

CLAIMS

1. An antibody or antigen binding fragment thereof that specifically binds one or more O-mannosylated threonine residues of E-cadherin, wherein said one or more O-mannosylated threonine residues are present within amino acid positions 467-472 of the E-cadherin sequence as depicted in Figure 1A.
- 5
2. An antibody or antigen binding fragment according to claim 1, wherein the binding of said antibody or antigen binding fragment to said E-cadherin is dependent on the presence of an O-mannosylated threonine residue at position 467, an O-mannosylated threonine residue at position 468, an O-mannosylated threonine residue at position 470, an O-mannosylated threonine residue at position 472, the glutamic acid residue at position 463, the serine residue at position 465, the serine residue at position 469, and/or the valine residue at position 477, of the E-cadherin sequence as depicted in Figure 1A.
- 10
3. An antibody or antigen binding fragment according to claim 1 or 2, wherein the binding of said antibody or antigen binding fragment to said E-cadherin is dependent on the presence of an O-mannosylated threonine residue at position 467 and/or an O-mannosylated threonine residue at position 468 and/or an O-mannosylated threonine residue at position 470 of the E-cadherin sequence as depicted in Figure 1A.
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- 20
4. An antibody or antigen binding fragment according to any one of claims 1-3, characterized in that said antibody or antigen binding fragment binds O-mannosylated truncated 70kDa E-cadherin better than O-mannosylated full length E-cadherin.
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5. An antibody or antigen binding fragment thereof that is able to bind O-mannosylated E-cadherin, wherein said antibody or antigen binding fragment comprises one or more, and optionally each, of:
- 30
- a. a heavy chain variable region CDR1 comprising the amino acid sequence GFX₁FSX₂AW, wherein X₁ is T or I and wherein X₂ is N or Y;
- or a heavy chain variable region CDR1 comprising an amino acid sequence differing from said GFX₁FSX₂AW sequence by 1, 2 or 3 conservative substitutions;

- b. a heavy chain variable region CDR2 comprising the amino acid sequence IKSKIDG X₁T X₂, wherein X₁ is G or E and wherein X₂ is T or I;
or a heavy chain variable region CDR2 comprising an amino acid sequence differing from said IKSKIDG X₁T X₂ sequence by 1, 2 or 3 conservative substitutions;
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- c. a heavy chain variable region CDR3 comprising the amino acid sequence TPGVGX₁NX₂PYYFDR, wherein X₁ is A or T and wherein X₂ is D or N;
or a heavy chain variable region CDR3 comprising an amino acid sequence differing from said TPGVGX₁NX₂PYYFDR sequence by 1, 2 or 3 conservative substitutions;
- 10
- d. a light chain variable region CDR1 comprising the amino acid sequence QSVLCRSNNKNC;
or a light chain variable region CDR1 comprising an amino acid sequence differing from said QSVLCRSNNKNC sequence by 1, 2 or 3 conservative substitutions;
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- e. a light chain variable region CDR2 comprising the amino acid sequence WAX₁, wherein X₁ is S or C;
or a light chain variable region CDR2 comprising an amino acid sequence differing from said WAX₁ sequence by 1, 2 or 3 conservative substitutions;
- 20
- f. a light chain variable region CDR3 comprising the amino acid sequence QQYSNTPQT;
or a light chain variable region CDR3 comprising an amino acid sequence differing from said QQYSNTPQT sequence by 1, 2 or 3 conservative substitutions.
- 25
6. An antibody or antigen binding fragment according to any one of claims 1-5, comprising:
- a. a heavy chain CDR1 comprising the sequence GFTFSNAW and a heavy chain CDR2 comprising the sequence IKSKIDGGTT and a heavy chain CDR3 comprising the sequence TPGVGANDPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- 30

- b. a heavy chain CDR1 comprising the sequence GFIFSNW and a heavy chain CDR2 comprising the sequence IKSKIDGGTT and a heavy chain CDR3 comprising the sequence TPGVGANDPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- c. a heavy chain CDR1 comprising the sequence GFIFSNW and a heavy chain CDR2 comprising the sequence IKSKIDGETT and a heavy chain CDR3 comprising the sequence TPGVGANDPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- d. a heavy chain CDR1 comprising the sequence GFTFSNw and a heavy chain CDR2 comprising the sequence IKSKIDGETT and a heavy chain CDR3 comprising the sequence TPGVGANDPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- e. a heavy chain CDR1 comprising the sequence GFTFSNw and a heavy chain CDR2 comprising the sequence IKSKIDGETT and a heavy chain CDR3 comprising the sequence TPGVGANNPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- f. a heavy chain CDR1 comprising the sequence GFTFSNw and a heavy chain CDR2 comprising the sequence IKSKIDGETT and a heavy chain CDR3 comprising the sequence TPGVGANNPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAc and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- g. a heavy chain CDR1 comprising the sequence GFTFSNw and a heavy chain CDR2 comprising the sequence IKSKIDGGTT and a heavy chain CDR3 comprising the sequence TPGVGANNPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or

- h. a heavy chain CDR1 comprising the sequence GFTFSNAW and a heavy chain CDR2 comprising the sequence IKSKIDGGTT and a heavy chain CDR3 comprising the sequence TPGVGTNNPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- 5
- i. a heavy chain CDR1 comprising the sequence GFTFSYAW and a heavy chain CDR2 comprising the sequence IKSKIDGGTT and a heavy chain CDR3 comprising the sequence TPGVGANDPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
- 10
- j. a heavy chain CDR1 comprising the sequence GFTFSNAW and a heavy chain CDR2 comprising the sequence IKSKIDGGTI and a heavy chain CDR3 comprising the sequence TPGVGANDPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
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- k. a heavy chain CDR1 comprising the sequence GFTFSYAW and a heavy chain CDR2 comprising the sequence IKSKIDGGTT and a heavy chain CDR3 comprising the sequence TPGVGANNPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
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- l. a heavy chain CDR1 comprising the sequence GFIFSYAW and a heavy chain CDR2 comprising the sequence IKSKIDGGTT and a heavy chain CDR3 comprising the sequence TPGVGANNPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT; or
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- 30
- m. a heavy chain CDR1 comprising the sequence GFIFSYAW and a heavy chain CDR2 comprising the sequence IKSKIDGETT and a heavy chain CDR3 comprising the sequence TPGVGANNPYYFDR and a light chain CDR1 comprising the sequence QSVLCRSNNKNC and a light chain CDR2 comprising the sequence WAS and a light chain CDR3 comprising the sequence QQYSNTPQT.
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7. An antibody or antigen binding fragment according to any one of claims 1-6, comprising:
- a heavy chain variable region comprising a sequence having at least 80% sequence identity with a VH sequence selected from the group consisting of SEQ ID NOs: 1-17;
 - 5 and/or
 - a light chain variable region comprising a sequence having at least 80% sequence identity with a VL sequence selected from the group consisting of SEQ ID NOs: 18-22.
8. An antibody or antigen binding fragment according to any one of claims 1-7, comprising:
- a VH sequence as depicted in SEQ ID NO: 1 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
 - a VH sequence as depicted in SEQ ID NO: 1 and a VL sequence as depicted in SEQ ID NO: 22, or sequences having at least 80% sequence identity thereto; or
 - 15 - a VH sequence as depicted in SEQ ID NO: 2 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
 - a VH sequence as depicted in SEQ ID NO: 3 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 90% sequence identity thereto; or
 - a VH sequence as depicted in SEQ ID NO: 4 and a VL sequence as depicted in SEQ ID NO: 19, or sequences having at least 80% sequence identity thereto; or
 - 20 - a VH sequence as depicted in SEQ ID NO: 5 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
 - a VH sequence as depicted in SEQ ID NO: 6 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
 - 25 - a VH sequence as depicted in SEQ ID NO: 6 and a VL sequence as depicted in SEQ ID NO: 20, or sequences having at least 80% sequence identity thereto; or
 - a VH sequence as depicted in SEQ ID NO: 7 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
 - a VH sequence as depicted in SEQ ID NO: 8 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
 - 30 - a VH sequence as depicted in SEQ ID NO: 9 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
 - a VH sequence as depicted in SEQ ID NO: 10 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or

- a VH sequence as depicted in SEQ ID NO: 10 and a VL sequence as depicted in SEQ ID NO: 21, or sequences having at least 80% sequence identity thereto; or
- a VH sequence as depicted in SEQ ID NO: 11 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
- 5 - a VH sequence as depicted in SEQ ID NO: 12 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
- a VH sequence as depicted in SEQ ID NO: 13 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
- a VH sequence as depicted in SEQ ID NO: 14 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
- 10 - a VH sequence as depicted in SEQ ID NO: 15 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
- a VH sequence as depicted in SEQ ID NO: 16 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto; or
- 15 - a VH sequence as depicted in SEQ ID NO: 17 and a VL sequence as depicted in SEQ ID NO: 18, or sequences having at least 80% sequence identity thereto.

9. An antibody or antigen binding fragment according to any one of claims 1-8, that is a human antibody or an antigen binding fragment thereof.
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10. An antibody or antigen binding fragment according to any one of claims 1-9, wherein said antibody is of the IgG isotype, preferably IgG1.
11. An antibody or antigen binding fragment according to any one of claims 1-10, that is afucosylated.
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12. An antibody or antigen binding fragment thereof that competes with an antibody according to any one of claims 1-11 for binding to O-mannosylated E-cadherin, preferably to O-mannosylated truncated 70kDa E-cadherin.
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13. An antibody or antigen binding fragment according to any one of claims 1-12, wherein said antibody or antigen binding fragment has one or more, and preferably each of, the following characteristics:
- 35 - binds to the extracellular (EC)3 domain of O-mannosylated E-cadherin;

- binds O-mannosylated truncated 70kDa E-cadherin better than O-mannosylated full length E-cadherin;

5 - binds tumor cells that co-express E-cadherin and an O-mannosyltransferase, preferably TMTC3.

14. An antibody or antigen binding fragment according to any one of claims 1-13, that is coupled to another compound, preferably to a compound selected from the group consisting of an immunomodulatory compound, a T cell-binding compound, a natural
10 killer cell (NK cell)-binding compound, a natural killer T cell (NKT cell)-binding compound, a gamma-delta T cell-binding compound, a CD3-specific binding compound, a TGFβ-specific binding compound, a cytokine, a second antibody or antigen binding part thereof, a detectable label, a drug, a chemotherapeutic drug, a cytotoxic agent, a toxic moiety, a hormone, an enzyme and a radioactive compound.

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15. A bispecific or multispecific binding compound, preferably a bispecific or multispecific antibody or antigen binding fragment thereof, that is able to bind O-mannosylated E-cadherin, comprising:

20 - an antibody or antigen binding fragment according to any one of claims 1-13; and
- an immunomodulatory compound.

16. An antibody-drug conjugate comprising an antibody or antigen binding fragment according to any one of claims 1-13 and a therapeutic compound.

25 17. An antibody or antigen binding fragment according to claim 14, or a bispecific or multispecific antibody or antigen binding fragment thereof according to claim 15, or an antibody-drug conjugate according to claim 16, wherein an antibody or antigen binding fragment according to any one of claims 1-13 is coupled to a CD3-specific binding compound or a TGFβ-specific binding compound.

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18. A bispecific antibody or antigen binding fragment thereof that is able to bind O-mannosylated E-cadherin, comprising:

- one Fab fragment of an antibody or antigen binding fragment according to any one of claims 1-13; and

- one Fab fragment of another antibody, specific for a T cell, a natural killer cell (NK cell), a natural killer T cell (NKT cell) or a gamma-delta T cell, preferably specific for CD3.
- 5 19. A bispecific antibody or antigen binding fragment thereof that is able to bind O-mannosylated E-cadherin, comprising:
- one Fab fragment of an antibody or antigen binding fragment according to any one of claims 1-13; and
- one Fab fragment of another antibody, specific for TGFβ.
- 10 20. A chimeric antigen receptor (CAR) T cell that is able to bind O-mannosylated E-cadherin, wherein the CAR T cell comprises the heavy chain CDR1, CDR2 and CDR3 sequences of an antibody according to any one of claims 1-13.
- 15 21. A chimeric antigen receptor (CAR) T cell according to claim 20, comprising a heavy chain CDR1, CDR2 and CDR3 sequence as recited in claim 5 or 6.
22. An isolated, synthetic or recombinant nucleic acid encoding an antibody or antigen binding fragment according to any one of claims 1-19, or encoding at least the
- 20 heavy chain CDR1, CDR2 and CDR3 sequences of an antibody according to any one of claims 1-19, or encoding at least the heavy chain CDR1, CDR2 and CDR3 sequences and the light chain CDR1, CDR2 and CDR3 sequences of an antibody according to any one of claims 1-19, or encoding at least the heavy chain variable region and/or the light chain variable region of an antibody or antigen binding fragment according to any one of
- 25 claims 1-19.
23. A nucleic acid according to claim 22, comprising a sequence that has at least 80% sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 23-39, and/or comprising a sequence that has at least 80% sequence identity with a
- 30 sequence selected from the group consisting of SEQ ID NOs: 40-44.
24. A nucleic acid according to any one of claims 22-23, that is codon optimized for expression in a non-human host cell.
- 35 25. A vector comprising a nucleic acid according to any one of claims 22-24.

26. A vector according to claim 25, wherein said vector is a CAR T cell vector comprising a nucleic acid sequence encoding a T cell activating domain and a nucleic acid sequence encoding an antigen recognition domain, wherein said antigen recognition domain comprises at least the heavy chain CDR1, CDR2 and CDR3 sequences of an antibody according to any one of claims 1-19, preferably at least the heavy chain CDR1, CDR2 and CDR3 sequences and the light chain CDR1, CDR2 and CDR3 sequences of an antibody according to any one of claims 1-19.
27. A vector according to claim 25 or 26, comprising:
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 23 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
 - a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 23 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 44, or sequences having at least 80% sequence identity thereto; or
 - a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 24 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto
 - a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 25 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
 - a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 26 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 41, or sequences having at least 80% sequence identity thereto; or
 - a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 27 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
 - a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 28 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
 - a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 28 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 42, or sequences having at least 80% sequence identity thereto; or

- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 29 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 30 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 31 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 32 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 32 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 43, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 33 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 34 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 35 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 36 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 37 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or
- a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 38 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto; or

a VH encoding nucleic acid sequence as depicted in SEQ ID NO: 39 and a VL encoding nucleic acid sequence as depicted in SEQ ID NO: 40, or sequences having at least 80% sequence identity thereto.

5 28. An isolated or recombinant host cell, or a non-human animal, comprising an antibody, antigen binding fragment, bispecific antibody, multispecific antibody, antibody-drug conjugate, CAR T cell, nucleic acid or vector according to any one of claims 1-27.

10 29. A cell according to claim 28, which is a mammalian cell, a bacterial cell, a plant cell, a HEK293T cell or a CHO cell.

30. A composition comprising an antibody, antigen binding fragment, bispecific antibody, multispecific antibody, antibody-drug conjugate, CAR T cell, nucleic acid
15 molecule, vector or host cell according to any one of claims 1-29.

31. The composition according to claim 30, wherein said composition is a pharmaceutical composition that also comprises a pharmaceutically acceptable carrier, diluent or excipient.
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32. The composition according to claim 30 or 31, further comprising another therapeutic agent for the treatment or prevention of a disorder that is associated with cells, preferably tumor cells, that comprise O-mannosylated E-cadherin.

25 33. A kit of parts comprising an antibody, antigen binding fragment, bispecific antibody, multispecific antibody, antibody-drug conjugate, CAR T cell, nucleic acid molecule, vector or host cell according to any one of claims 1-29 and another therapeutic agent for the treatment or prevention of a disorder that is associated with cells, preferably tumor cells, that comprise O-mannosylated E-cadherin.

30 34. A method for producing an antibody or antigen binding fragment or antibody-drug conjugate or CAR T cell according to any one of claims 1-21, the method comprising culturing a cell comprising a nucleic acid or vector according to any one of claims 22-27 and allowing said cell to translate said nucleic acid or vector, thereby producing said
35 antibody or antigen binding fragment or antibody-drug conjugate or CAR T cell

according to any one of claims 1-21, the method preferably further comprising recovering said antibody or antigen binding fragment or antibody-drug conjugate or CAR T cell from said cell and/or from the culture medium.

- 5 35. An antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell or nucleic acid or vector or host cell according to any one of claims 1-29, for use as a medicament or prophylactic agent or diagnostic agent.
- 10 36. An antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell or nucleic acid or vector or host cell according to any one of claims 1-29 for use in a method for treating or preventing a disorder that is associated with cells, preferably tumor cells, that comprise O-mannosylated E-cadherin.
- 15 37. An antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell or nucleic acid or vector or host cell according to any one of claims 1-29 for use in diagnosis of a disorder that is associated with cells, preferably tumor cells, that comprise O-mannosylated E-cadherin.
- 20 38. A composition according to claim 32, a kit of parts according to claim 33, or an antibody or antigen binding fragment or bispecific antibody or multispecific antibody or CAR T cell or nucleic acid or vector or host cell for use according to claim 36 or 37, wherein said disorder is selected from the group consisting of epithelial cancer,
- 25 adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma, anaplastic carcinoma, large cell carcinoma, small cell carcinoma, colorectal cancer, colon cancer, stomach cancer, gastric cancer, gastroesophageal junction carcinoma, breast cancer, pancreatic cancer, esophageal cancer, gastroesophageal junction carcinoma, bladder cancer, lung cancer, small cell lung cancer, non-small cell lung cancer, lung
- 30 adenocarcinoma, urinary tract cancer, prostate cancer, brain cancer, thyroid cancer, laryngeal cancer, carcinoid cancer, liver cancer, hepatocellular carcinoma, head and neck cancer, ovary cancer, cervical cancer, ovarian cancer, endometrial cancer, intraepithelial carcinoma, clear cell carcinoma, melanoma, multiple myeloma, kidney cancer, renal cell carcinoma, renal transitional cell cancer, fallopian tube cancer and peritoneal cancer,
- 35 preferably selected from the group consisting of colorectal cancer, colon cancer, colon

cancer subtype CMS1, colon cancer subtype CMS2, colon cancer subtype CMS3, colon cancer subtype CMS4, laryngeal cancer, head and neck cancer, breast cancer, pancreatic cancer, esophageal cancer, bladder cancer, lung cancer, stomach cancer, urinary tract cancer, prostate cancer and ovary cancer.

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39. An antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell or nucleic acid or vector or host cell for use according to any one of claims 36-38, whereby said antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or
 10 CAR T cell or nucleic acid or vector or host cell is combined with another therapeutic agent useful in the treatment and/or prevention of a disorder that is associated with cells, preferably tumor cells, that comprise O-mannosylated E-cadherin.

40. Use of an antibody or antigen binding fragment or bispecific antibody or
 15 multispecific antibody or antibody-drug conjugate or CAR T cell according to any one of claims 1-21 for determining whether a sample comprises cells, preferably tumor cells, that comprise O-mannosylated E-cadherin.

41. A method for determining whether cells, preferably tumor cells, that comprise
 20 O-mannosylated E-cadherin are present in a sample, the method comprising:
 - contacting said sample with an antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell according to any one of claims 1-21, and
 - allowing said antibody or antigen binding fragment or bispecific antibody or
 25 multispecific antibody or antibody-drug conjugate or CAR T cell to bind to cells, preferably tumor cells, that comprise O-mannosylated E-cadherin, if present, and
 - determining whether or not cells are bound to said antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell, thereby determining whether or not cells, preferably tumor cells, that
 30 comprise O-mannosylated E-cadherin are present in said sample.

42. A method for determining whether a human or non-human individual is suffering from a cancer that is positive for O-mannosylated E-cadherin, the method comprising:
 - contacting tumor cells of said individual with an antibody or antigen binding fragment
 35 or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell

according to any one of claims 1-21,

- allowing said antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell to bind tumor cells that comprise O-mannosylated E-cadherin, if present, and

- 5 - determining whether or not tumor cells are bound to said antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell, thereby determining whether or not said individual is suffering from a cancer that comprises O-mannosylated E-cadherin and an O-mannosyltransferase, preferably TMTC3.

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43. A method for treating or preventing a disorder associated with cells, preferably tumor cells, that comprise O-mannosylated E-cadherin, the method comprising administering to an individual in need thereof a therapeutically effective amount of an antibody or antigen binding fragment or bispecific antibody or multispecific antibody or
15 antibody-drug conjugate or CAR T cell or nucleic acid or vector or host cell or composition or kit of parts according to any one of claims 1-33, optionally in association with a further therapeutic agent or therapeutic procedure.

44. Use of an antibody or antigen binding fragment or bispecific antibody or
20 multispecific antibody or antibody-drug conjugate or CAR T cell or nucleic acid or vector or host cell according to any one of claims 1-29 for the manufacture of a medicament.

45. Use of an antibody or antigen binding fragment or bispecific antibody or multispecific antibody or antibody-drug conjugate or CAR T cell or nucleic acid or vector
25 or host cell according to any one of claims 1-29 for the manufacture of a medicament for treating or preventing a disorder associated with cells, preferably tumor cells, that comprise O-mannosylated E-cadherin.

46. A method according to claim 43 or a use according to claim 44 or 45, wherein said
30 disorder is selected from the group consisting of epithelial cancer, adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma, anaplastic carcinoma, large cell carcinoma, small cell carcinoma, colorectal cancer, colon cancer, stomach cancer, gastric cancer, gastroesophageal junction carcinoma, breast cancer, pancreatic cancer, esophageal cancer, gastroesophageal junction carcinoma, bladder cancer, lung cancer,
35 small cell lung cancer, non-small cell lung cancer, lung adenocarcinoma, urinary tract

cancer, prostate cancer, brain cancer, thyroid cancer, laryngeal cancer, carcinoid cancer, liver cancer, hepatocellular carcinoma, head and neck cancer, ovary cancer, cervical cancer, ovarian cancer, endometrial cancer, intraepithelial carcinoma, clear cell carcinoma, melanoma, multiple myeloma, kidney cancer, renal cell carcinoma, renal
5 transitional cell cancer, fallopian tube cancer and peritoneal cancer, preferably selected from the group consisting of colorectal cancer, colon cancer, colon cancer subtype CMS1, colon cancer subtype CMS2, colon cancer subtype CMS3, colon cancer subtype CMS4, laryngeal cancer, head and neck cancer, breast cancer, pancreatic cancer, esophageal cancer, bladder cancer, lung cancer, stomach cancer, urinary tract cancer, prostate
10 cancer and ovary cancer.

47. An antibody or antigen binding fragment or antibody-drug conjugate or CAR T cell when obtained by a method according to claim 34.

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