frequency of administration, but may be used at lower dosages and/or less frequently. When administered as monotherapy, the anti-cMet ADC will typically be administered on a schedule that provides therapeutic benefit. It is contemplated that anti-cMet ADCs administered once a week, once every two weeks, once every three weeks, once every four weeks, once every five weeks, once every six weeks, once every seven weeks or once every eight weeks will provide therapeutic benefit, although more or less frequent administration may be beneficial. When administered adjunctive to or with another therapy and/or agent, the anti-cMet ADC may be administered before, after or concurrently with the other therapy or agent.

[011] The anti-cMet ADCs may be administered via a variety of routes or modes of administration, including but not limited to, intravenous infusion and/or injection and subcutaneous injection. The amount administered will depend upon the route of administration, the dosing schedule, the type of cancer being treated, the stage of the cancer being treated, and other parameters such as the age and weight of the patient, as is well known in the art. Specific exemplary dosing schedules expected to provide therapeutic benefit are provided in the Detailed Description. Generally, an amount of anti-cMet ADC in the range of about 0.005 to 15 mg/kg when administered intravenously on a weekly basis from once weekly to and including once every eight weeks is expected to provide therapeutic benefit.

[012] Accordingly, in one embodiment, the present disclosure provides ADCs that specifically bind cMet ("anti-cMet ADCs"). The anti-cMet ADCs comprise cytotoxic and/or cytostatic agents linked by way of linkers to an antigen binding moiety that specifically binds cMet. In some embodiments, the antigen binding moiety is an antibody and/or an antigen binding fragment.

[012a] In one aspect, there is provided an anti-cMet antibody drug conjugate ("ADC") comprising an antimitotic agent linked to an anti-cMet antibody by way of a linker, wherein the ADC has the structure of formula (I):

(I) $[D–L–XY–]_n–Ab$

or a salt thereof, wherein:

D is the antimitotic agent;

L is the linker;

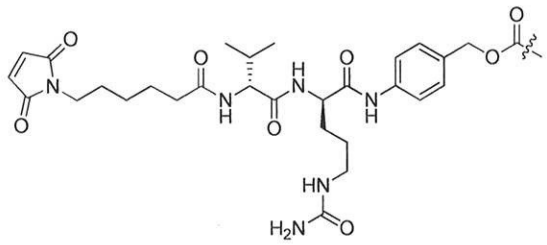
Ab is the anti-cMet antibody;

XY represents a covalent linkage linking linker L to antibody Ab; and

n is an integer ranging from 2 to 8;

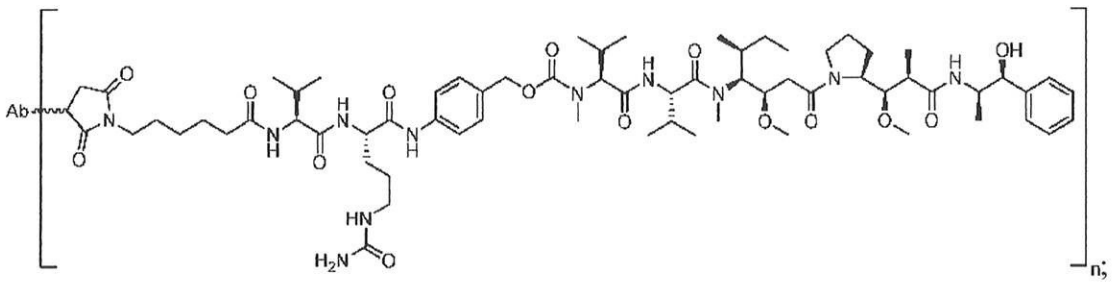
wherein

L comprises a valine-citrulline (vc) linker, and has the structure of formula (IVb.2):



(IVb.2)

D is a monomethyl auristatin E ("MMAE"), and the ADC of structural formula (I) has the following structure:



and

Ab comprises an anti-cMet antibody which comprises (i) a VH chain comprising three CDRs; and (ii) a VL chain comprising three CDRs, wherein:

V_H CDR#1 has an amino acid sequence:	GYIFTAYTMH	(SEQ ID NO:112),
V_H CDR#2 has an amino acid sequence:	WIKPNNGLANYAQKFQG	(SEQ ID NO:113),
V_H CDR#3 has an amino acid sequence:	SEITTEFDY	(SEQ ID NO:114),
V_L CDR#1 has an amino acid sequence:	KSSESVDSYANSFLH	(SEQ ID NO:115),
V_L CDR#2 has an amino acid sequence:	RASTRES	(SEQ ID NO:116),
and V_L CDR#3 has an amino acid sequence:	QQSKEDPLT	(SEQ ID NO:117),

and (iii) a modified hinge region having an amino acid sequence of PKSCDCHCPPCP (SEQ ID NO:170).

[012b] In one aspect, there is provided a pharmaceutical composition comprising the ADC disclosed herein, and a pharmaceutically acceptable carrier.

[012c] In one aspect, there is provided an anti-cMet antibody drug conjugate ("ADC") comprising a DNA cross-linking agent linked to an anti-cMet antibody by way of a linker, wherein the ADC has the structure of formula (I):

(I) $[D–L–XY–]_n–Ab$

or a salt thereof, wherein:

D is the DNA cross-linking agent;

L is the linker;

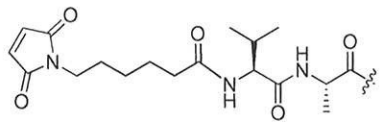
Ab is the anti-cMet antibody;

XY represents a covalent linkage linking linker L to antibody Ab; and

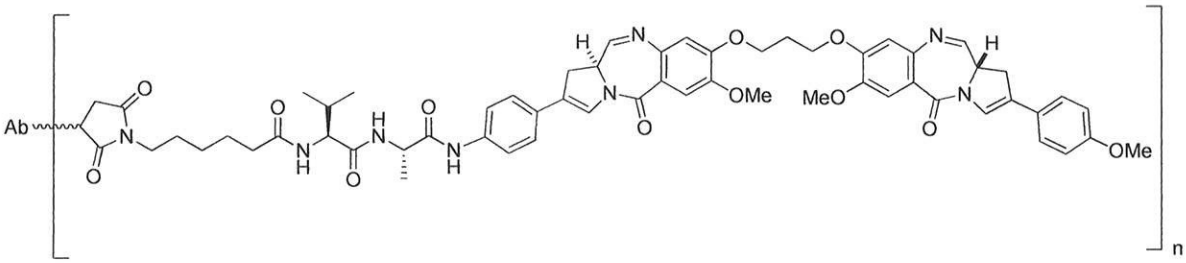
n is an integer ranging from 2 to 8;

wherein

L comprises a valine-alanine (va) linker, and has the structure of formula (IVd.3):

(IVd.3) 

D is a pyrrolobenzodiazepine ("PBD") dimer, and the ADC of structural formula (I) has the following structure:



and

Ab comprises an anti-cMet antibody which comprises (i) a VH chain comprising three CDRs; and (ii) a VL chain comprising three CDRs, wherein:

V_H CDR#1 has an amino acid sequence:	GYIFTAYTMH	(SEQ ID NO:173),
V_H CDR#2 has an amino acid sequence:	WIKPNNGLANYAQKFQG	(SEQ ID NO:174),
V_H CDR#3 has an amino acid sequence:	SEITTEFDY	(SEQ ID NO:175),
V_L CDR#1 has an amino acid sequence:	KSSESVDSYANSFLH	(SEQ ID NO:176),
V_L CDR#2 has an amino acid sequence:	RASTRES	(SEQ ID NO:177),
and V_L CDR#3 has an amino acid sequence:	QQSKEDPLT	(SEQ ID NO:178),

and (iii) a modified hinge region having an amino acid sequence of PKSCDCHCPPCP (SEQ ID NO:170).

[0012d] In one aspect, there is provided use of a pharmaceutical composition comprising an anti cMet antibody drug conjugate ("ADC") and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating a solid tumor cancer that overexpresses cMet, wherein the medicament is to be administered in an amount and for a period of time sufficient to provide a therapeutic benefit, and wherein the ADC has the structure of formula (I):

(I) $[D–L–XY–]_n–Ab$

or a salt thereof, wherein:

D is the antimitotic agent;

L is the linker;

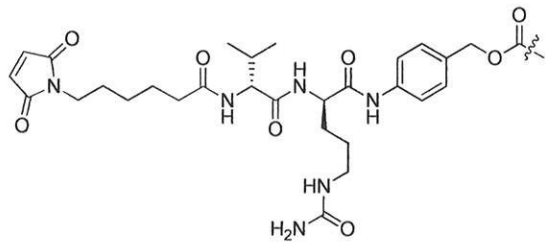
Ab is the anti-cMet antibody;

XY represents a covalent linkage linking linker L to antibody Ab; and

n is an integer ranging from 2 to 8;

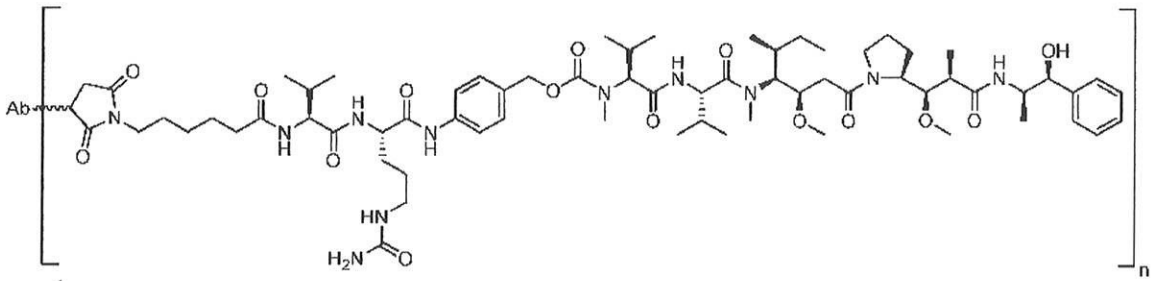
wherein

L comprises a valine-citrulline (vc) linker, and has the structure of formula (IVb.2):



(IVb.2)

D is a monomethyl auristatin E ("MMAE"), and the ADC of structural formula (I) has the following structure:



; and

Ab comprises an anti-cMet antibody which comprises (i) a VH chain comprising three CDRs; and (ii) a VL chain comprising three CDRs, wherein:

V_H CDR#1 has an amino acid sequence:	GYIFTAYTMH	(SEQ ID NO:112),
V_H CDR#2 has an amino acid sequence:	WIKPNNGLANYAQKFQG	(SEQ ID NO:113),
V_H CDR#3 has an amino acid sequence:	SEITTEFDY	(SEQ ID NO:114),
V_L CDR#1 has an amino acid sequence:	KSSESVDSYANSFLH	(SEQ ID NO:115),
V_L CDR#2 has an amino acid sequence:	RASTRES	(SEQ ID NO:116),
and V_L CDR#3 has an amino acid sequence:	QQSKEDPLT	(SEQ ID NO:117),

and (iii) a modified hinge region having an amino acid sequence of PKSCDCHCPPCP (SEQ ID NO:170).

[013] Antibodies and/or binding fragments composing the anti-cMet ADCs generally comprise a heavy chain comprising a variable region (V_H) having three complementarity determining regions ("CDRs") referred to herein (in N→C order) as V_H CDR#1, V_H CDR#2, and V_H CDR#3, and a light chain comprising a variable region (V_L) having three complementarity determining regions

referred to herein (in N→C order) as V_L CDR#1, V_L CDR#2, and V_L CDR#3. The amino acid sequences of exemplary CDRs, as well as the amino acid sequence of the V_H and V_L regions of the heavy and light chains of exemplary anti-cMet antibodies and/or binding fragments that can compose the anti-cMet ADCs are provided herein. Specific embodiments of anti-cMet ADCs include, but are not limited to, ABT-700 and STI-0602.

[014] For therapeutic uses, it may be desirable to utilize anti-cMet ADCs that bind cMet with an affinity of at least 100 nM. Accordingly, in some embodiments, the anti- cMet ADCs comprise an anti- cMet and/or anti- cMet binding fragment that binds cMet with an affinity of at least about 100 nM, or even higher, for example, at least about 90 nM, 80 nM, 70 nM, 60 nM, 50 nM, 40 nM, 30 nM, 25 nM, 20 nM, 15 nM, 10 nM, 7 nM, 6 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, 0.1 nM,

WE CLAIM:

1. An anti-cMet antibody drug conjugate ("ADC") comprising an antimitotic agent linked to an anti-cMet antibody by way of a linker, wherein the ADC has the structure of formula (I):

(I) $[D–L–XY–]_n–Ab$

or a salt thereof, wherein:

D is the antimitotic agent;

L is the linker;

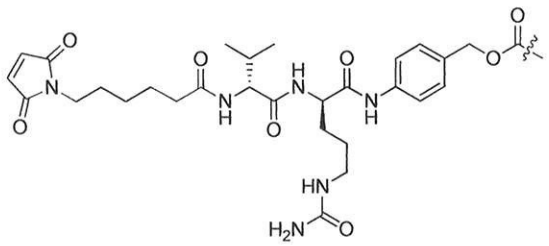
Ab is the anti-cMet antibody;

XY represents a covalent linkage linking linker L to antibody Ab; and

n is an integer ranging from 2 to 8;

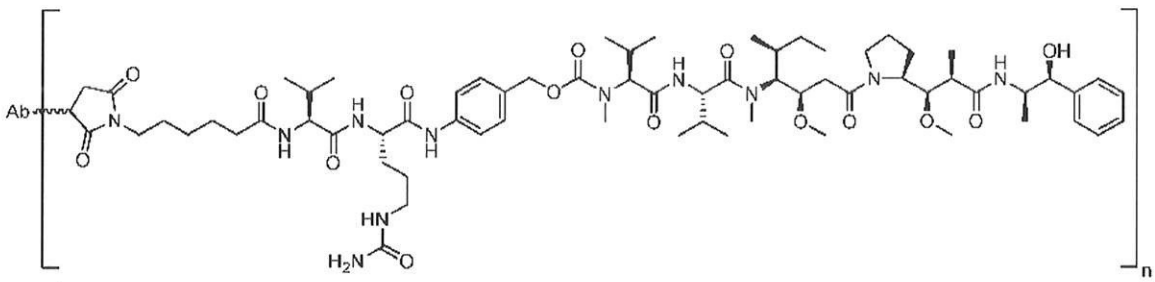
wherein

L comprises a valine-citrulline (vc) linker, and has the structure of formula (IVb.2):



(IVb.2)

D is a monomethyl auristatin E ("MMAE"), and the ADC of structural formula (I) has the following structure:



; and

Ab comprises an anti-cMet antibody which comprises (i) a VH chain comprising three CDRs; and (ii) a VL chain comprising three CDRs, wherein:

V_H CDR#1 has an amino acid sequence:	GYIFTAYTMH	(SEQ ID NO:112),
V_H CDR#2 has an amino acid sequence:	WIKPNNGLANYAQKFQG	(SEQ ID NO:113),
V_H CDR#3 has an amino acid sequence:	SEITTEFDY	(SEQ ID NO:114),
V_L CDR#1 has an amino acid sequence:	KSSESVDSYANSFLH	(SEQ ID NO:115),

V_L CDR#2 has an amino acid sequence: RASTRES (SEQ ID NO:116),

and V_L CDR#3 has an amino acid sequence: QQSKEDPLT (SEQ ID NO:117),

and (iii) a modified hinge region having an amino acid sequence of PKSCDCHCPPCP (SEQ ID NO:170).

2. The ADC of claim 1, wherein the anti-cMet antibody comprises a VH chain of SEQ ID NO:78 and a VL chain of SEQ ID NOS:79 or 81.

3. The ADC of claim 1, wherein the anti-cMet antibody comprises a heavy chain of SEQ ID NOS:86 or 88 and a light chain of SEQ ID NO:87.

4. A pharmaceutical composition comprising the ADC of claim 3, and a pharmaceutically acceptable carrier.

5. The pharmaceutical composition of claim 4, having a drug antibody ratio ("DAR") of about 3.1.

6. An anti-cMet antibody drug conjugate ("ADC") comprising a DNA cross-linking agent linked to an anti-cMet antibody by way of a linker, wherein the ADC has the structure of formula (I):

(I) $[D–L–XY–]_n–Ab$

or a salt thereof, wherein:

D is the DNA cross-linking agent;

L is the linker;

Ab is the anti-cMet antibody;

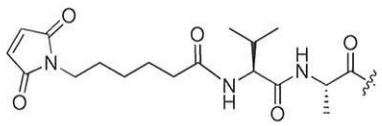
XY represents a covalent linkage linking linker L to antibody Ab; and

n is an integer ranging from 2 to 8;

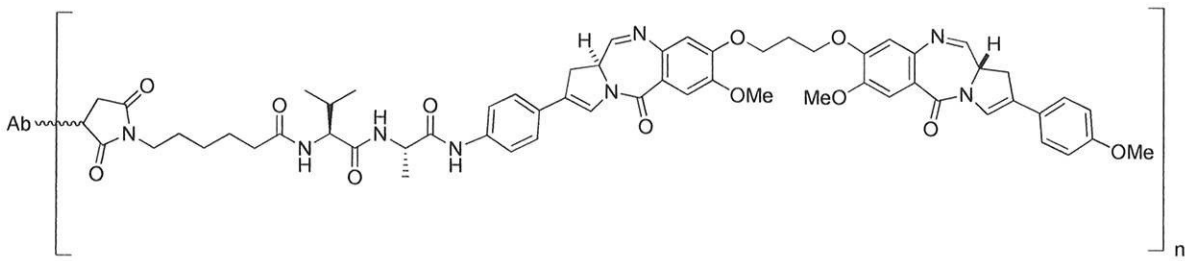
wherein

L comprises a valine-alanine (va) linker, and has the structure of formula (IVd.3):

(IVd.3)



D is a pyrrolobenzodiazepine ("PBD") dimer, and the ADC of structural formula (I) has the following structure:



and

Ab comprises an anti-cMet antibody which comprises (i) a VH chain comprising three CDRs; and (ii) a VL chain comprising three CDRs, wherein:

V_H CDR#1 has an amino acid sequence: GYIFTAYTMH (SEQ ID NO:173),

V_H CDR#2 has an amino acid sequence: WIKPNNGLANYAQKFQG (SEQ ID NO:174),

V_H CDR#3 has an amino acid sequence: SEITTEFDY (SEQ ID NO:175),

V_L CDR#1 has an amino acid sequence: KSSESVDSYANSFLH (SEQ ID NO:176),

V_L CDR#2 has an amino acid sequence: RASTRES (SEQ ID NO:177),

and V_L CDR#3 has an amino acid sequence: QQSKEDPLT (SEQ ID NO:178),

and (iii) a modified hinge region having an amino acid sequence of PKSCDCHCPPCP (SEQ ID NO:170).

7. The ADC of claim 6, wherein the anti-cMet antibody comprises a VH chain of SEQ ID NO:78 and a VL chain of SEQ ID NOS:79 or 81.

8. The ADC of claim 6, wherein the anti-cMet antibody comprises a heavy chain of SEQ ID NO:171 and a light chain of SEQ ID NO:172.

9. Use of a pharmaceutical composition comprising an anti cMet antibody drug conjugate ("ADC") and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating a solid tumor cancer that overexpresses cMet, wherein the medicament is to be administered in an amount and for a period of time sufficient to provide a therapeutic benefit, and wherein the ADC has the structure of formula (I):

(I) $[D–L–XY–]_n–Ab$

or a salt thereof, wherein:

D is the antimitotic agent;

L is the linker;

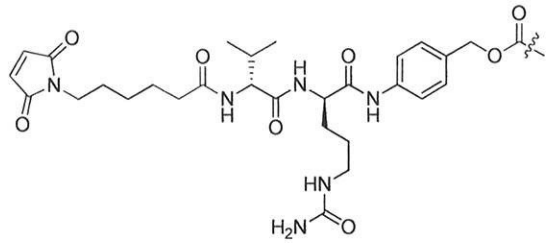
Ab is the anti-cMet antibody;

XY represents a covalent linkage linking linker L to antibody Ab; and

n is an integer ranging from 2 to 8;

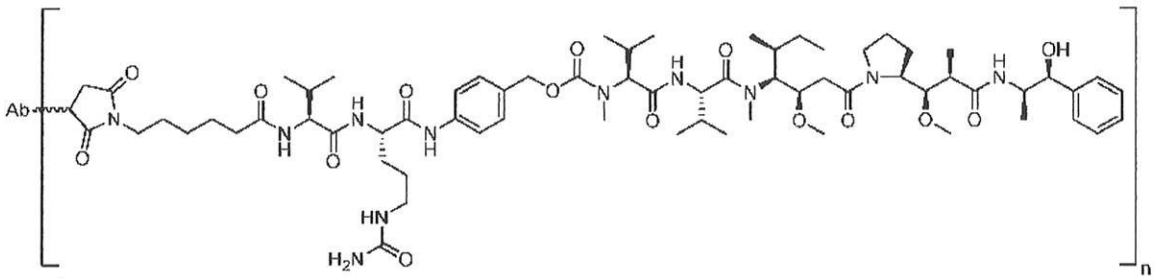
wherein

L comprises a valine-citrulline (vc) linker, and has the structure of formula (IVb.2):



(IVb.2)

D is a monomethyl auristatin E ("MMAE"), and the ADC of structural formula (I) has the following structure:



; and

Ab comprises an anti-cMet antibody which comprises (i) a VH chain comprising three CDRs; and (ii) a VL chain comprising three CDRs, wherein:

V_H CDR#1 has an amino acid sequence:	GYIFTAYTMH	(SEQ ID NO:112),
V_H CDR#2 has an amino acid sequence:	WIKPNNGLANYAQKFQG	(SEQ ID NO:113),
V_H CDR#3 has an amino acid sequence:	SEITTEFDY	(SEQ ID NO:114),
V_L CDR#1 has an amino acid sequence:	KSSESVDSYANSFLH	(SEQ ID NO:115),
V_L CDR#2 has an amino acid sequence:	RASTRES	(SEQ ID NO:116),
and V_L CDR#3 has an amino acid sequence:	QQSKEDPLT	(SEQ ID NO:117),

and (iii) a modified hinge region having an amino acid sequence of PKSCDCHCPPCP (SEQ ID NO:170).

10. The use of claim 9, wherein the anti-cMet antibody comprises a VH chain of SEQ ID NO:78 and a VL chain of SEQ ID NOS:79 or 81.

11. The use of claim 9, wherein the anti-cMet antibody comprises a heavy chain of SEQ ID NOS:86 or 88 and a light chain of SEQ ID NO:87.

12. The use of claim 9, wherein the cMet overexpressing cancer is non-small cell lung cancer ("NSCLC").

13. The use of claim 12, wherein the NSCLC is squamous NSCLC or an adenocarcinoma.

14. The use of claim 13, wherein the squamous NSCLC has a biopsy IHC score of 2+ to 3+.

15. The use of claim 13, in which a biopsy of the adenocarcinoma tumor tissue has an IHC score of 3+ and/or an H-score greater than 225.

16. The use of claim 9, in which the anti-cMet ADC is to be administered adjunctive to an additional anticancer agent.

17. The use of claim 16, in which the additional anticancer agent is an inhibitor of epidermal growth factor receptor ("EGFR").

18. The use of claim 17, in which the additional anticancer agent is erlotinib.