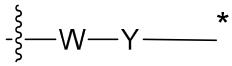
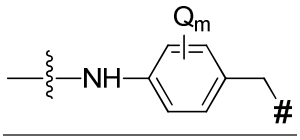
X is the activateable self-immolative moiety, wherein the activateable self-immolative moiety is of formula (i):

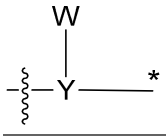


(i)

wherein the wavy line indicates covalent attachment of W to A, B, or Z depending on the presence or absence of A or B, and the asterisk (*) indicates covalent attachment of Y to the oxygen atom of the methylene carbamate unit; W is an Activation Unit; and Y is a self-immolative Spacer Unit, wherein the Activation Unit comprises a sequence of 1 to 12 amino acids having an amide linkage to the self-immolative Spacer Unit wherein the amide linkage is cleavable by the action of a tumor associated protease to initiate release of free drug, and the self-immolative Spacer Unit is a PAB group having the structure of:

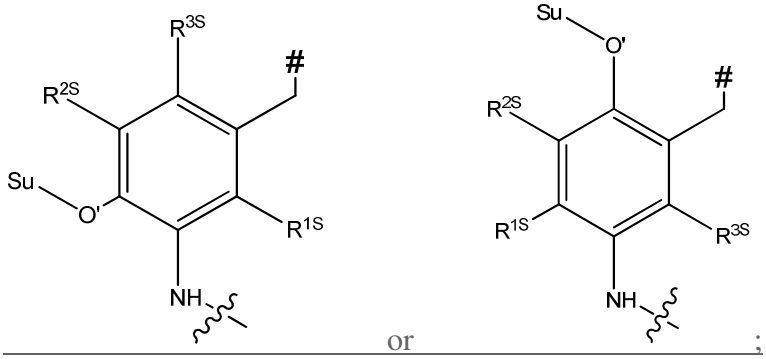


wherein the wavy line indicates the site of covalent attachment to the Activation Unit and the hashtag (#) indicates the site of covalent attachment to the benzylic carbon atom of the PAB group to the methylene carbamate unit; and Q is independently -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), or other electron donating group and subscript m is 0, 1 or 2, or the activateable self-immolative moiety is of formula (ii):



(ii)

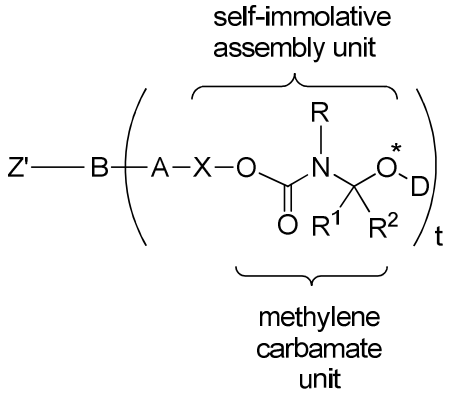
wherein the wavy line indicates covalent attachment of Y to A, B, or Z, depending on the presence or absence of A or B, and the asterisk (*) indicates the site of covalent attachment of Y to the oxygen atom of the methylene carbamate unit, wherein formula (ii) is a Glucuronide Unit having the structure of formula XIXa or XIXb:



(XIXa) or (XIXb);

wherein Su is a Sugar moiety; -O'-represents the oxygen atom of glycosidic bond cleavable by a glycosidase; R^{1S}, R^{2S} and R^{3S} are independently selected from the group consisting of hydrogen, halogen, -CN and $-NO_2$; the wavy line indicates the site of covalent attachment to the Stretcher Unit (Z), either directly or indirectly through the Connector Unit (A); and # indicates the site of attachment to the oxygen atom of the methylene carbamate unit~~, wherein activation of the activateable self-immolative moiety is by a protease or a glucosidase~~; R is hydrogen, optionally substituted C_1-C_6 alkyl that is optionally a Basic Unit, optionally substituted C_{6-14} aryl that is optionally a Basic Unit, or optionally substituted C-linked C_3-C_8 heteroaryl that is optionally a Basic Unit, R^1 and R^2 independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_{6-14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl, or both R and R^1 together with the nitrogen and carbon atoms to which they are attached define an azetidinyl, pyrrolodinyl, piperidinyl or homopiperidinyl moiety and R^2 is hydrogen; and wherein activation of the activateable self-immolative moiety (X) results in release of free drug having the formula of D-T*H.

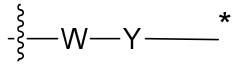
[0006b] In another aspect, the present disclosure refers to a Drug-Linker compound, wherein the Drug-Linker compound comprises a Drug Unit and a Linker Unit, wherein the Linker Unit comprises a Self-Immolative Assembly Unit having a methylene carbamate unit and an activateable self-immolative moiety wherein the Drug Unit is covalently attached to the methylene carbamate unit, wherein the Drug-Linker compound has the structure of:



,

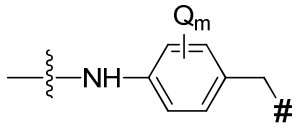
or a pharmaceutically acceptable salt thereof; wherein D is a Drug Unit having an aromatic hydroxyl functional group that has been incorporated into the indicated methylene carbamate unit; O* is the oxygen atom from said functional group that becomes incorporated into the indicated methylene carbamate unit;

R is hydrogen, optionally substituted C_1-C_6 alkyl that is optionally a Basic Unit, optionally substituted C_{6-14} aryl that is optionally a Basic Unit, or optionally substituted C-linked C_3-C_8 heteroaryl that is optionally a Basic Unit, R^1 and R^2 independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_{6-14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl, or both R and R^1 together with the nitrogen and carbon atoms to which they are attached comprise an azetidinyl, pyrrolodinyl, piperidinyl or homopiperidinyl moiety and R^2 is hydrogen; X is an activateable self-immolative moiety, wherein the activateable self-immolative moiety is of formula (i):

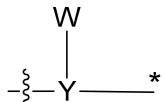


(i)

wherein the wavy line indicates covalent attachment of W to A, B, or Z depending on the presence or absence of A or B, and the asterisk (*) indicates covalent attachment of Y to the oxygen atom of the methylene carbamate unit; W is an Activation Unit; and Y is a self-immolative Spacer Unit, wherein the Activation Unit comprises a sequence of 1 to 12 amino acids having an amide linkage to the self-immolative Spacer Unit wherein the amide linkage is cleavable by the action of a tumor associated protease to initiate release of free drug, and the self-immolative Spacer Unit is a PAB group having the structure of:

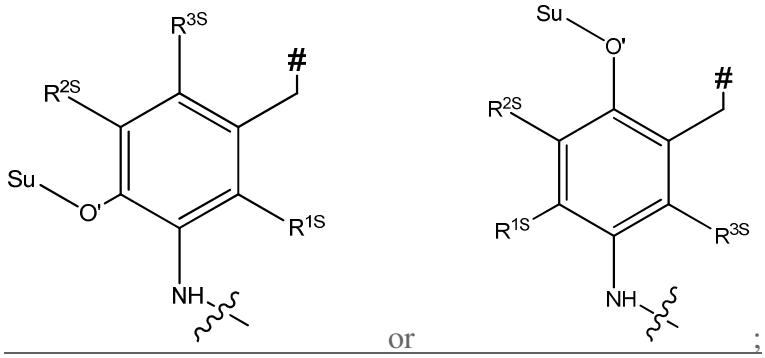


wherein the wavy line indicates the site of covalent attachment to the Activation Unit and the hashtag (#) indicates the site of covalent attachment to the benzylic carbon atom of the PAB group to the methylene carbamate unit; and Q is independently -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), or other electron donating group and subscript m is 0, 1 or 2, or the activateable self-immolative moiety is of formula (ii):



(ii)

wherein the wavy line indicates covalent attachment of Y to A, B, or Z, depending on the presence or absence of A or B, and the asterisk (*) indicates the site of covalent attachment of Y to the oxygen atom of the methylene carbamate unit, wherein formula (ii) is a Glucuronide Unit having the structure of formula XIXa or XIXb:



or ;

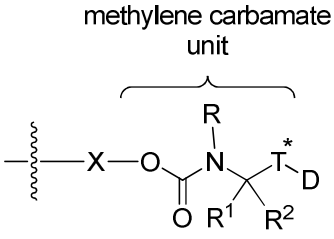
(XIXa) (XIXb)

wherein Su is a Sugar moiety; -O'-represents the oxygen atom of glycosidic bond cleavable by a glycosidase; R^{1S}, R^{2S} and R^{3S} are independently selected from the group consisting of hydrogen, halogen, -CN and -NO_2; the wavy line indicates the site of covalent attachment to the Stretcher Unit (Z), either directly or indirectly through the Connector Unit (A); and # indicates the site of attachment to the oxygen atom of the methylene carbamate unit~~, wherein activation of the activateable self-immolative moiety is by a protease or a glucosidase~~; Z' is a Stretcher Unit precursor to a Stretcher Unit (Z) of a Ligand Drug Conjugate compound as described herein and comprises a maleimide functional group that provides for covalent attachment of a Ligand Unit to Z; B is an optional Branching Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or polyamine residues or combinations thereof that is present when subscript t is greater than 1 and is absent when subscript t is 1; A is an optional Connector Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or diamino residues or combinations thereof; and subscript t ranges from 1 to 4; and wherein activation of the activateable self-immolative moiety (X) results in release of free drug having the formula of D-T^{*}H.

[0006c] In another aspect, the present disclosure refers to a method of preparing an Antibody Drug Conjugate compound as described herein, in which the Stretcher Unit (Z) comprises a succinimide moiety or an succinic acid-amide moiety; and wherein the Ligand Unit is an antibody, the method comprising the step of: contacting a Drug Linker compound as described herein in which the Stretcher Unit precursor (Z') is comprised of a maleimide moiety ~~moeity~~ with an antibody having a reactive cysteine thiol functional group obtained from interchain disulfide bond reduction and/or from an engineered cysteine residue, wherein said contacting converts Z' to Z by formation of a covalent bond between the reactive cysteine sulfur atom of the antibody and the succinimide moiety ~~moeity~~ of Z, optionally followed by spontaneous hydrolysis of the succinimide moiety to an acid amide moiety, whereby the Antibody Drug Conjugate compound is obtained.

CLAIMS

1. A Ligand-Drug Conjugate compound comprising a Ligand Unit, a Drug Unit and a Linker Unit, wherein the Linker Unit comprises a Self-immolative (SI) Assembly Unit having a methylene carbamate unit and an activateable self-immolative moiety wherein the methylene carbamate unit is covalently attached to the Drug Unit, and wherein the SI Assembly Unit covalently attached to the Drug Unit is represented by the structure of formula SI:



(SI)

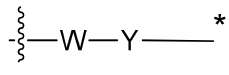
or a pharmaceutically acceptable salt thereof, wherein

the wavy line indicates covalent attachment to the remainder of the Linker Unit;

D is the Drug Unit having an aromatic hydroxyl functional group that has been incorporated into the methylene carbamate unit;

T* is the oxygen atom from said functional group that becomes incorporated into the indicated methylene carbamate unit;

X is the activateable self-immolative moiety, wherein the activateable self-immolative moiety is of formula (i):



(i)

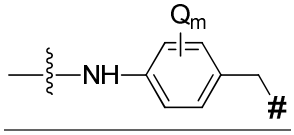
wherein the wavy line indicates covalent attachment of W to A, B, or Z depending on the presence or absence of A or B, and the asterisk (*) indicates covalent attachment of Y to the oxygen atom of the methylene carbamate unit;

W is an Activation Unit; and

Y is a self-immolative Spacer Unit,

wherein the Activation Unit comprises a sequence of 1 to 12 amino acids having an amide linkage to the self-immolative Spacer Unit wherein the amide linkage is cleavable by the action of a tumor associated protease to initiate release of free drug, and

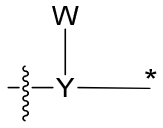
the self-immolative Spacer Unit is a PAB group having the structure of:



wherein the wavy line indicates the site of covalent attachment to the Activation Unit and the hashtag (#) indicates the site of covalent attachment to the benzylic carbon atom of the PAB group to the methylene carbamate unit; and

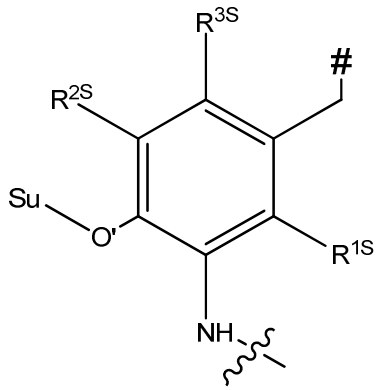
Q is independently -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), or other electron donating group and subscript m is 0, 1 or 2, or

the activateable self-immolative moiety is of formula (ii):



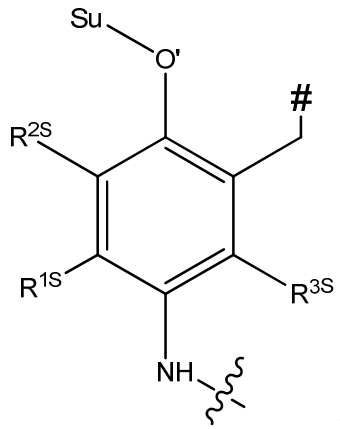
(ii)

wherein the wavy line indicates covalent attachment of Y to A, B, or Z, depending on the presence or absence of A or B, and the asterisk (*) indicates the site of covalent attachment of Y to the oxygen atom of the methylene carbamate unit, wherein formula (ii) is a Glucuronide Unit having the structure of formula XIXa or XIXb:



(XIXa)

or



(XIXb)

;

wherein Su is a Sugar moiety; -O'-represents the oxygen atom of glycosidic bond cleavable by a glycosidase;

R^{1S}, R^{2S} and R^{3S} are independently selected from the group consisting of hydrogen, halogen, -CN and -NO_2;

the wavy line indicates the site of covalent attachment to the Stretcher Unit (Z), either directly or indirectly through the Connector Unit (A); and

# indicates the site of attachment to the oxygen atom of the methylene carbamate unit

~~, wherein activation of the activateable self-immolative moiety is by a protease or a glucosidase~~;

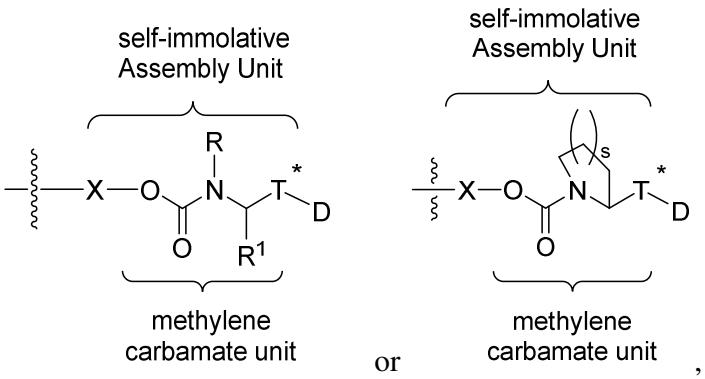
R is hydrogen, optionally substituted C_1-C_6 alkyl that is optionally a Basic Unit, optionally substituted C_{6-14} aryl that is optionally a Basic Unit, or optionally substituted C-linked C_3-C_8 heteroaryl that is optionally a Basic Unit,

R^1 and R^2 independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_{6-14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl, or

both R and R^1 together with the nitrogen and carbon atoms to which they are attached define an azetidinyl, pyrrolodinyl, piperidinyl or homopiperidinyl moiety and R^2 is hydrogen; and

wherein activation of the activateable self-immolative moiety (X) results in release of free drug having the formula of D-T^*H.

2. The Ligand-Drug Conjugate compound of claim **1**, wherein the SI Assembly Unit covalently attached to the Drug Unit is represented by the structure of:

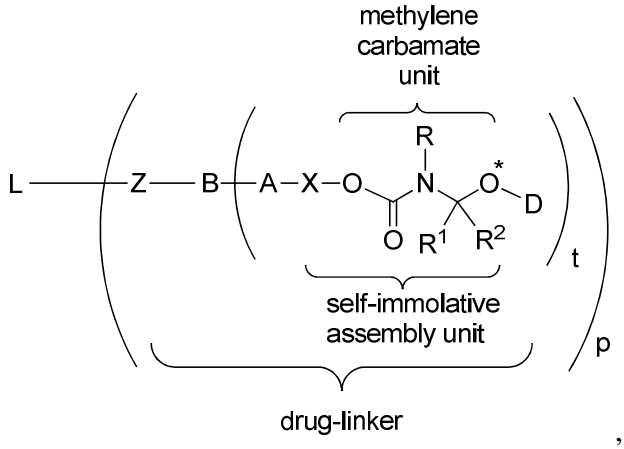


,

or a pharmaceutically acceptable salt thereof, wherein subscript s is 0, 1, 2 or 3 to define an azetidinyl, pyrrolodinyl, piperidinyl or homopiperidinyl moiety.

3. The Ligand-Drug Conjugate compound of claim **2**, wherein R and R^1 are independently selected from the group consisting of hydrogen, optionally substituted C_1-C_6 alkyl and optionally substituted C_{6-14} aryl; and subscript s is 0, 1, or 2.

4. The Ligand-Drug Conjugate Compound of claim **1**, wherein the Ligand-Drug Conjugate compound has the structure of:



,

or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Z is a Stretcher Unit comprising a thio-substituted succinimide or succinic acid-amide moiety;

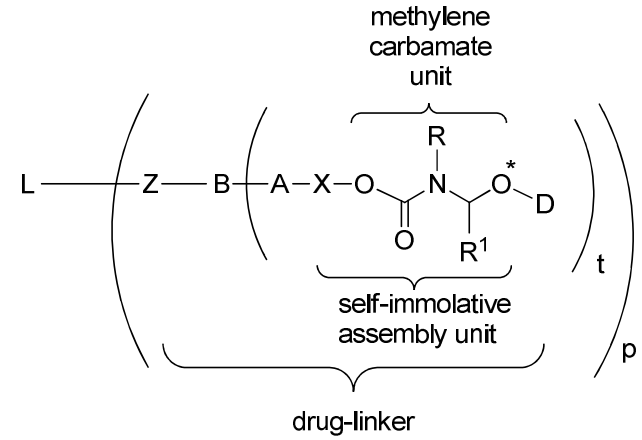
B is an optional Branching Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or polyamine residues or combinations thereof and is present when subscript t is greater than 1 and is absent when subscript t is 1;

A is an optional Connector Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or diamino residues or combinations thereof;

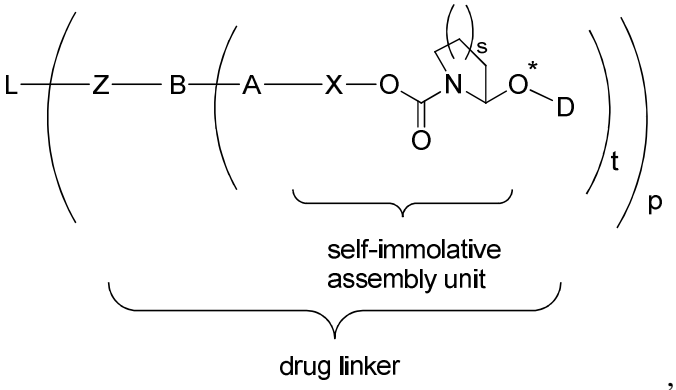
subscript t ranges from 1 to 4; and

subscript p is an integer ranging from 1 to 16.

5. The Ligand-Drug Conjugate compound of claim **4**, wherein the Ligand-Drug Conjugate compound has the structure of:



,



,

or a pharmaceutically acceptable salt thereof, wherein

R and R^1 independently are hydrogen, optionally substituted C_1-C_6 alkyl or optionally substituted C_{6-14} aryl; and

subscript s is 1 or 2.

6. The Ligand-Drug Conjugate compound of claim 4, wherein R and R^1 are independently hydrogen, optionally substituted C_{1-4} alkyl or optionally substituted phenyl.

7. The Ligand-Drug Conjugate Compound of claim **5**, wherein R is a saturated C_{1-6} alkyl, optionally substituted with a basic group.

8. The Ligand-Drug Conjugate compound of any one of claims **1-5**, wherein R is a Basic Unit wherein the basic functional group of the Basic Unit is an amine or a nitrogen-containing 3, 4, 5, or 6 membered heterocycle that is C-linked or N-linked and is optionally substituted.

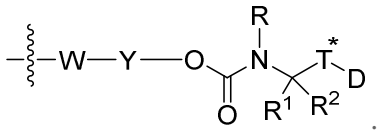
9. The Ligand-Drug Conjugate compound of claim **8**, wherein the basic functional group of the Basic Unit is $–N(R^{op})_2$, wherein R^{op} are independently selected from the group consisting of hydrogen and C_{1-6} alkyl.

10. The Ligand-Drug Conjugate compound of claim **8**, wherein the basic functional group of the Basic Unit is $–N(R^{op})_2$, wherein R^{op} are independently selected from the group consisting of hydrogen and methyl.

11. The Ligand-Drug Conjugate compound of claim **8**, wherein the Basic Unit is $–CH_2CH_2N(R^{op})_2$, wherein R^{op} are independently selected from the group consisting of hydrogen and methyl.

12. The Ligand-Drug Conjugate compound of any one of claims **1-11**, wherein R^1 is hydrogen.

13. The Ligand-Drug Conjugate compound of claim **1**, wherein its SI Assembly Unit covalently attached to the Drug Unit is represented by the structure of:



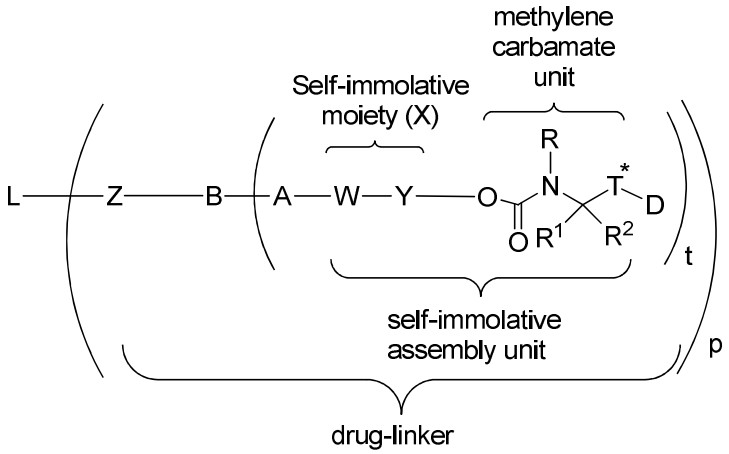
~~wherein~~

~~W is an Activation Unit; and~~

~~Y is a self-immolative Spacer Unit,~~

~~wherein enzymatic cleavage of W results in release of free drug.~~

14. The Ligand-Drug Conjugate compound of claim **13**, wherein the Ligand-Drug Conjugate compound has the structure of:



or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Z is a Stretcher Unit comprising a thio-substituted succinimide or succinic acid-amide moiety;

B is an optional Branching Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or polyamine residues or combinations thereof and is present when subscript t is greater than 1 and is absent when subscript t is 1;

A is an optional Connector Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or diamino residues or combinations thereof;

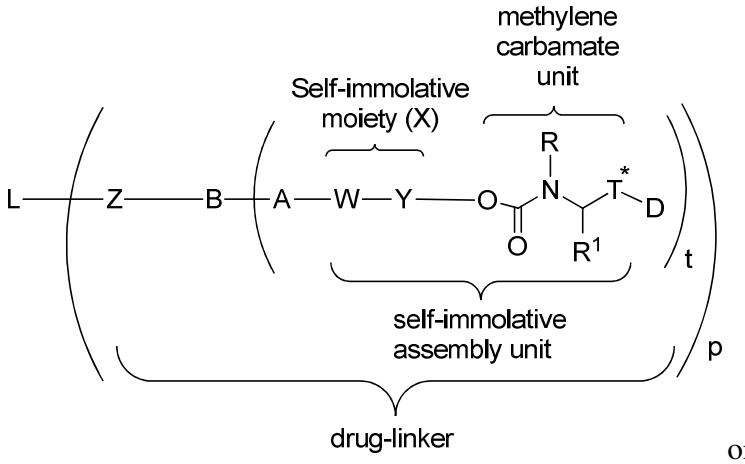
~~W is an Activation Unit;~~

~~Y is a self-immolative Spacer Unit;~~

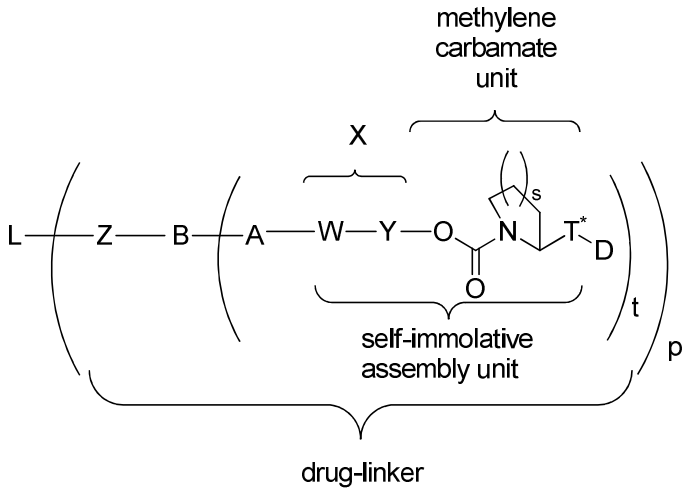
subscript t ranges from 1 to 4; and

subscript p is an integer ranging from 1 to 16.

15. The Ligand-Drug Conjugate compound of claim **14**, wherein the Ligand-Drug Conjugate compound has the structure of:



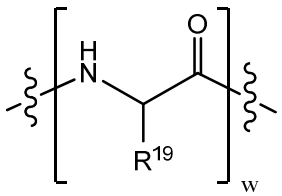
or



wherein R and R^1 independently are hydrogen, optionally substituted C_1-C_6 alkyl, or optionally substituted C_{6-14} aryl; and

subscript s is 1 or 2.

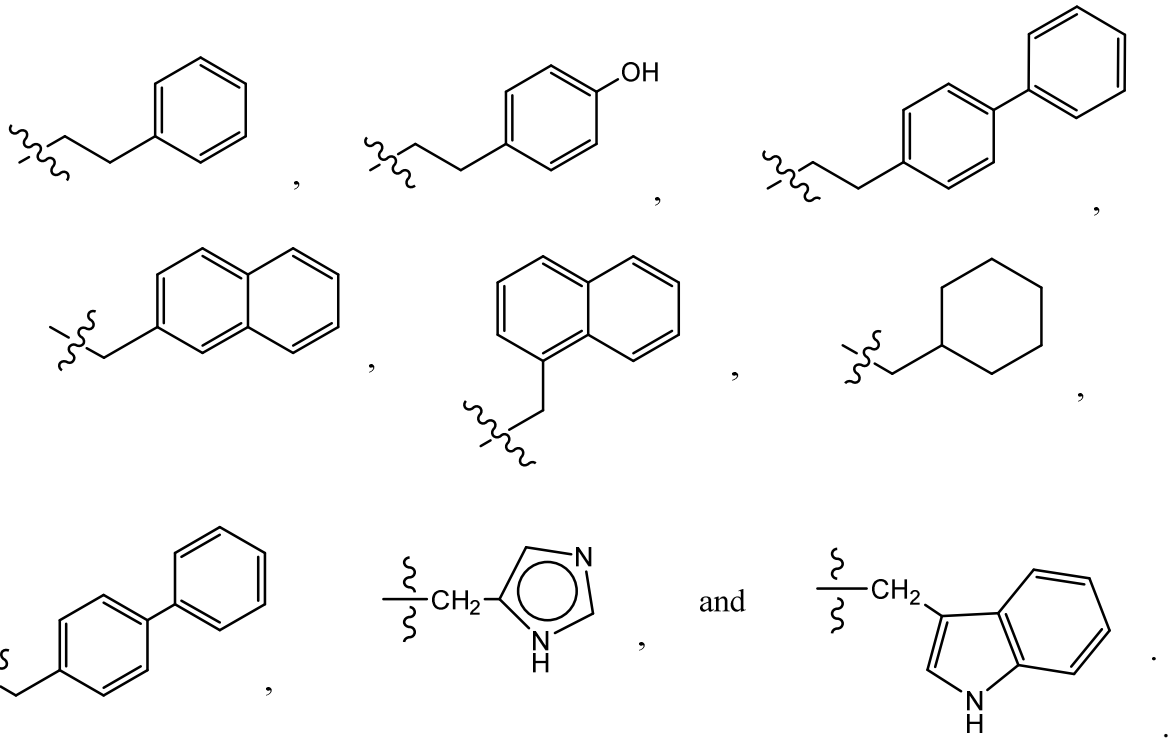
16. The Ligand-Drug Conjugate compound of claim **14** or **15**, wherein W has the formula of:



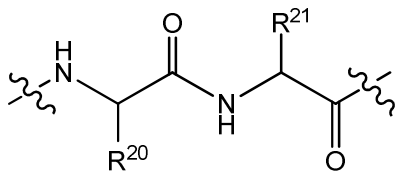
wherein, the wavy line adjacent to the carbonyl is attached to the self-immolative Spacer Unit and the other wavy line is attached to a Stretcher Unit (Z), directly or indirectly through an intervening Connector Unit (A), and/or Branching unit (B);

w is an integer ranging from 1 to 12;

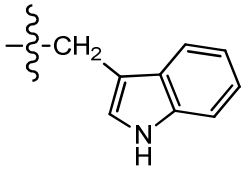
R^{19} is, in each instance, independently selected from the group consisting of hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, benzyl, *p*-hydroxybenzyl, $-CH_2OH$, $-CH(OH)CH_3$, $-CH_2CH_2SCH_3$, $-CH_2CONH_2$, $-CH_2COOH$, $-CH_2CH_2CONH_2$, $-CH_2CH_2COOH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_3NH_2$, $-(CH_2)_3NHCOCH_3$, $-(CH_2)_3NHCHO$, $-(CH_2)_4NHC(=NH)NH_2$, $-(CH_2)_4NH_2$, $-(CH_2)_4NHCOCH_3$, $-(CH_2)_4NHCHO$, $-(CH_2)_3NHCONH_2$, $-(CH_2)_4NHCONH_2$, $-CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-, phenyl, cyclohexyl,



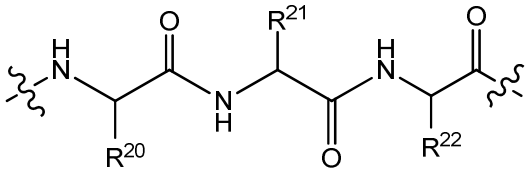
17. The Ligand-Drug Conjugate compound of claim **16**, wherein W has the formula of:



wherein R^{20} and R^{21} are as follows:

R^{20}	R^{21}
benzyl	$(CH_2)_4NH_2$
methyl	$(CH_2)_4NH_2$
isopropyl	$(CH_2)_4NH_2$
isopropyl	$(CH_2)_3NHCONH_2$
benzyl	$(CH_2)_3NHCONH_2$
isobutyl	$(CH_2)_3NHCONH_2$
sec-butyl	$(CH_2)_3NHCONH_2$
	$(CH_2)_3NHCONH_2$
benzyl	methyl
benzyl	$(CH_2)_3NHC(=NH)NH_2$.

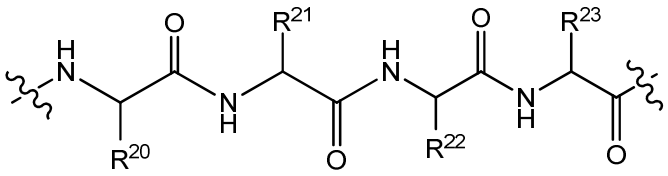
18. The Ligand-Drug Conjugate compound of claim **16**, wherein W has the formula of:



wherein R^{20}, R^{21} and R^{22} are as follows:

R^{20}	R^{21}	R^{22}
benzyl	benzyl	$(CH_2)_4NH_2$
isopropyl	benzyl	$(CH_2)_4NH_2$
H	benzyl	$(CH_2)_4NH_2$.

19. The Ligand-Drug Conjugate compound of claim **16**, wherein W has the formula of:

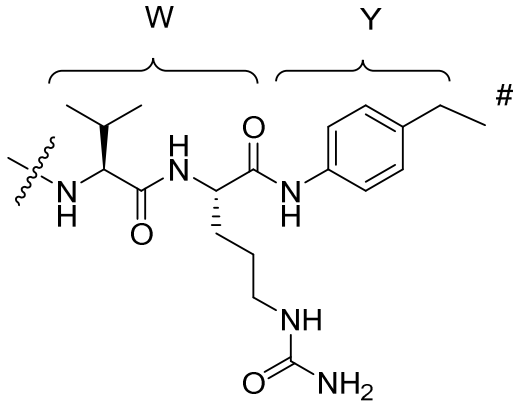


wherein R^{20}, R^{21}, R^{22} and R^{23} are as follows:

R^{20}	R^{21}	R^{22}	R^{23}
H	benzyl	isobutyl	H
methyl	isobutyl	methyl	isobutyl.

20. The Ligand-Drug Conjugate compound of claim **16**, wherein W is -Val-Cit-, -Phe-Lys- or –Val-Ala-.

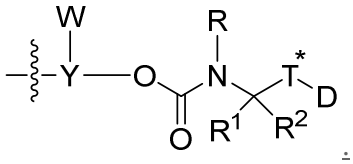
21. The Ligand-Drug Conjugate compound of claim **13**, **14** or **15**, wherein –W-Y- has the structure of:



wherein the wavy line indicates covalent attachment to a Stretcher Unit Z, either directly or indirectly through the Connector Unit (A) and/or Branching Unit (B); and

the hash mark (#) indicates covalent attachment of the benzylic carbon to the methylene carbamate unit.

22. The Ligand-Drug Conjugate compound of claim **1**, wherein its SI Assembly Unit covalently attached to the Drug Unit is represented by the structure of:



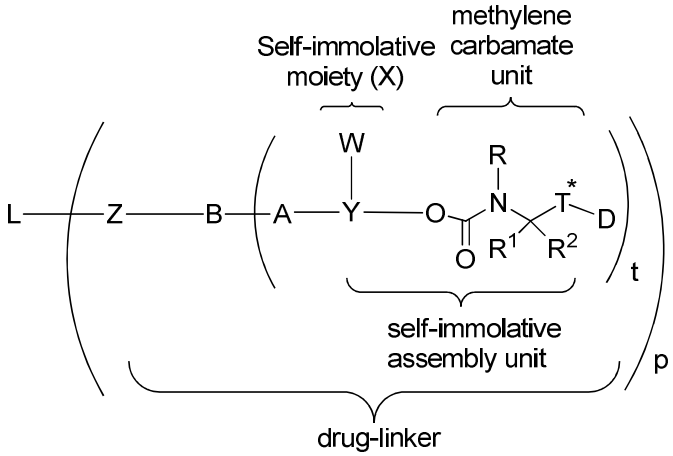
~~wherein W is an activation unit; and~~

~~Y is a self-immolative Spacer Unit,~~

~~wherein the activation unit is a sugar moiety attached to Y through a glycosidic bond so that –Y(W)– is a glycoside unit, wherein enzymatic cleavage of the glycosidic bond initiates self-immolation of Y to release free drug; and~~

~~wherein the wavy line indicates covalent attachment to a Stretcher Unit Z, either directly or indirectly through a Connector Unit (A) and/or Branching Unit (B).~~

23. The Ligand-Drug Conjugate compound of claim **22**, wherein the Ligand-Drug Conjugate compound has the structure of:



or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Z is a Stretcher Unit comprising a thio-substituted succinimide or succinic acid-amide moiety;

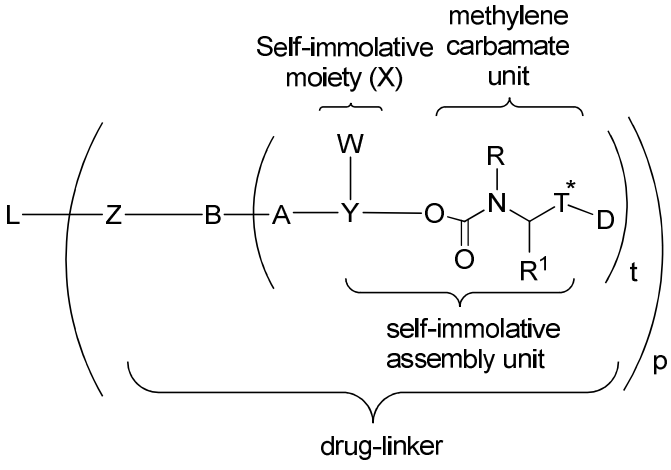
B is an optional Branching Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or polyamine residues or combinations thereof and is present when subscript t is greater than 1 and is absent when subscript t is 1;

A is an optional Connector Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or diamino residues or combinations thereof;

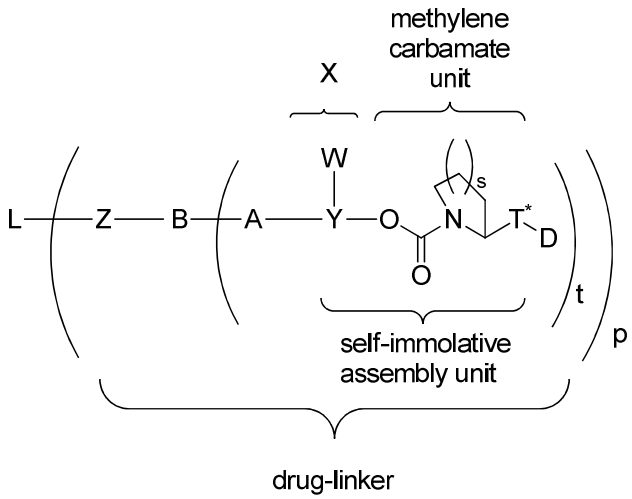
subscript t ranges from 1 to 4; and

subscript p is an integer ranging from 1 to 16.

24. The Ligand-Drug Conjugate compound of claim **23**, wherein the Ligand-Drug Conjugate compound has the structure of:



or



or a pharmaceutically acceptable salt thereof, wherein

R and R^1 independently are hydrogen, optionally substituted C_1-C_6 alkyl or optionally substituted C_{6-14} aryl; and

subscript s is 1 or 2.

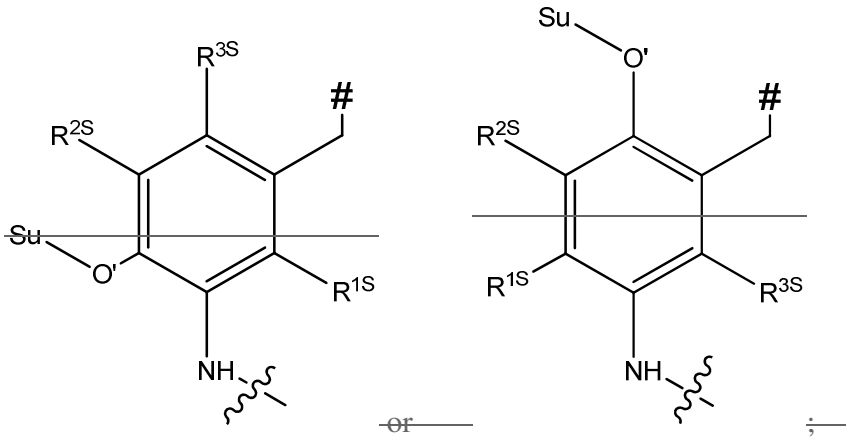
25. The Ligand-Drug Conjugate compound of claim **15** or **24**, wherein R and R^1 are independently hydrogen or optionally substituted C_1-C_4 alkyl.

26. The Ligand-Drug Conjugate compound of claim **25**, wherein the optional substituents are independently selected from the group consisting of -X, -OH, -OR^{op}, -$N(R^{op})_2$, -$N(R^{op})_3$, -CX_3, -CN, -NO_2, -$S(=O)_2R^{op}$ and -$C(=NR^{op})N(R^{op})_2$, wherein each X is independently selected from the group consisting of a halogen: -F, -Cl, -Br, and -I; and each R^{op} is independently selected from the group consisting of hydrogen and -C_1-C_{20} alkyl.

27. The Ligand-Drug Conjugate compound of claim **26**, wherein the optional substituent is selected from the group consisting of –$N(R^{op})_2$, -$N(R^{op})_3$, -$C(=NR)N(R^{op})_2$ and -$S(=O)_2R^{op}$.

28. The Ligand-Drug Conjugate compound of claim **15** or **24**, wherein R is a Basic Unit or a PEG Unit and R^1 is hydrogen.

~~**29.** The Ligand-Drug Conjugate compound of claim **22**, **23** or **24**, wherein the glycoside unit has the structure of:~~



~~wherein Su is the sugar moiety;~~

~~-O'- represents the oxygen atom of the glycosidic bond;~~

~~R^{1S}, R^{2S} and R^{3S} independently are hydrogen, halogen, -CN, or -NO_2; and~~

~~wherein the wavy line indicates covalent attachment to a Stretcher Unit (Z) either directly or indirectly through a Connector Unit (A) and/or Branching Unit (B);~~

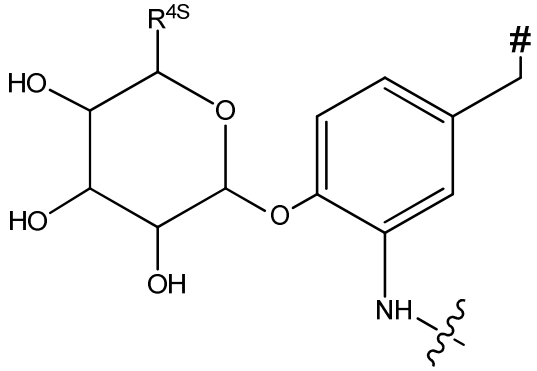
~~and the hash mark (#) indicates covalent attachment to the methylene carbamate unit.~~

~~30~~29**.** The Ligand-Drug Conjugate compound of claim ~~29~~22, 23, or 24, wherein R^{1S}, R^{2S} and R^{3S} are each hydrogen.

~~31~~30**.** The Ligand-Drug Conjugate compound of claim ~~29~~22, 23, or 24, wherein R^{2S} is $-NO_2$, and R^{1S} and R^{3S} are each hydrogen.

se

~~32~~31**.** The Ligand-Drug Conjugate compound of claim ~~29~~22, 23, or 24, wherein the ~~glycoside~~ Glucuronide unit has the structure of:

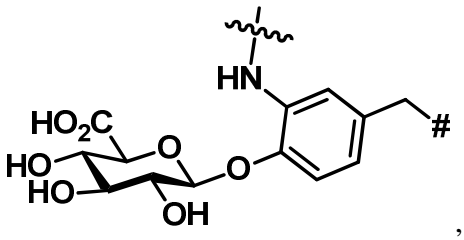


wherein R^{4S} is CH_2OH or $–CO_2H$;

the wavy line indicates covalent attachment to a Stretcher Unit (Z), either directly or indirectly through a Connector Unit (A) and/or Branching Unit (B); and

the hash mark (#) indicates covalent attachment to the methylene carbamate unit.

~~33~~32**.** The Ligand-Drug Conjugate compound of claim ~~32~~31, wherein the ~~glycoside~~ Glucuronide unit ~~is a Glucuronide Unit having~~ has the structure of:

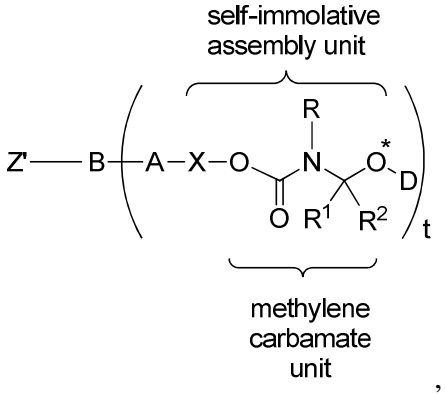


,

or pharmaceutically acceptable salt thereof.

~~34~~33. A Drug-Linker compound, wherein the Drug-Linker compound comprises a Drug Unit and a Linker Unit, wherein the Linker Unit comprises a Self-Immolative Assembly Unit having a methylene carbamate unit and an activateable self-immolative moiety wherein the Drug Unit is covalently attached to the methylene carbamate unit,

wherein the Drug-Linker compound has the structure of:



,

or a pharmaceutically acceptable salt thereof; wherein

D is a Drug Unit having an aromatic hydroxyl functional group that has been incorporated into the indicated methylene carbamate unit;

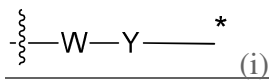
O* is the oxygen atom from said functional group that becomes incorporated into the indicated methylene carbamate unit;

R is hydrogen, optionally substituted C_1-C_6 alkyl that is optionally a Basic Unit, optionally substituted C_{6-14} aryl that is optionally a Basic Unit, or optionally substituted C-linked C_3-C_8 heteroaryl that is optionally a Basic Unit,

R^1 and R^2 independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_{6-14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl, or

both R and R^1 together with the nitrogen and carbon atoms to which they are attached comprise an azetidinyl, pyrrolodinyl, piperidinyl or homopiperidinyl moiety and R^2 is hydrogen;

X is an activateable self-immolative moiety, wherein the activateable self-immolative moiety is of formula (i):



(i)

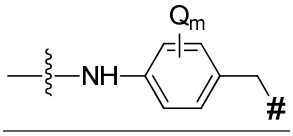
wherein the wavy line indicates covalent attachment of W to A, B, or Z depending on the presence or absence of A or B, and the asterisk (*) indicates covalent attachment of Y to the oxygen atom of the methylene carbamate unit;

W is an Activation Unit; and

Y is a self-immolative Spacer Unit,

wherein the Activation Unit comprises a sequence of 1 to 12 amino acids having an amide linkage to the self-immolative Spacer Unit wherein the amide linkage is cleavable by the action of a tumor associated protease to initiate release of free drug, and

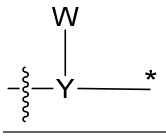
the self-immolative Spacer Unit is a PAB group having the structure of:



wherein the wavy line indicates the site of covalent attachment to the Activation Unit and the hashtag (#) indicates the site of covalent attachment to the benzylic carbon atom of the PAB group to the methylene carbamate unit; and

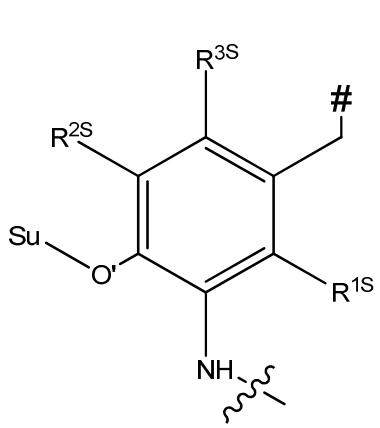
Q is independently -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), or other electron donating group and subscript m is 0, 1 or 2, or

the activateable self-immolative moiety is of formula (ii):

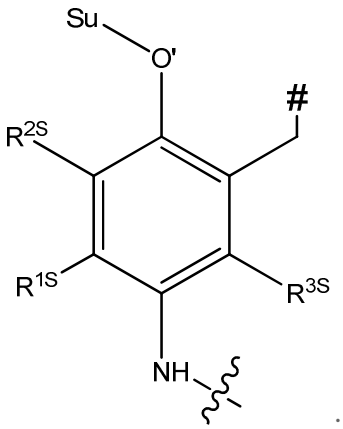


(ii)

wherein the wavy line indicates covalent attachment of Y to A, B, or Z, depending on the presence or absence of A or B, and the asterisk (*) indicates the site of covalent attachment of Y to the oxygen atom of the methylene carbamate unit, wherein formula (ii) is a Glucuronide Unit having the structure of formula XIXa or XIXb:



or



;

(XIXa) (XIXb)

wherein Su is a Sugar moiety; -O'-represents the oxygen atom of glycosidic bond cleavable by a glycosidase;

R^{1S}, R^{2S} and R^{3S} are independently selected from the group consisting of hydrogen, halogen, -CN and -NO_2;

the wavy line indicates the site of covalent attachment to the Stretcher Unit (Z), either directly or indirectly through the Connector Unit (A); and

# indicates the site of attachment to the oxygen atom of the methylene carbamate unit

~~, wherein activation of the activateable self-immolative moiety is by a protease or a glucosidase~~;

Z' is a Stretcher Unit precursor to a Stretcher Unit (Z) of a Ligand-Drug Conjugate compound of claim **4** and comprises a maleimide functional group that provides for covalent attachment of a Ligand Unit to Z;

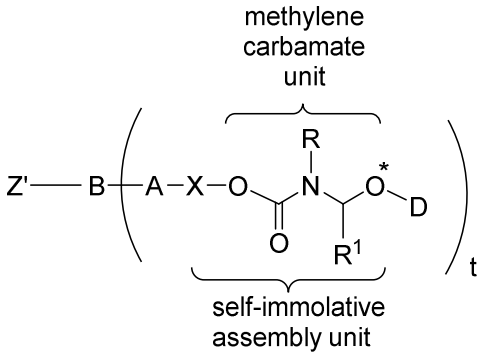
B is an optional Branching Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or polyamine residues or combinations thereof that is present when subscript t is greater than 1 and is absent when subscript t is 1;

A is an optional Connector Unit comprising one or more natural or non-natural amino acid, amino alcohol, amino aldehyde, or diamino residues or combinations thereof; and

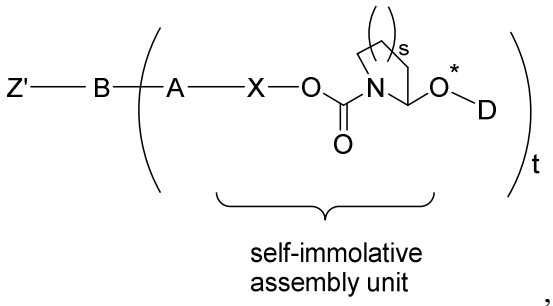
subscript t ranges from 1 to 4; and

wherein activation of the activateable self-immolative moiety (X) results in release of free drug having the formula of D-T^{*}H.

~~35~~34**.** The Drug-Linker compound of claim ~~34~~33, wherein the Drug-Linker compound has the structure of:



,



,

or a pharmaceutically acceptable salt thereof, wherein

R and R^1 independently are hydrogen, optionally substituted C_1-C_6 alkyl or optionally substituted C_{6-14} aryl; and

subscript s is 1 or 2.

~~36~~35**.** The Drug-Linker compound of claim ~~35~~34, wherein R and R^1 are independently hydrogen, optionally substituted C_{1-4} alkyl or optionally substituted phenyl.

~~37~~36**.** The Drug-Linker Compound of claim ~~35~~34, wherein R is a saturated C_{1-6} alkyl, optionally substituted with a basic group.

~~38~~37**.** The Drug-Linker compound of claim ~~34~~33 or ~~35~~34, wherein R is a Basic Unit, wherein the basic functional group of the Basic Unit is an amine or a nitrogen-containing 3-, 4-, 5-, or 6-membered heterocycle that is C-linked or N-linked and is optionally substituted.

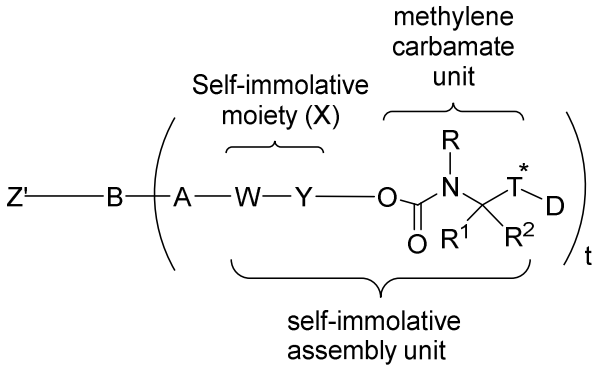
~~39~~38. The Drug-Linker compound of claim ~~38~~37, wherein the basic functional group of the Basic Unit is $–N(R^{op})_2$, wherein R^{op} are independently selected from the group consisting of hydrogen and C_{1-6} alkyl.

~~40~~39. The Drug-Linker compound of claim ~~38~~37, wherein the basic functional group of the Basic Unit is $–N(R^{op})_2$, wherein R^{op} are independently selected from the group consisting of hydrogen and methyl.

~~41~~40. The Drug-Linker compound of claim ~~38~~37, wherein R is a Basic Unit, wherein the Basic Unit is $–CH_2CH_2N(R^{op})_2$, wherein R^{op} are independently selected from the group consisting of hydrogen and methyl.

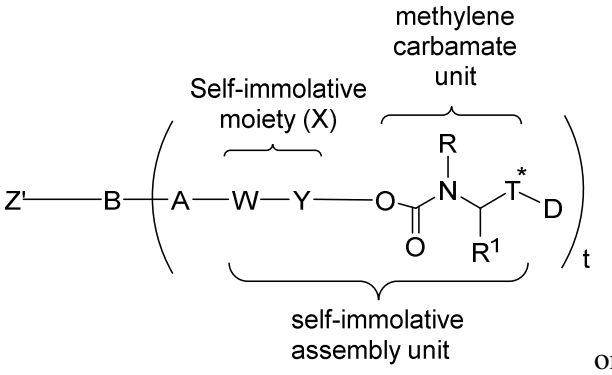
~~42~~41. The Drug-Linker compound of any one of claims ~~34-41~~33-40, wherein R^1 is hydrogen.

~~43~~42. The Drug-Linker compound of claim ~~34~~33, wherein the Drug-Linker compound has the structure of:

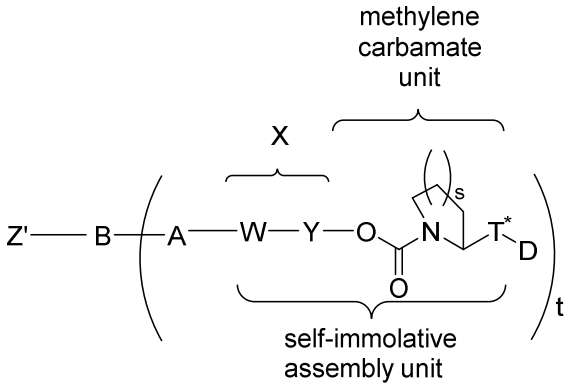


or a pharmaceutically acceptable salt thereof, wherein

~~44~~43. The Drug-Linker compound of claim ~~43~~42, wherein the Drug-Linker compound has the structure of:



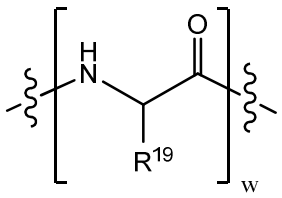
or



wherein R and R^1 independently are hydrogen, optionally substituted C_1-C_6 alkyl or optionally substituted C_{6-14} aryl; and

subscript s is 1 or 2.

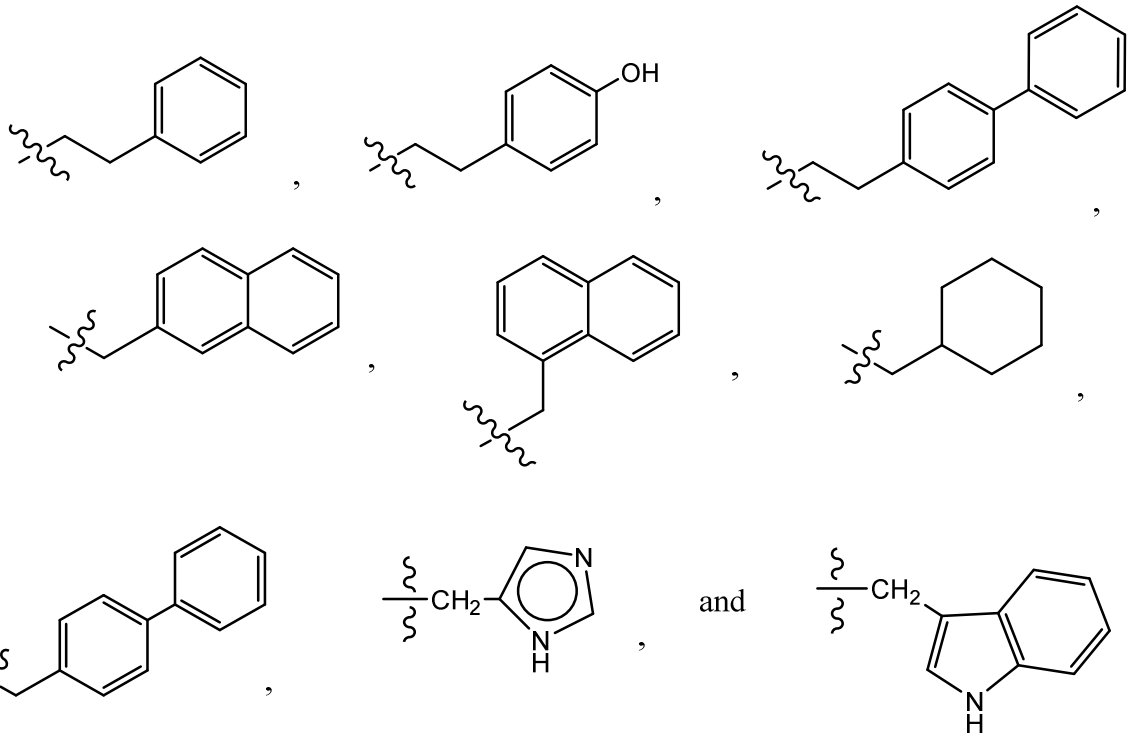
~~45~~44**.** The Drug-Linker compound of claim ~~43~~42 or ~~44~~43, wherein W has the formula of:



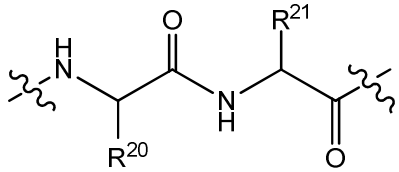
wherein, the wavy line adjacent to the carbonyl is attached to the self-immolative Spacer Unit and the other wavy line is attached to a Stretcher Unit (Z), directly or indirectly through an intervening Connector Unit (A), and/or Branching unit (B);

w is an integer ranging from 1 to 12;

R^{19} is, in each instance, independently selected from the group consisting of hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, benzyl, *p*-hydroxybenzyl, $-CH_2OH$, $-CH(OH)CH_3$, $-CH_2CH_2SCH_3$, $-CH_2CONH_2$, $-CH_2COOH$, $-CH_2CH_2CONH_2$, $-CH_2CH_2COOH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_3NH_2$, $-(CH_2)_3NHCOCH_3$, $-(CH_2)_3NHCHO$, $-(CH_2)_4NHC(=NH)NH_2$, $-(CH_2)_4NH_2$, $-(CH_2)_4NHCOCH_3$, $-(CH_2)_4NHCHO$, $-(CH_2)_3NHCONH_2$, $-(CH_2)_4NHCONH_2$, $-CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-, phenyl, cyclohexyl,

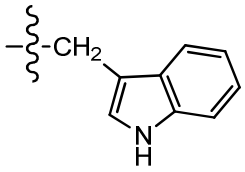


~~46~~45**.** The Drug-Linker compound of claim ~~45~~44 wherein W has the formula of:

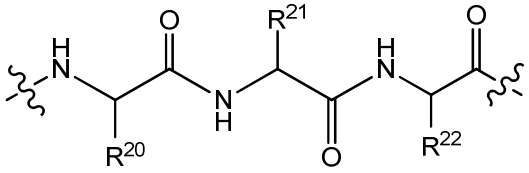


wherein R^{20} and R^{21} are as follows:

R^{20}	R^{21}
benzyl	$(CH_2)_4NH_2$

methyl	$(CH_2)_4NH_2$
isopropyl	$(CH_2)_4NH_2$
isopropyl	$(CH_2)_3NHCONH_2$
benzyl	$(CH_2)_3NHCONH_2$
isobutyl	$(CH_2)_3NHCONH_2$
sec-butyl	$(CH_2)_3NHCONH_2$
	$(CH_2)_3NHCONH_2$
benzyl	methyl
benzyl	$(CH_2)_3NHC(=NH)NH_2$.

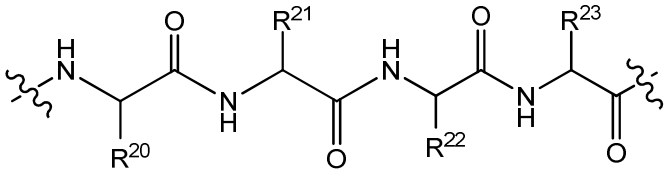
~~47~~46**.** The Drug-Linker compound of claim ~~45~~44 wherein W has the formula of:



wherein R^{20}, R^{21} and R^{22} are as follows:

R^{20}	R^{21}	R^{22}
benzyl	benzyl	$(CH_2)_4NH_2$
isopropyl	benzyl	$(CH_2)_4NH_2$
H	benzyl	$(CH_2)_4NH_2$.

~~48~~47**.** The Drug-Linker compound of claim ~~45~~44, wherein W has the formula of:



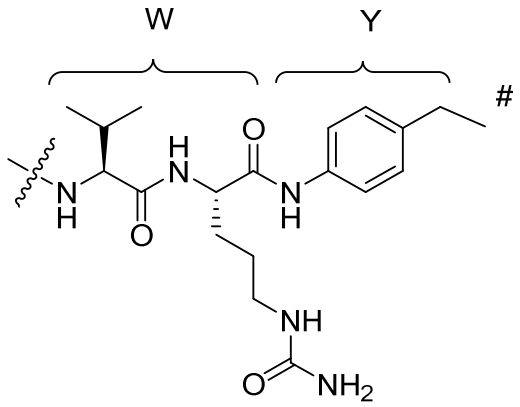
wherein R^{20}, R^{21}, R^{22} and R^{23} are as follows:

R^{20}	R^{21}	R^{22}	R^{23}

H	benzyl	isobutyl	H
methyl	isobutyl	methyl	isobutyl.

~~49~~48. The Drug-Linker compound of claim ~~45~~44, wherein W is -Val-Cit-, -Phe-Lys- or –Val-Ala-.

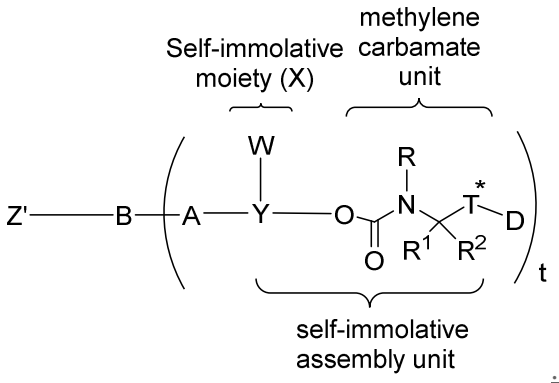
~~50~~49. The Drug-Linker compound of claim ~~43~~42 or ~~44~~43, wherein –W-Y- has the structure of:



wherein the wavy line indicates covalent attachment to a Stretcher Unit Z, either directly or indirectly through the Connector Unit (A) and/or Branching Unit (B); and

the hash mark (#) indicates covalent attachment of the benzylic carbon to the methylene carbamate unit.

~~51~~50. The Drug-Linker compound of claim ~~34~~33, wherein the Drug-Linker compound has the structure of:



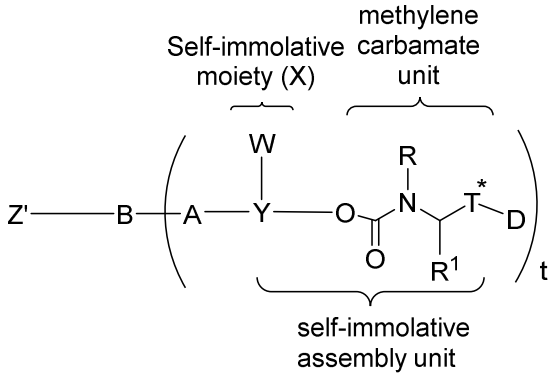
~~or a pharmaceutically acceptable salt thereof, wherein~~

~~W is an activation unit; and~~

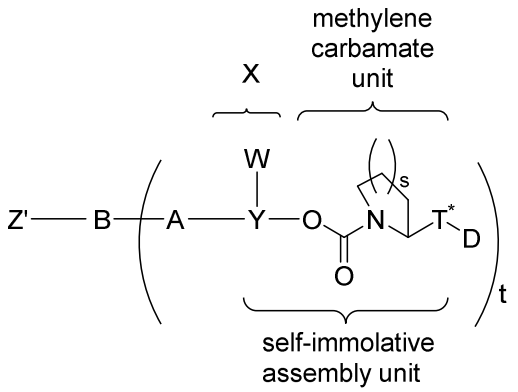
~~Y is a self-immolative Spacer Unit,~~

~~wherein the activation unit is a sugar moiety attached to Y through a glycosidic bond so that Y(W) is a glycoside unit, wherein enzymatic cleavage of the glycosidic bond initiates self-immolation of Y to release free drug~~

~~52~~51**.** The Drug-Linker compound of claim ~~51~~50, wherein the Drug-Linker compound has the structure of:



or



or a pharmaceutically acceptable salt thereof, wherein

R and R^1 independently are hydrogen, optionally substituted C_1-C_6 alkyl or optionally substituted C_{6-14} aryl; and

subscript s is 1 or 2.

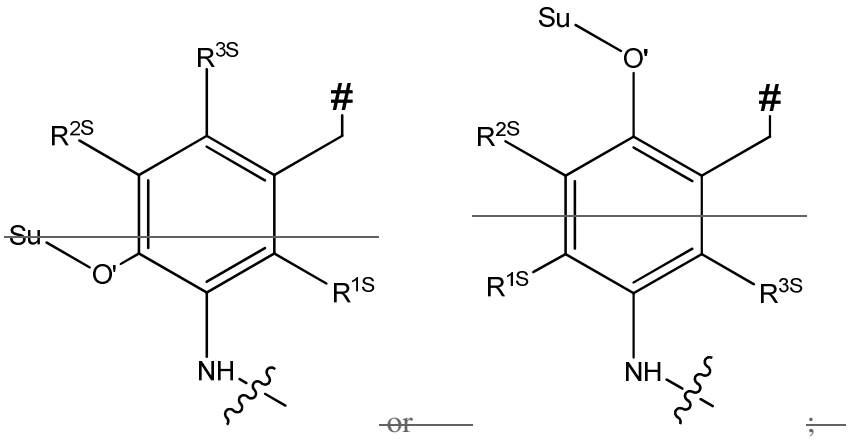
~~53~~52**.** The Drug-Linker compound of claim ~~44~~43 or ~~52~~51, wherein R and R^1 are independently hydrogen or optionally substituted C_1-C_4 alkyl.

~~54~~53. The Drug-Linker compound of claim ~~53~~52, wherein the optional substituents are independently selected from the group consisting of -X, -OH, -OR^{op}, -$N(R^{op})_2$, -$N(R^{op})_3$, -CX_3, -CN, -NO_2, -$S(=O)_2R^{op}$ and -$C(=NR^{op})N(R^{op})_2$, wherein each X is independently selected from the group consisting of a halogen: -F, -Cl, -Br, and -I; and each R^{op} is independently selected from the group consisting of hydrogen and -C_1- C_{20} alkyl.

~~55~~54. The Drug-Linker compound of claim ~~54~~53 wherein the optional substituent is selected from the group consisting of –$N(R^{op})_2$, -$N(R^{op})_3$, -$C(=NR)N(R^{op})_2$ and -$S(=O)_2R^{op}$.

~~56~~55. The Drug-Linker compound of claim ~~44~~43 or ~~52~~51, wherein R is a Basic Unit or a PEG Unit and R^1 is hydrogen.

~~57. The Drug-Linker compound of claim 51 or 52, wherein the glycoside unit has the structure of:~~



~~or~~ ;

~~wherein Su is the sugar moiety;~~

~~O' represents the oxygen atom of the glycosidic bond;~~

~~R^{1S}, R^{2S} and R^{3S} independently are hydrogen, halogen, CN, or NO_2; and~~

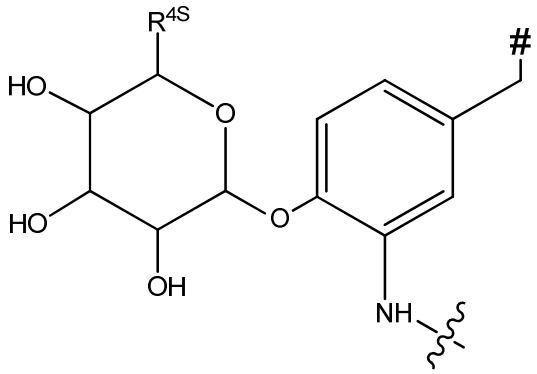
~~wherein the wavy line indicates covalent attachment to a Stretcher Unit (Z) either directly or indirectly through a Connector Unit (A) and/or Branching Unit (B);~~

~~and # indicates covalent attachment to the methylene carbamate unit.~~

~~58~~56. The Drug-Linker compound of claim ~~57~~50 or 51, wherein R^{1S}, R^{2S} and R^{3S} are each hydrogen.

~~59~~57. The Drug-Linker compound of claim ~~57~~50 or 51, wherein R^{2S} is $-NO_2$, and R^{1S} and R^{3S} are each hydrogen.

~~60~~58. The Drug-Linker compound of claim ~~57~~50 or 51, wherein the ~~glycoside~~ Glucuronide unit has the structure of:

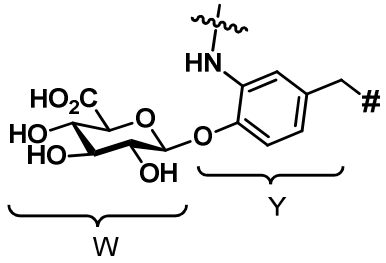


wherein R^{4S} is CH_2OH or $–CO_2H$;

the wavy line indicates covalent attachment to a Stretcher Unit (Z), either directly or indirectly through a Connector Unit (A) and/or Branching Unit (B); and

the hash mark (#) indicates covalent attachment to the methylene carbamate unit.

~~61~~59. The Drug-Linker compound of claim ~~57~~50 or 51, wherein the ~~glycoside~~ Glucuronide unit ~~is a Glucuronide Unit having~~ has the structure of:



wherein the wavy bond adjacent to the nitrogen of Y indicates covalent attachment to Z', A or B, depending on the presence or absence of A and/or B, and the hash mark (#) indicates covalent attachment of the benzylic carbon of Y to the methylene carbamate unit.

~~**62.** The Drug-Linker compound of any one of claims **34-61**, wherein Z' comprises a maleimide moiety.~~

~~63~~**60.** A method of preparing an Antibody Drug Conjugate compound of claim **4**, in which the Stretcher Unit (Z) comprises a succinimide moiety or an succinic acid-amide moiety; and wherein the Ligand Unit is an antibody, the method comprising the step of:

contacting a Drug-Linker compound of claim ~~62~~**33** in which the Stretcher Unit precursor (Z') comprises a maleimide ~~moeity~~ moiety with an antibody having a reactive cysteine thiol functional group obtained from interchain disulfide bond reduction and/or from an engineered cysteine residue,

wherein said contacting converts Z' to Z by formation of a covalent bond between the reactive cysteine sulfur atom of the antibody and the succinimide ~~moeity~~ moiety of Z, optionally followed by spontaneous hydrolysis of the succinimide moiety to an acid amide moiety, whereby the Antibody Drug Conjugate compound is obtained.

~~64~~**61.** The Ligand-Drug Conjugate compound of claim **1**, wherein the Drug Unit is a cytotoxic drug.

~~65~~**62.** The Ligand-Drug Conjugate compound of claim **1**, for use as a medicament.

~~66~~**63.** Use of a Ligand-Drug Conjugate compound of claim **61**~~64~~ in the manufacture of a medicament for the treatment of a cancer.

~~67~~**64.** The use according to claim ~~66~~**63**, wherein the cancer is a hematological cancer.

~~68~~**65.** The use according to claim ~~67~~**64**, wherein the cancer is in the form of a solid tumor.