a first sequence and a second sequence located in the AB and EF structural loops of the CH3 domain, respectively, wherein the first and second sequence have the sequence set forth in SEQ ID NOs **10 and 11 [FS22-172-003]**, respectively.

2. The antibody molecule according to claim 1, wherein the antibody molecule comprises the VH domain and the VL domain set forth in:

- (i) SEQ ID NOs **70 and 76, respectively [FS28-256-271];**
- (ii) SEQ ID NOs **58 and 54, respectively [FS28-024-052];**
- (iii) SEQ ID NOs **70 and 68, respectively [FS28-256-021];**
- (iv) SEQ ID NOs **70 and 64, respectively [FS28-256-012];**
- (v) SEQ ID NOs **74 and 68, respectively [FS28-256-023];**
- (vi) SEQ ID NOs **70 and 78, respectively [FS28-256-024];**
- (vii) SEQ ID NOs **74 and 78, respectively [FS28-256-026];**

- (viii) SEQ ID NOs **70 and 76**, respectively **[FS28-256-027]**;
- (ix) SEQ ID NOs **66 and 68**, respectively **[FS28-256-001]**;
- (x) SEQ ID NOs **66 and 78**, respectively **[FS28-256-005]**;
- (xi) SEQ ID NOs **72 and 64**, respectively **[FS28-256-014]**;
- (xii) SEQ ID NOs **74 and 64**, respectively **[FS28-256-018]**;
- (xiii) SEQ ID NOs **62 and 64**, respectively **[FS28-256]**;
- (xiv) SEQ ID NOs **56 and 54**, respectively **[FS28-024-051]**;
- (xv) SEQ ID NOs **60 and 54**, respectively **[FS28-024-053]**; or
- (xvi) SEQ ID NOs **12 and 54**, respectively **[FS28-024]**.

3. The antibody molecule according to claim 1 or 2, wherein the antibody molecule comprises:

- (i) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 set forth in SEQ ID NOs **42, 33, 44, 20, 22, and 80, respectively [FS28-256-271]**; and/or
- (ii) the VH domain and VL domain set forth in SEQ ID NOs **70 and 76**, respectively **[FS28-256-271]**.

4. The antibody molecule according to claim 1 or 2, wherein the antibody molecule comprises:

- (i) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 set forth in SEQ ID NOs **14, 16, 27, 20, 22 and 24**, respectively **[FS28-024-052]**; and/or
- (ii) the VH domain and VL domain set forth in SEQ ID NOs **58 and 54**, respectively **[FS28-024-052]**.

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

- (i) the first sequence is located between positions 14 and 17 of the CH3 domain of the antibody molecule; and/or
 - (ii) wherein the second sequence is located between 91 and 99 of the CH3 domain of the antibody molecule; and
- wherein the amino acid residue numbering is according to the IMGT numbering scheme.

6. 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: 8 **[FS22-172-003]**.

7. The antibody molecule according to claim 6, wherein the CH3 domain sequence comprises an additional lysine residue (K) at the immediate C-terminus of the CH3 domain sequence.
8. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule comprises the heavy chain and light chain of antibody:
- (i) **FS22-172-003-AA/FS28-256-271** set forth in SEQ ID NOs **3 and 84**, respectively;
 - (ii) **FS22-172-003-AA/FS28-024-052** set forth in SEQ ID NOs **102 and 85**, respectively;
 - (iii) **FS22-172-003-AA/FS28-256-021** set forth in SEQ ID NOs **125 and 82**, respectively;
 - (iv) **FS22-172-003-AA/FS28-256-012** set forth in SEQ ID NOs **125 and 116**, respectively;
 - (v) **FS22-172-003-AA/FS28-256-023** set forth in SEQ ID NOs **133 and 82**, respectively;
 - (vi) **FS22-172-003-AA/FS28-256-024** set forth in SEQ ID NOs **125 and 83**, respectively;
 - (vii) **FS22-172-003-AA/FS28-256-026** set forth in SEQ ID NOs **133 and 83**, respectively;
 - (viii) **FS22-172-003-AA/FS28-256-027** set forth in SEQ ID NOs **125 and 84**, respectively;
 - (ix) **FS22-172-003-AA/FS28-256-001** set forth in SEQ ID NOs **120 and 82**, respectively;
 - (x) **FS22-172-003-AA/FS28-256-005** set forth in SEQ ID NOs **120 and 83**, respectively;
 - (xi) **FS22-172-003-AA/FS28-256-014** set forth in SEQ ID NOs **129 and 116**, respectively;
 - (xii) **FS22-172-003-AA/FS28-256-018** set forth in SEQ ID NOs **133 and 116**, respectively;
 - (xiii) **FS22-172-003-AA/FS28-256** set forth in SEQ ID NOs **114 and 116**, respectively;
 - (xiv) **FS22-172-003-AA/FS28-024-051** set forth in SEQ ID NOs **98 and 85**, respectively;
 - (xv) **FS22-172-003-AA/FS28-024-053** set forth in SEQ ID NOs **106 and 85**, respectively;
- or
- (xvi) **FS22-172-003-AA/FS28-024** set forth in SEQ ID NOs **94 and 85**, respectively.
9. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule comprises the heavy chain and light chain set forth in SEQ ID NOs **3 and 84**, respectively [**FS22-172-003-AA/FS28-256-271**].
10. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule comprises the heavy chain and light chain set forth in SEQ ID NOs **3 and 84**, respectively [**FS22-172-003-AA/FS28-256-271**], and wherein the CH3 domain in the heavy chain sequence comprises an additional lysine residue (K) at the immediate C-terminus of the CH3 domain sequence.
11. An antibody molecule that binds to mesothelin (MSLN) and CD137, comprising the heavy chain and light chain set forth in SEQ ID NOs **3 and 84**, respectively [**FS22-172-003-AA/FS28-256-271**].

12. An antibody molecule that binds to mesothelin (MSLN) and CD137, comprising the heavy chain and light chain set forth in SEQ ID NOs **3 and 84**, respectively [**FS22-172-003-AA/FS28-256-271**], wherein the CH3 domain in the heavy chain sequence comprises an additional lysine residue (K) at the immediate C-terminus of the CH3 domain sequence.
13. The antibody molecule according to any one of claims 1 to 8, wherein the antibody molecule comprises the heavy chain and light chain set forth in SEQ ID NOs **102 and 85**, respectively [**FS22-172-003-AA/FS28-024-052**].
14. The antibody molecule according to any one of claims 1 to 8 or claim 13, wherein the antibody molecule comprises the heavy chain and light chain set forth in SEQ ID NOs **102 and 85**, respectively [**FS22-172-003-AA/FS28-024-052**], and wherein the CH3 domain in the heavy chain sequence comprises an additional lysine residue (K) at the immediate C-terminus of the CH3 domain sequence.
15. An antibody molecule that binds to mesothelin (MSLN) and CD137, comprising the heavy chain and light chain set forth in SEQ ID NOs **102 and 85**, respectively [**FS22-172-003-AA/FS28-024-052**].
16. An antibody molecule that binds to mesothelin (MSLN) and CD137, comprising the heavy chain and light chain set forth in SEQ ID NOs **102 and 85**, respectively [**FS22-172-003-AA/FS28-024-052**], wherein the CH3 domain in the heavy chain sequence comprises an additional lysine residue (K) at the immediate C-terminus of the CH3 domain sequence.
17. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule does not bind to Fcγ receptors.
18. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule binds to immobilised MSLN with a higher affinity than to soluble MSLN.
19. The antibody molecule according to any one of the preceding claims, wherein the antibody molecule is capable of activating CD137 on an immune cell in the presence of tumour cell-surface bound MSLN.

20. The antibody molecule according to any one of the preceding claims, wherein binding of the antibody molecule to CD137 on an immune cell and to tumour cell-surface bound MSLN causes clustering of CD137 on the immune cell.
21. A nucleic acid molecule or molecules encoding the antibody molecule according to any one of the preceding claims.
22. A vector or vectors comprising the nucleic acid molecule or molecules according to claim 21.
23. A recombinant host cell comprising the nucleic acid molecule(s) according to claim 21, or the vector(s) according to claim 22.
24. A method of producing the antibody molecule according to any one of claims 1 to 20 comprising culturing the recombinant host cell of claim 23 under conditions for production of the antibody molecule.
25. A pharmaceutical composition comprising the antibody molecule according to any one of claims 1 to 20 and a pharmaceutically acceptable excipient.
26. A pharmaceutical composition for the treatment of cancer in an individual, comprising the antibody molecule according to any one of claims 1 to 20.
27. The pharmaceutical composition according to claim 26, further comprising a second therapeutic.