

of cMET on a human cancer cell. In some embodiments, a binding agent does not have detectable cMET agonist activity. In some embodiments, a binding agent induces or promotes death of a cell to which it binds. In certain embodiments a binding agent is conjugated to an anti-neoplastic agent.

[0010]

- 5 In some aspects, a binding agent described herein specifically binds to cMET, or a portion thereof. In some aspects, a binding agent described herein specifically binds to cMET, or a portion thereof with a KD of 10 nM or less, or 1 nM or less. In some aspects, an affinity of a binding agent for cMET, or a portion thereof, comprises a KD of 10 nM or less, or 1 nM or less

[0011]

- 10 In some embodiments, a binding agent that specifically binds to cMET further comprises a second antigen binding portion that specifically binds to another antigen (e.g., an antigen that is not cMET, or a portion thereof). For example, in some embodiments, a binding agent comprises a first antigen binding domain that specifically binds to cMET and a second antigen binding domain that specifically binds to another polypeptide.

- 15 [0012]

- In certain aspects, presented herein are methods of treating a subject having or suspected of having a neoplastic disorder or cancer. In one embodiment, a method includes administering a therapeutically effective amount of a binding agent described herein to a subject. In some embodiments, a method comprises contacting a cell of the subject (e.g., a neoplastic or cancerous cell) with the binding agent. In 20 certain embodiments, the binding agent is configured to specifically bind to the extracellular domain of cMET expressed on one or more cells of the subject. In certain embodiments, the binding agent decreases, inhibits or reduces mitosis of, and/or promotes or induces death of the one or more cells expressing cMET. In certain embodiments, the neoplastic disorder or cancer comprises a lung carcinoma, breast carcinoma, ovarian carcinoma, kidney carcinoma, colorectal carcinoma, gastric carcinoma, thyroid carcinoma, 25 pancreas carcinoma, neuroblastoma, or a squamous cell carcinoma of the head and neck, cervical cancer, hepatocellular cancer, sarcomas, mesothelioma, glioblastoma, multiple myeloma, melanoma, prostate and esophageal carcinoma.

[0013]

- In some embodiments, a pharmaceutical composition which comprises the binding agent is provided. In 30 some embodiments, a pharmaceutical composition comprises, in addition to the binding agent, a pharmaceutically acceptable excipient, diluent, additive and/or carrier. In some embodiments, a pharmaceutical composition is formulated as a sterile, lyophilized powder, that upon reconstitution, is suitable for intravenous administration to a mammal.

[0013a]

- 35 In certain embodiments, there is provided a binding agent selected from the group consisting of: (i) a binding agent having a CDR-L1 of SEQ ID NO 1 or 2, a CDR-L2 of SEQ ID NO 16 or 17, a CDR-L3 of SEQ ID NO 26 or 27, a CDR-H1 of SEQ ID NO 50 or 51, a CDR-H2 of SEQ ID NO 62 or 63, and a CDR-H3 of SEQ ID NO 79 or 80; (ii) a binding agent having a CDR-L1 of SEQ ID NO 3 or 4, a CDR-L2 of SEQ ID NO 18 or 19, a CDR-L3 of SEQ ID NO 28 or 29, a CDR-H1 of SEQ ID NO 52 or 53, a CDR- 40 H2 of SEQ ID NO 64 or 65, and a CDR-H3 of SEQ ID NO 81 or 82; (iii) a binding agent having a CDR-L1 of SEQ ID NO 5 or 6, a CDR-L2 of SEQ ID NO 20 or 21, a CDR-L3 of SEQ ID NO 30 or 31, a CDRH1 of SEQ ID NO 54 or 55, a CDR-H2 of SEQ ID NO 66 or 67, and a CDR-H3 of SEQ ID NO 83 or 84; (iv) a binding agent having a CDR-L1 of SEQ ID NO 7 or 8, a CDR-L2 of SEQ ID NO 22 or 23, a CDR-L3 of SEQ ID NO 34 or 35, a CDR-H1 of SEQ ID NO 56 or 57, a CDR-H2 of SEQ ID NO 68 or 69, 45 and a CDR-H3 of SEQ ID NO 85 or 86; (v) a binding agent having a CDR-L1 of SEQ ID NO 9 or 10, a CDR-L2 of SEQ ID NO 24 or 25, a CDRL3 of SEQ ID NO 34 or 35, a CDR-H1 of SEQ ID NO 58 or 59, a CDR-H2 of SEQ ID NO 70 or 71, and a CDR-H3 of SEQ ID NO 87 or 88; (vi) a binding agent having a CDR-L1 of SEQ ID NO 11 or 12, a CDR-L2 of SEQ ID NO 24 or 25, a CDR-L3 of SEQ ID NO 34 or 35, a CDR-H1 of SEQ ID NO 58 or 59, a CDR-H2 of SEQ ID NO 74 or 75, and a CDR-H3 of SEQ ID NO 50 90 or 91; and (vii) a binding agent having a CDR-L1 of SEQ ID NO 11 or 12, a CDR-L2 of SEQ ID NO 24 or 25, a CDR-L3 of SEQ ID NO 34 or 35, a CDR-H1 of SEQ ID NO 58 or 59, a CDR-H2 of SEQ ID NO 72 or 73, and a CDR-H3 of SEQ ID NO 88 or 89; wherein the binding agent specifically binds to an extracellular domain of mesenchymal epithelial transition factor (cMET).

[0014]

- 55 Certain aspects of the technology are described further in the following description, examples, claims and drawings.

in terms of what the invention does not include aspects that are not expressly excluded in the invention are nevertheless disclosed herein.

[0156]

5 The technology illustratively described herein suitably can be practiced in the absence of any element(s) not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising," "consisting essentially of," and "consisting of" can be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and use of such terms and expressions do not exclude any equivalents of the features shown and described or segments thereof, and various modifications are possible within the scope of the technology claimed. The term "a" or "an" can refer to one of or a plurality of the elements it modifies (e.g., "a reagent" can mean one or more reagents) unless it is contextually clear either one of the elements or more than one of the elements is described. The term "about" as used herein refers to a value within 10% of the underlying parameter (i.e., plus or minus 10%), and use of the term "about" at the beginning of a string of values modifies each of the values (i.e., "about 1, 2 and 3" refers to about 1, about 2 and about 3). For example, a weight of "about 100 grams" can include weights between 90 grams and 110 grams. The term, "substantially" as used herein refers to a value modifier meaning "at least 95%", "at least 96%", "at least 97%", "at least 98%", or "at least 99%" and may include 100%. For example, a composition that is substantially free of X, may include less than 5%, less than 4%, less than 3%, less than 2%, or less than 1% of X, and/or X may be absent or undetectable in the composition.

[00156a]

25 The discussion of documents, acts, materials, devices, articles and the like is included in this specification solely for the purpose of providing a context for the present invention. It is not suggested or represented that any or all of these matters formed part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

30 [0157]

Thus, it should be understood that although the present technology has been specifically disclosed by representative embodiments and optional features, modification and variation of the concepts herein disclosed can be resorted to by those skilled in the art, and such modifications and variations are considered within the scope of this technology.

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Claims

1. A binding agent selected from the group consisting of:
- 5 (i) a binding agent having a CDR-L1 of SEQ ID NO 1 or 2,
a CDR-L2 of SEQ ID NO 16 or 17,
a CDR-L3 of SEQ ID NO 26 or 27,
a CDR-H1 of SEQ ID NO 50 or 51,
a CDR-H2 of SEQ ID NO 62 or 63, and
a CDR-H3 of SEQ ID NO 79 or 80;
- 10 (ii) a binding agent having
a CDR-L1 of SEQ ID NO 3 or 4,
a CDR-L2 of SEQ ID NO 18 or 19,
a CDR-L3 of SEQ ID NO 28 or 29,
a CDR-H1 of SEQ ID NO 52 or 53,
15 a CDR-H2 of SEQ ID NO 64 or 65, and
a CDR-H3 of SEQ ID NO 81 or 82;
- (iii) a binding agent having
a CDR-L1 of SEQ ID NO 5 or 6,
a CDR-L2 of SEQ ID NO 20 or 21,
20 a CDR-L3 of SEQ ID NO 30 or 31,
a CDR-H1 of SEQ ID NO 54 or 55,
a CDR-H2 of SEQ ID NO 66 or 67, and
a CDR-H3 of SEQ ID NO 83 or 84;
- (iv) a binding agent having
25 a CDR-L1 of SEQ ID NO 7 or 8,
a CDR-L2 of SEQ ID NO 22 or 23,
a CDR-L3 of SEQ ID NO 34 or 35,
a CDR-H1 of SEQ ID NO 56 or 57,
a CDR-H2 of SEQ ID NO 68 or 69, and
30 a CDR-H3 of SEQ ID NO 85 or 86;
- (v) a binding agent having
a CDR-L1 of SEQ ID NO 9 or 10,

a CDR-L2 of SEQ ID NO 24 or 25,
 a CDR-L3 of SEQ ID NO 34 or 35,
 a CDR-H1 of SEQ ID NO 58 or 59,
 a CDR-H2 of SEQ ID NO 70 or 71, and
 5 a CDR-H3 of SEQ ID NO 87 or 88;
 (vi) a binding agent having
 a CDR-L1 of SEQ ID NO 11 or 12,
 a CDR-L2 of SEQ ID NO 24 or 25,
 a CDR-L3 of SEQ ID NO 34 or 35,
 10 a CDR-H1 of SEQ ID NO 58 or 59,
 a CDR-H2 of SEQ ID NO 74 or 75, and
 a CDR-H3 of SEQ ID NO 90 or 91; and
 (vii) a binding agent having
 a CDR-L1 of SEQ ID NO 11 or 12,
 15 a CDR-L2 of SEQ ID NO 24 or 25,
 a CDR-L3 of SEQ ID NO 34 or 35,
 a CDR-H1 of SEQ ID NO 58 or 59,
 a CDR-H2 of SEQ ID NO 72 or 73, and
 a CDR-H3 of SEQ ID NO 88 or 89;
 20 wherein the binding agent specifically binds to an extracellular domain of
 mesenchymal epithelial transition factor (cMET).

2. The binding agent according to claim 1, having:
 a CDR-L1 of SEQ ID NO 9 or 10,
 25 a CDR-L2 of SEQ ID NO 24 or 25,
 a CDR-L3 of SEQ ID NO 34 or 35,
 a CDR-H1 of SEQ ID NO 58 or 59,
 a CDR-H2 of SEQ ID NO 70 or 71, and
 a CDR-H3 of SEQ ID NO 87 or 88.

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3. The binding agent according to claim 2, having a humanized light chain
 variable region selected from the group consisting of SEQ ID NOS 46-49 and a

humanized heavy chain variable region selected from the group consisting of SEQ ID NOS 105-108.

4. The binding agent according to claim 3, having SEQ ID NO 47 and 108.
5. The binding agent according to claim 3, having SEQ ID NO 47 and 106.
6. The binding agent according to claim 3, having SEQ ID NO 47 and 105.
7. The binding agent according to claim 3, having SEQ ID NO 48 and 108.
8. The binding agent of any one of claims 1 to 7, wherein the binding agent is an antibody, or a binding fragment thereof.
9. The binding agent of any one of claims 1 to 7, wherein the binding agent is an antibody.
10. The binding agent of any one of claims 1 to 9, wherein the binding agent induces internalization of cMET on a human cancer cell.
11. The binding agent of any one of claims 1 to 9, wherein the binding agent induces degradation of cMET on a human cancer cell.
12. The binding agent of any one of claims 1 to 11, wherein the binding agent comprises an anti-neoplastic agent.
13. A composition comprising a first binding agent that is the binding agent of any one of claims 1 to 11, and a second binding agent that does not bind specifically to cMET.
14. The composition of claim 13, wherein the first binding agent is the binding agent that specifically binds to the extracellular domain of cMET and the

second binding agent is conjugated to the first binding agent.

15. Use of a therapeutically effective amount of the binding agent of any one of claims 1 to 12 or the composition of claim 13 or 14 in the manufacture of a medicament for treating a subject having, or suspected of having, a cMET expressing neoplastic disorder or cMET expressing cancer.

16. The use of claim 15, wherein the binding agent specifically binds to the extracellular domain of cMET expressed on one or more cells of the subject.

17. The use of claim 15 or 16, wherein the binding agent inhibits mitosis of, and/or induces death of the one or more cells expressing cMET.

18. The use of any one of claims 15 to 17, wherein the cMET expressing neoplastic disorder or cMET expressing cancer comprises a lung carcinoma, breast carcinoma, ovarian carcinoma, kidney carcinoma, colorectal carcinoma, gastric carcinoma, thyroid carcinoma, pancreas carcinoma, neuroblastoma, or a squamous cell carcinoma of the head and neck, cervical cancer, hepatocellular cancer, sarcomas, mesothelioma, glioblastoma, multiple myeloma, melanoma, prostate and esophageal carcinoma.

19. A pharmaceutical composition comprising the binding agent of any one of claims 1 to 12, and a pharmaceutically acceptable excipient, diluent, additive or carrier.

20. The binding agent of any one of claims 1 to 12 or the composition of claim 13 or 14 for use in treating a subject having, or suspected of having, a cMET expressing neoplastic disorder or cMET expressing cancer.

21. The binding agent or the composition for use according to claim 20, wherein the binding agent specifically binds to the extracellular domain of cMET expressed on one or more cells of the subject.

22. The binding agent or the composition for use according to claim 20 or 21, wherein the binding agent inhibits mitosis of, and/or induces death of the one or more cells expressing cMET.

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23. The binding agent or the composition for use according to any one of claims 20 to 22, wherein the cMET expressing neoplastic disorder or cMET expressing cancer comprises a lung carcinoma, breast carcinoma, ovarian carcinoma, kidney carcinoma, colorectal carcinoma, gastric carcinoma, thyroid carcinoma, pancreas carcinoma, neuroblastoma, or a squamous cell carcinoma of the head and neck, cervical cancer, hepatocellular cancer, sarcomas, mesothelioma, glioblastoma, multiple myeloma, melanoma, prostate and esophageal carcinoma.

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