

Claims:

1. An antibody molecule comprising:
 - a first antigen-binding domain that binds epidermal growth factor receptor (EGFR); and
 - a second antigen-binding domain that binds c-Met,
 wherein the first antigen-binding domain comprises:
 - (i) a heavy chain variable (VH) region comprising the following complementarity determining regions (CDRs):
 - HCDR1 having the amino acid sequence of SEQ ID NO: 1
 - HCDR2 having the amino acid sequence of SEQ ID NO: 2
 - HCDR3 having the amino acid sequence of SEQ ID NO: 3,
 or a variant thereof in which one or two or three amino acids in one or more of HCDR1, HCDR2, or HCDR3 are substituted with another amino acid; and
 - (ii) a light chain variable (VL) region comprising the following CDRs:
 - LCDR1 having the amino acid sequence of SEQ ID NO: 4
 - LCDR2 having the amino acid sequence of SEQ ID NO: 5
 - LCDR3 having the amino acid sequence of SEQ ID NO: 6,
 or a variant thereof in which one or two or three amino acids in one or more of HCDR1, HCDR2, or HCDR3 are substituted with another amino acid.

2. The antibody molecule according to claim 1, wherein the first antigen-binding domain comprises:
 - (i) a VH region comprising the following CDRs:
 - HCDR1 having the amino acid sequence of SEQ ID NO: 1
 - HCDR2 having the amino acid sequence of SEQ ID NO: 2
 - HCDR3 having the amino acid sequence of SEQ ID NO: 3; and
 - (ii) a VL region comprising the following CDRs:
 - LCDR1 having the amino acid sequence of SEQ ID NO: 4
 - LCDR2 having the amino acid sequence of SEQ ID NO: 5
 - LCDR3 having the amino acid sequence of SEQ ID NO: 6.

3. The antibody molecule according to claim 1 or claim 2, wherein the first antigen-binding domain binds to human EGFR with an affinity having a K_d that is:
 - (i) equal to 10 nM or higher;
 - (ii) equal to 30 nM or higher; or
 - (iii) equal to 40 nM or higher.

4. The antibody molecule according to claim 1 or claim 2, wherein the first antigen-binding domain binds to human EGFR with an affinity having a K_d that is:
 - (i) between 10 and 100 nM;
 - (ii) between 20 and 80 nM;
 - (iii) between 30 and 75 nM; or

(iv) between 35 and 50 nM.

5. The antibody molecule according to any one of claims 1 to 4, wherein the first antigen-binding domain binds to human EGFR with an affinity that is lower than the affinity that an antigen-binding domain comprising the variable heavy region sequence and variable light region sequence of antibody molecule QD6, the sequences set forth in SEQ ID NOs: 18 and 22, respectively.

6. The antibody molecule according to any one of the preceding claims, wherein the first antigen-binding domain comprises:

a VH region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 16; and

a VL region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 20.

7. The antibody molecule according to any one of the preceding claims, wherein the second antigen-binding domain comprises:

(i) a heavy chain variable (VH) region comprising the following complementarity determining regions (CDRs):

HCDR1 having the amino acid sequence of SEQ ID NO: 24

HCDR2 having the amino acid sequence of SEQ ID NO: 25

HCDR3 having the amino acid sequence of SEQ ID NO: 26,

or a variant thereof in which one or two or three amino acids in one or more of HCDR1, HCDR2, or HCDR3 are substituted with another amino acid; and

(ii) a light chain variable (VL) region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 27

LCDR2 having the amino acid sequence of SEQ ID NO: 28

LCDR3 having the amino acid sequence of SEQ ID NO: 29,

or a variant thereof in which one or two or three amino acids in one or more of HCDR1, HCDR2, or HCDR3 are substituted with another amino acid.

8. The antibody molecule according to claim 7, wherein the second antigen-binding domain comprises:

(i) a VH region comprising the following CDRs:

HCDR1 having the amino acid sequence of SEQ ID NO: 24

HCDR2 having the amino acid sequence of SEQ ID NO: 25

HCDR3 having the amino acid sequence of SEQ ID NO: 26; and

(ii) a VL region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 27

LCDR2 having the amino acid sequence of SEQ ID NO: 28

LCDR3 having the amino acid sequence of SEQ ID NO: 29.

9. The antibody molecule according to claim 7 or claim 8, wherein the second antigen-binding domain binds to cMet with an affinity having a K_d that is:
- (i) lower than 10 nM; or
 - (ii) lower than 5 nM.
10. The antibody molecule according to any one of claims 3 to 5 and claim 9, wherein the affinity is measured by surface plasmon resonance.
11. The antibody molecule according to any one of claims 7 to 10, wherein the second antigen-binding domain comprises:
- a VH region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 38; and
 - a VL region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 40.
12. The antibody molecule according to any one of the preceding claims, wherein antibody molecule comprises:
- a first heavy chain, wherein the first heavy chain comprises the VH region of the first antigen-binding domain, and a first heavy chain constant (CH) region or a fragment thereof;
 - a first light chain, wherein the first light chain comprises the VL region of the first antigen-binding domain, and a first light chain constant (CL) region or a fragment thereof;
 - a second heavy chain, wherein the second heavy chain comprises the VH region of the second antigen-binding domain, and a second heavy chain constant (CH) region or a fragment thereof; and
 - a second light chain, wherein the second light chain comprises the VL region of the second antigen-binding domain, and a second light chain constant (CL) region or a fragment thereof.
13. The antibody molecule according to claim 12, wherein the first and second CH region comprises an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 42.
14. The antibody molecule according to claim 12 or claim 13, wherein the first and second heavy chain form a heterodimer, optionally wherein one of the first and second heavy chains comprises a cysteine (C) residue at position 354 and a tryptophan (W) residue at position 366 and the other heavy chain comprises a cysteine (C) residue at position 349, a valine (V) residue at position 407, a serine (S) at position 366 and an alanine (A) at position 368, wherein the numbering of the constant region is as per the EU index.
15. The antibody molecule according to any one of claims 12 to 14, wherein the antibody molecule comprises:
- (a) a modified CH region, wherein the modified CH region comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid; and

(b) a modified corresponding CL region, wherein the modified CL comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid,

wherein either:

(i) the first heavy chain comprises the modified CH region and the first light chain comprises the modified corresponding CL region; or

(ii) the second heavy chain comprises the modified CH region and the second light chain comprises the modified corresponding CL region, and

wherein the substituted cysteine of the modified CH region and the substituted cysteine of the modified corresponding light chain can form a disulphide bond.

16. The antibody molecule according to claim 15, wherein the modified CH region comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid at position 126; and the modified corresponding CL region comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid at position 121, wherein the numbering of the constant region is as per the EU index.

17. The antibody molecule according to any one of claims 12 to 16, wherein the first and/or second CH region comprise a mutation to reduce or abrogate binding of the antibody molecule to one of more Fcγ receptors.

18. The antibody molecule according to any one of claims 12 to 17, wherein the first and/or second CH region comprise a phenylalanine at position 234, glutamic acid at position 235, and serine at position 331, wherein the numbering of the constant region is as per the EU index.

19. The antibody molecule according to any one of claims 12 to 18, wherein the first CH region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NOs: 45, 46 or 63; and the second CH region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 43, 44 or 64, and optionally wherein the first CL region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 49 or 65; and the second CL region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 47 or 48.

20. The antibody molecule according to claim 19, wherein the first CH region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 63; and the second CH region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 64, and wherein the first CL region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 65; and the second CL region

comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 47.

21. The antibody molecule according to claim 19, wherein the first heavy chain comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NOs: 56, 57 or 59; and the second heavy chain comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NOs: 50, 51 or 60, and optionally wherein the first light chain comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 58 or 61; and the second light chain comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 52 or 62.

22. The antibody molecule according to claim 20, wherein the first heavy chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 59; the second heavy chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 60; the first light chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 61; and the second light chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 62.

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

- (i) the first antigen-binding domain that binds to EGFR binds to cynomolgus EGFR;
- (ii) the first antigen-binding domain that binds to EGFR binds to mouse EGFR;
- (iii) the second antigen-binding domain that binds to c-Met binds to cynomolgus c-Met;
- (iv) the first antigen-binding domain is specific for EGFR;
- (v) the second antigen-binding domain is specific for c-Met;
- (vi) the antibody molecule is capable of concurrently engaging EGFR and c-Met;
- (vii) the antibody molecule is capable of being internalised into a cell;
- (viii) the antibody molecule has cytotoxic activity when measured in an *in vitro* cell viability assay; and/or
- (ix) the antibody molecule is capable of blocking ligand dependent signalling of EGFR and/or c-Met.

24. An antibody molecule comprising:

a first antigen-binding domain that binds epidermal growth factor receptor (EGFR);

wherein the first antigen-binding domain comprises:

- (i) a heavy chain variable (VH) region comprising the following complementarity determining regions (CDRs):

HCDR1 having the amino acid sequence of SEQ ID NO: 1

HCDR2 having the amino acid sequence of SEQ ID NO: 2

HCDR3 having the amino acid sequence of SEQ ID NO: 3,

or a variant thereof in which one or two or three amino acids in one or more of HCDR1, HCDR2, or HCDR3 are substituted with another amino acid; and

(ii) a light chain variable (VL) region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 4

LCDR2 having the amino acid sequence of SEQ ID NO: 5

LCDR3 having the amino acid sequence of SEQ ID NO: 6,

or a variant thereof in which one or two or three amino acids in one or more of LCDR1, LCDR2, or LCDR3 are substituted with another amino acid.

25. An antibody molecule comprising:

a first antigen-binding domain that binds c-MET;

wherein the first antigen-binding domain comprises:

(i) a heavy chain variable (VH) region comprising the following complementarity determining regions (CDRs):

HCDR1 having the amino acid sequence of SEQ ID NO: 24

HCDR2 having the amino acid sequence of SEQ ID NO: 25

HCDR3 having the amino acid sequence of SEQ ID NO: 26,

or a variant thereof in which one or two or three in one or more of HCDR1, HCDR2, or HCDR3 are substituted with another amino acid; and

(ii) a light chain variable (VL) region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 27

LCDR2 having the amino acid sequence of SEQ ID NO: 28

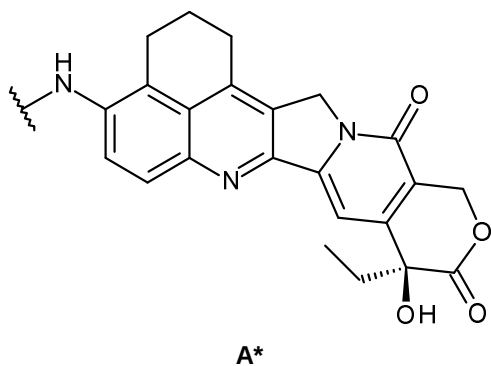
LCDR3 having the amino acid sequence of SEQ ID NO: 29,

or a variant thereof in which one or two or three in one or more of HCDR1, HCDR2, or HCDR3 are substituted with another amino acid.

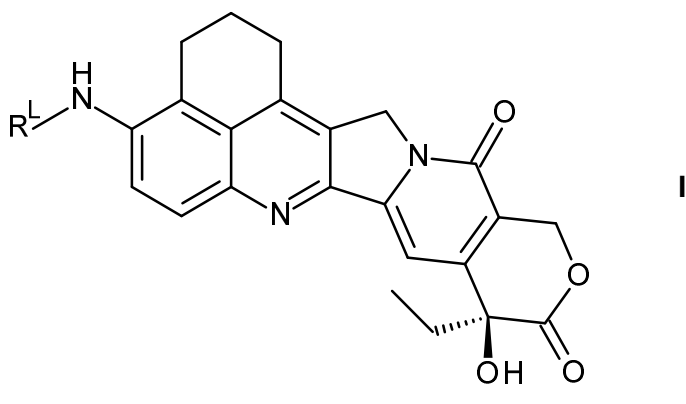
26. A conjugate comprising the antibody molecule of any one of the preceding claims conjugated to a drug.

27. The conjugate according to claim 26, wherein the drug comprises a cytotoxin, a radioisotope, an immunomodulator, a cytokine, a lymphokine, a chemokine, a growth factor, a tumor necrosis factor, a hormone, a hormone antagonist, an enzyme, an oligonucleotide, a DNA, an RNA, an siRNA, an RNAi, a microRNA, a photoactive therapeutic agent, an anti-angiogenic agent, a pro-apoptotic agent, a peptide, a lipid, a carbohydrate, a chelating agent, or combinations thereof.

28. The conjugate according to claim 26 or claim 27, wherein the drug is a topoisomerase I inhibitor having formula A*

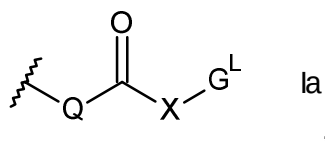


29. The conjugate according to claim 28, wherein the topoisomerase I inhibitor has formula I:



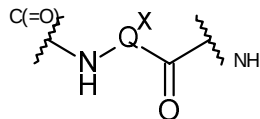
or a salt or solvates thereof, wherein R^L is a linker for connection to the antibody molecule, optionally wherein said linker is selected from:

(ia):



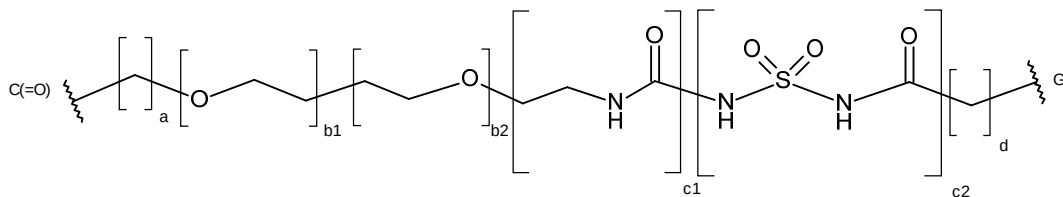
wherein

Q is:



, where Q^X is such that Q is an amino-acid residue, a dipeptide residue, a tripeptide residue or a tetrapeptide residue;

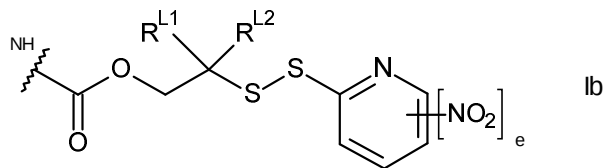
X is:



where $a = 0$ to 5 , $b_1 = 0$ to 16 , $b_2 = 0$ to 16 , $c_1 = 0$ or 1 , $c_2 = 0$ or 1 , $d = 0$ to 5 , wherein at least b_1 or $b_2 = 0$ (i.e. only one of b_1 and b_2 may not be 0) and at least c_1 or $c_2 = 0$ (i.e. only one of c_1 and c_2 may not be 0);

G^L is a linker for connecting to the antibody molecule; or

(ib):



where R^{L1} and R^{L2} are independently selected from H and methyl, or together with the carbon atom to which they are bound form a cyclopropylene or cyclobutylene group; and

e is 0 or 1 .

30. The conjugate of any one of claims 26 to 29 having the formula IV:



or a pharmaceutically acceptable salt or solvate thereof,

wherein:

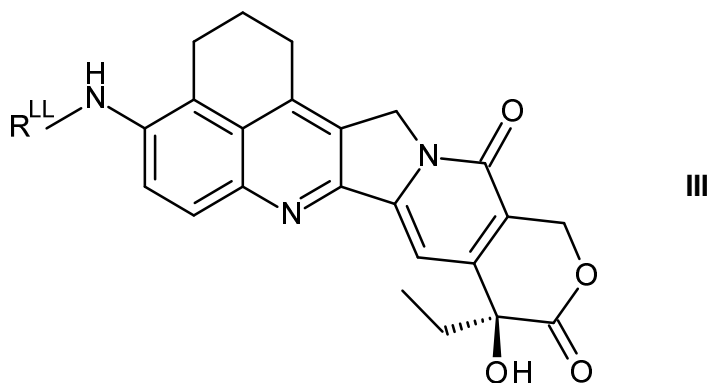
L is the antibody molecule;

D^L is drug having a linker; and

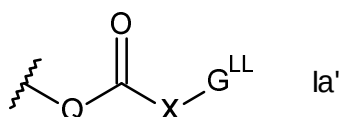
p is an integer from 1 to 20 .

31. The conjugate according to claim 30, wherein p is a range selected from 2 to 8 , 3 to 7 , 4 to 7 or 5 to 7 .

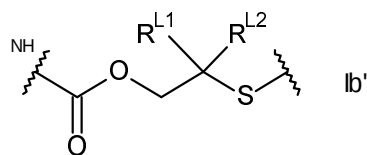
32. The conjugate according to claim 30 or 31, wherein D^L is a topoisomerase I inhibitor having a linker that is of formula III:



R^{LL} is a linker connected to the antibody molecule, wherein the linker is selected from (Ia'):

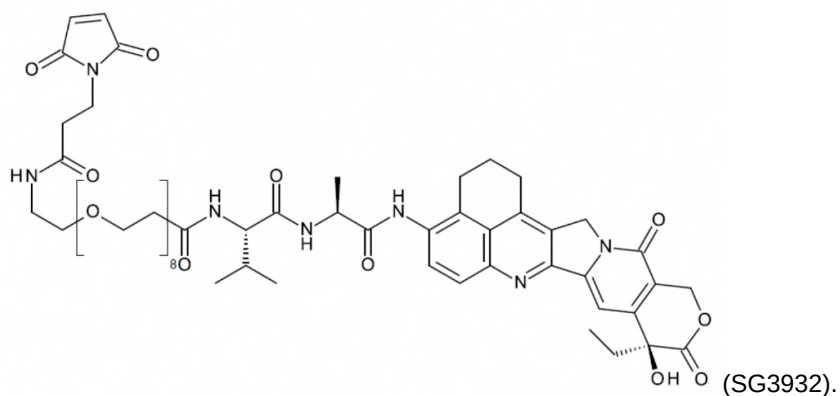


where Q and X are as defined in claim 29 and G^{LL} is a linker connected to the antibody molecule; and (1b'):



where R^{L1} and R^{L2} are as defined in claim 29.

33. The conjugate of any one of claims 26 to 32, wherein the antibody molecule is conjugated to a topoisomerase I inhibitor having the following formula:



34. The conjugate according to any one of claims 26 to 33, wherein:

- (i) the conjugate is capable of concurrently engaging EGFR and c-Met;
- (ii) the conjugate is capable of being internalised into a cell;
- (iii) the conjugate has cytotoxic activity when measured in an *in vitro* cell viability assay;

and/or

(iv) the conjugate is capable of inhibiting the development or progression of a cancer when measured in an *in vivo* model.

35. A pharmaceutical composition comprising an antibody molecule according to any one of claims 1 to 25, or a conjugate according to any one of claims 26 to 34, and a pharmaceutically acceptable carrier.

36. An antibody molecule according to any one of claims 1 to 25, a conjugate according to any one of claims 26 to 34, or the pharmaceutical composition according to claim 35, for use in treatment of the human or animal body.

37. An antibody molecule according to any one of claims 1 to 25, a conjugate according to any one of claims 26 to 34, or the pharmaceutical composition according to claim 35, for use in treating a cancer.
38. Use of an antibody molecule according to any one of claims 1 to 25, a conjugate according to any one of claims 26 to 34, or the pharmaceutical composition according to claim 35, in the manufacture of a medicament for the treatment of a cancer.
39. An antibody molecule, conjugate or pharmaceutical composition for use according to claim 37, or use according to claim 38, wherein the cancer is lung cancer (such as Non-Small Cell Lung Cancer (NSCLC)), pancreatic cancer, breast cancer, colorectal cancer, gastric cancer, squamous cell carcinoma of head and neck (SCCHN or SQHN), ovarian cancer or glioblastoma.
40. An antibody molecule, conjugate or pharmaceutical composition for use according to claim 37, or use according to claim 38, wherein the cancer is lung cancer (such as Non-Small Cell Lung Cancer (NSCLC)) or squamous cell carcinoma of head and neck (SCCHN or SQHN).
41. A nucleic acid, or a plurality of nucleic acids, optionally isolated, encoding an antibody molecule according to any one of claims 1 to 25.
42. An expression vector, or a plurality of expression vectors, comprising a nucleic acid or a plurality of nucleic acids according to claim 41.
43. A recombinant host cell comprising the nucleic acid or plurality of nucleic acids according to claim 41, or the expression vector or plurality of expression vectors of claim 42.
44. A method of producing an antibody molecule according to any one of claims 1 to 25, comprising culturing the recombinant host cell according to claim 43 under conditions for production of the antibody molecule.
45. The method according to claim 44 further comprising isolating and/or purifying the antibody molecule.