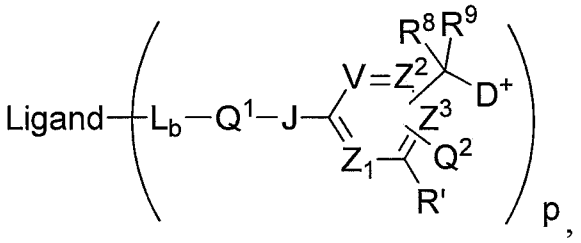
[0009a] In one aspect, there is provided a Ligand Drug Conjugate (LDC) composition, wherein the LDC composition is represented by the structure of Formula 1:



(Formula 1)

wherein

"Ligand" is a Ligand Unit (L), wherein L is an antibody or fragment thereof, thereby defining an antibody drug conjugate (ADC), wherein the antibody is capable of selective binding to an antigen, wherein the antigen is an extracellularly accessible cell-surface protein or glycoprotein preferentially displayed by abnormal cells in comparison to normal cells, wherein the cells are mammalian cells;

L_b is a primary linker;

Q^1 is A_a-W_w, wherein A is an optional Stretcher unit so that subscript a is 0 when A is absent or 1 when A is present and is optionally comprised of two, three or four subunits;

Q^2 is $W'_{w'}$-E-, wherein Q^2, when present, is bonded to V, Z^1, Z^2 or Z^3;

W_w and $W'_{w'}$ are Cleavable units, wherein

W_w of Q^1 is capable of selective cleavage by an intracellular or regulatory protease in comparison to serum proteases, or by glutathione through disulfide exchange, or is more reactive to hydrolysis under more acidic conditions present in lysosomes in comparison to physiological pH of serum,

W'-E of Q^2 provides a glycosidic bond cleavable by a glycosidase located intracellularly, and

subscript w is 0 or 1 so that W is absent when subscript w is 0 or W is present when subscript w is 1, and subscript w' is 0 or 1, wherein W'-E is absent when subscript w' is 0 or W'-E is present when subscript w' is 1, and wherein w + w' is 1 so that one and only one of W, W' is present;

V, Z^1, Z^2 and Z^3 are $=C(R^{24})$-, wherein R^{24} is hydrogen or alkyl, alkenyl or alkynyl, optionally substituted, or halogen, -NO_2, -CN or other electron withdrawing

group, an electron donating group, -Q^2, or –$C(R^8)(R^9)$-D^+, wherein at least one of V, Z^1, Z^2 and Z^3 is =$C(R^{24})$- when subscript w is 1, and at least two of V, Z^1, Z^2 and Z^3 are =$C(R^{24})$- when w' is 1,

provided that when subscript w is 1, Q^2 is absent and one and only one R^{24} is –$C(R^8)(R^9)$-D^+ so that –$C(R^8)(R^9)$-D^+ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is =$C(R^{24})$- and the Q^1-J- and –$C(R^8)(R^9)$-D^+ substituents are *ortho* or *para* to each other,

provided that when subscript w' is 1, one and only one R^{24} is –$C(R^8)(R^9)$-D^+ so that –$C(R^8)(R^9)$-D^+ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is =$C(R^{24})$- and one and only one other R^{24} is Q^2 so that Q^2 is bonded to another one of V, Z^1, Z^2, Z^3 when that variable group is =$C(R^{24})$-, and the Q^2 and –$C(R^8)(R^9)$-D^+ substituents are *ortho* or *para* to each other;

one of R^8 and R^9 is hydrogen and the other is hydrogen, alkyl, alkenyl or alkynyl, optionally substituted, or aryl or heteroaryl, optionally substituted;

R' is hydrogen or is halogen, -NO_2, -CN or other electron withdrawing group, or is an electron donating group;

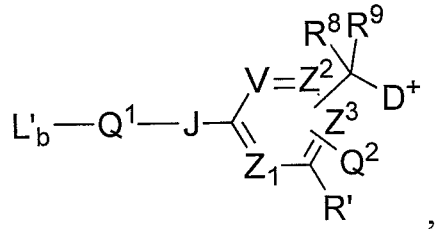
E and J independently are –O-, -S- or –$N(R^{33})$-, wherein R^{33} is hydrogen or optionally substituted alkyl;

D^+ represents a structure of a quaternized tertiary amine-containing drug, wherein the tertiary amine-containing drug is quaternized at the nitrogen atom of its tertiary amine; and

subscript p is an average drug loading having a number ranging from 1 to 24; and

wherein said protease cleavage, disulfide exchange, acid hydrolysis or glycosidase cleavage results in release of tertiary amine-containing drug (D) from a Ligand Drug Conjugate compound of the composition.

[0009b] In another aspect, there is provided a Drug-Linker compound, wherein the Drug Linker compound has the structure of Formula I:



(Formula I)

wherein

L'_b is a ligand covalent binding moiety precursor;

Q^1 is A_a-W_w, wherein A is an optional Stretcher unit so that subscript a is 0 when A is absent or 1 when A is present and is optionally comprised of two, three or four subunits;

Q^2 is $W'_{w'}$-E-, wherein Q^2, when present, is bonded to V, Z^1, Z^2 or Z^3;

W_w and $W'_{w'}$ are Cleavable units, wherein

W_w of Q^1 is capable of selective cleavage by an intracellular or regulatory protease in comparison to serum proteases, or by glutathione through disulfide exchange, or is more reactive to hydrolysis under more acidic conditions present in lysosomes in comparison to physiological pH of serum,

W'-E of Q^2 provides a glycosidic bond cleavable by a glycosidase located intracellularly, and

subscript w is 0 or 1 so that W is absent when subscript w is 0 or W is present when subscript w is 1, and subscript subscript w' is 0 or 1, wherein W'-E is absent when subscript w' is 0 or W'-E is present when subscript w' is 1, and wherein w + w' is 1 so that one and only one of W, W' is present;

V, Z^1, Z^2 and Z^3 are $=C(R^{24})$-, wherein R^{24} is hydrogen or alkyl, alkenyl or alkynyl, optionally substituted, or halogen, -NO_2, -CN or other electron withdrawing group, an electron donating group, -Q^2, or $-C(R^8)(R^9)$-D^+, wherein at least one of V, Z^1, Z^2 and Z^3 is $=C(R^{24})$- when subscript w is 1, and at least two of V, Z^1, Z^2 and Z^3 are $=C(R^{24})$- when subscript w' is 1,

provided that when subscript w is 1, Q^2 is absent and one and only one R^{24} is $-C(R^8)(R^9)$-D^+ so that $-C(R^8)(R^9)$-D^+ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})$- and the Q^1-J- and $-C(R^8)(R^9)$-D^+ substituents are *ortho* or *para* to each other,

provided that when subscript w' is 1, one only one R^{24} is $-C(R^8)(R^9)$-D^+ so that $-C(R^8)(R^9)$-D^+ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})$- and one and only one other R^{24} is Q^2 so that Q^2 is bonded to another one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})$-, and the Q^2 and $-C(R^8)(R^9)$-D^+ substituents are *ortho* or *para* to each other;

one of R^8 and R^9 is hydrogen and the other is hydrogen, alkyl, alkenyl or alkynyl, optionally substituted, or aryl or heteroaryl, optionally substituted;

R' is hydrogen or is halogen, -NO_2, -CN or other electron withdrawing group, or is an electron donating group;

E and J independently are –O-, -S- or –N(R^{33})-, wherein R^{33} is hydrogen or optionally substituted alkyl;

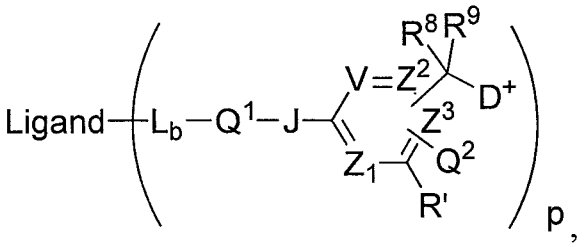
D^+ represents a structure of a quaternized tertiary amine-containing drug, wherein the tertiary amine-containing drug is quaternized at the nitrogen atom of its tertiary amine, and is cytotoxic or cytostatic towards mammalian cells; and

wherein said protease cleavage, disulfide exchange, acid hydrolysis or glycosidase cleavage results in expulsion of free tertiary amine-containing drug (D) from the Drug-Linker Compound, or a Ligand Drug Conjugate compound or N-acetyl-cysteine Conjugate derived therefrom..

[0010] In some embodiments, the targeting moiety is an antibody, thereby defining an antibody drug conjugate (ADC), and the targeted moiety is an cell-surface antigen of targeted abnormal cells that is capable of cellular internalization of bound ADC, wherein the antigen is preferentially present on the abnormal cells in comparison to normal cells.

WHAT IS CLAIMED IS:

1. A Ligand Drug Conjugate (LDC) composition, wherein the LDC composition is represented by the structure of Formula 1:



(Formula 1)

wherein

"Ligand" is a Ligand Unit (L), wherein L is an antibody or fragment thereof, thereby defining an antibody drug conjugate (ADC), wherein the antibody is capable of selective binding to an antigen, wherein the antigen is an extracellularly accessible cell-surface protein or glycoprotein preferentially displayed by abnormal cells in comparison to normal cells, wherein the cells are mammalian cells;

L_b is a primary linker;

Q^1 is A_a-W_w, wherein A is an optional Stretcher unit so that subscript a is 0 when A is absent or 1 when A is present and is optionally comprised of two, three or four subunits;

Q^2 is $W'_{w'}$-E-, wherein Q^2, when present, is bonded to V, Z^1, Z^2 or Z^3;

W_w and $W'_{w'}$ are Cleavable units, wherein

W_w of Q^1 is capable of selective cleavage by an intracellular or regulatory protease in comparison to serum proteases, or by glutathione through disulfide exchange, or is more reactive to hydrolysis under more acidic conditions present in lysosomes in comparison to physiological pH of serum,

W'-E of Q^2 provides a glycosidic bond cleavable by a glycosidase located intracellularly, and

subscript w is 0 or 1 so that W is absent when subscript w is 0 or W is present when subscript w is 1, and subscript w' is 0 or 1, wherein W'-E is absent when subscript w' is 0 or W'-E is present when subscript w' is 1, and wherein w + w' is 1 so that one and only one of W, W' is present;

V, Z^1, Z^2 and Z^3 are $=C(R^{24})$-, wherein R^{24} is hydrogen or alkyl, alkenyl or alkynyl, optionally substituted, or halogen, $-NO_2$, -CN or other electron withdrawing group, an

electron donating group, $-Q^2$, or $-C(R^8)(R^9)-D^+$, wherein at least one of V, Z^1, Z^2 and Z^3 is $=C(R^{24})-$ when subscript w is 1, and at least two of V, Z^1, Z^2 and Z^3 are $=C(R^{24})-$ when w' is 1,

provided that when subscript w is 1, Q^2 is absent and one and only one R^{24} is $-C(R^8)(R^9)-D^+$ so that $-C(R^8)(R^9)-D^+$ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})-$ and the Q^1-J- and $-C(R^8)(R^9)-D^+$ substituents are *ortho* or *para* to each other,

provided that when subscript w' is 1, one and only one R^{24} is $-C(R^8)(R^9)-D^+$ so that $-C(R^8)(R^9)-D^+$ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})-$ and one and only one other R^{24} is Q^2 so that Q^2 is bonded to another one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})-$, and the Q^2 and $-C(R^8)(R^9)-D^+$ substituents are *ortho* or *para* to each other;

one of R^8 and R^9 is hydrogen and the other is hydrogen, alkyl, alkenyl or alkynyl, optionally substituted, or aryl or heteroaryl, optionally substituted;

R' is hydrogen or is halogen, $-NO_2$, -CN or other electron withdrawing group, or is an electron donating group;

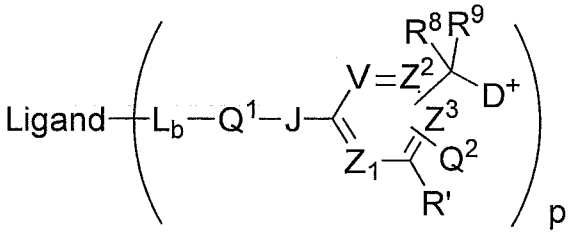
E and J independently are –O-, -S- or $-N(R^{33})-$, wherein R^{33} is hydrogen or optionally substituted alkyl;

D^+ represents a structure of a quaternized tertiary amine-containing drug, wherein the tertiary amine-containing drug is quaternized at the nitrogen atom of its tertiary amine; and

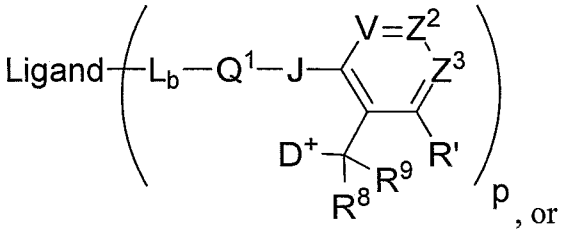
subscript p is an average drug loading having a number ranging from 1 to 24; and

wherein said protease cleavage, disulfide exchange, acid hydrolysis or glycosidase cleavage results in release of tertiary amine-containing drug (D) from a Ligand Drug Conjugate compound of the composition.

2. The LDC composition of claim 1 wherein the structure of the composition is represented by Formula 2A or Formula 2B:



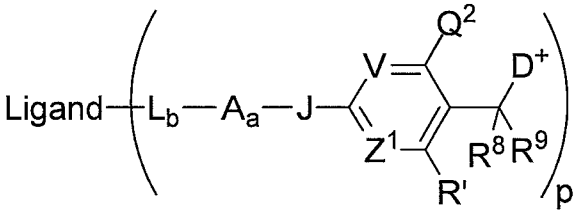
(Formula 2A)



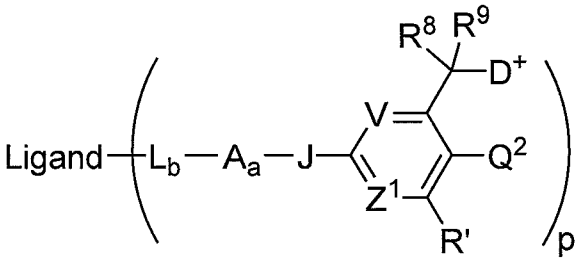
, or

(Formula 2B)

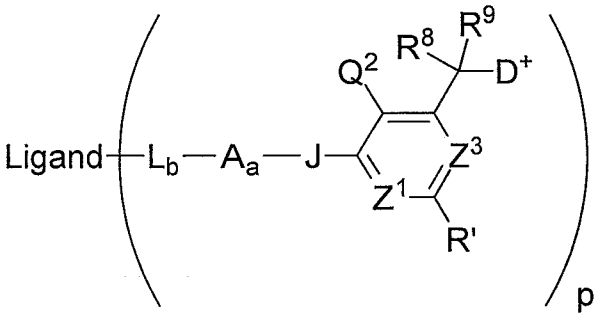
wherein the structure of the composition is represented by the structure of Formula 3A, Formula 3B, Formula 3C, Formula 3D, Formula 3E, or Formula 3F:



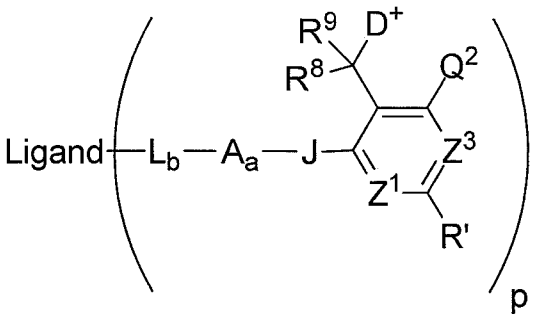
(Formula 3A)



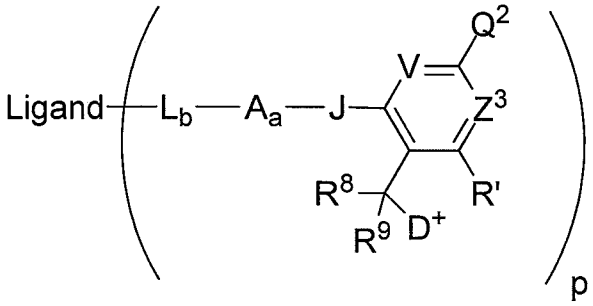
(Formula 3B)



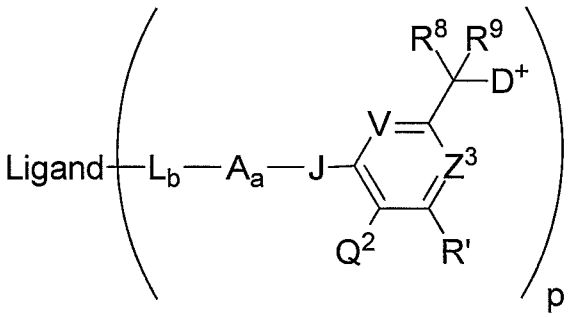
(Formula 3C)



(Formula 3D)



(Formula 3E)



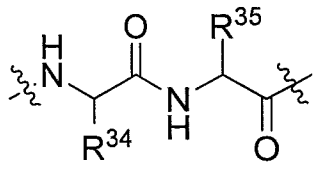
(Formula 3F)

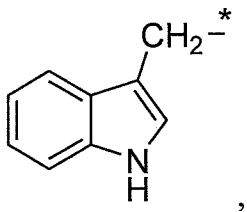
wherein the tertiary amine-containing drug is cytotoxic or cytostatic towards the mammalian cells.

3. The LDC composition of claim 1 or 2, wherein W of Q^1 is comprised or consists of a peptide moiety having a peptide bond to J that is selectively cleavable by an intracellular or regulatory protease in comparison to serum proteases wherein action of the regulatory protease on W causes release of tertiary amine-containing drug (D) from a Ligand Drug Conjugate compound of the composition, and W' of Q^2 is a glycoside-bonded carbohydrate, wherein the glycoside bond W'-E of Q^2 provides for a cleavage site for a glycosidase located intracellularly, wherein action of the glycosidase on W'-E causes

release of tertiary amine-containing drug (D) from a Ligand Drug Conjugate compound of the composition.

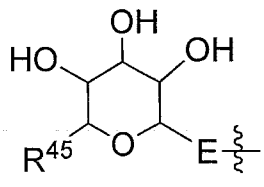
4. The LDC composition of claim 3, wherein the peptide moiety of W is comprised or consists of a dipeptide moiety having the structure of Formula 6:


(Formula 6),

wherein R^{34} is benzyl, methyl, isopropyl, isobutyl, sec-butyl, -CH(OH)CH_3 or has the structure of , wherein the asterisk indicates covalent bonding to the dipeptide backbone; and R^{35} is methyl, $-(CH_2)_4$-NH_2, -$(CH_2)_3NH(C{=}O)NH_2$, -$(CH_2)_3NH(C{=}NH)NH_2$, or -$(CH_2)_2CO_2H$,

wherein the wavy bond to the dipeptide's C-terminus indicates covalent bonding to J of the arylene moiety of Formula 2A or 2B and the wavy bond to the dipeptide's N-terminus indicates covalent bonding to the remainder of W, if any such remainder is present, or to A, or a subunit thereof, when subscript a is 1 or to L_b when subscript a is 0, and wherein the dipeptide's bond to J is cleavable by an intracellular or regulatory protease, and

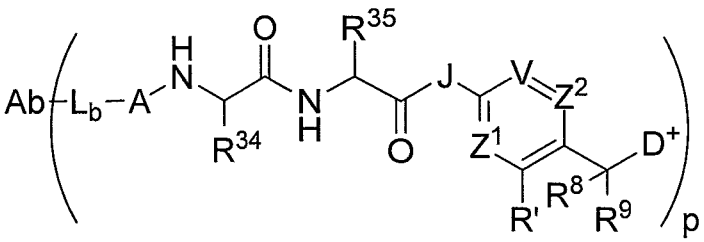
wherein W' in Q^2 is a carbohydrate moiety that is glycoside-bonded to E, wherein the glycosidic bond is cleavable by a glycosidase located intracellularly, and wherein W'-E has the structure of Formula 7:


(Formula 7),

wherein the wavy line represents E bonded to one of V, Z^1, Z^2, or Z^3 when that variable group is $=C(R^{24})$, wherein E is –O-, -S- , or $–N(R^{33})$-, wherein R^{33} is hydrogen or methyl; and

wherein R^{45} is $–CH_2OH$ or $–CO_2H$.

5. The LDC composition of claim 4, wherein the structure of the composition is represented by Formula 9:



(Formula 9)

wherein

Ab is the antibody Ligand Unit;

R' is hydrogen or an electron donating group;

R^8 is hydrogen;

R^9 is hydrogen, optionally substituted C_1-C_6 alkyl, or optionally substituted phenyl;

R^{34} is methyl, isopropyl or $-CH(OH)CH_3$;

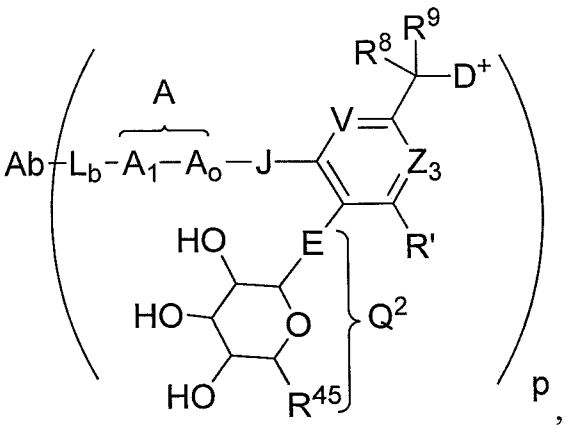
R^{35} is methyl, $-(CH_2)_3NH(C=O)NH_2$ or $-(CH_2)_2CO_2H$;

J is $–N(R^{33})$-, wherein R^{33} is hydrogen or methyl; and

V, Z^2 and Z^1 are each =CH-,

or

the structure of the composition is represented by the structure of Formula 11:



(Formula 11)

wherein

Ab is the antibody Ligand Unit;

A_1 and A_O are independently selected subunits of A, wherein A_O is an optional subunit of A so that A_1 becomes A when A_O is absent and A is $-A_1-A_O-$ when A_O is present;

E is –O- or –NH-;

J is $-N(R^{33})-$, wherein R^{33} is hydrogen or methyl;

V and Z^3 are each =CH-;

R' is hydrogen or an electron withdrawing group;

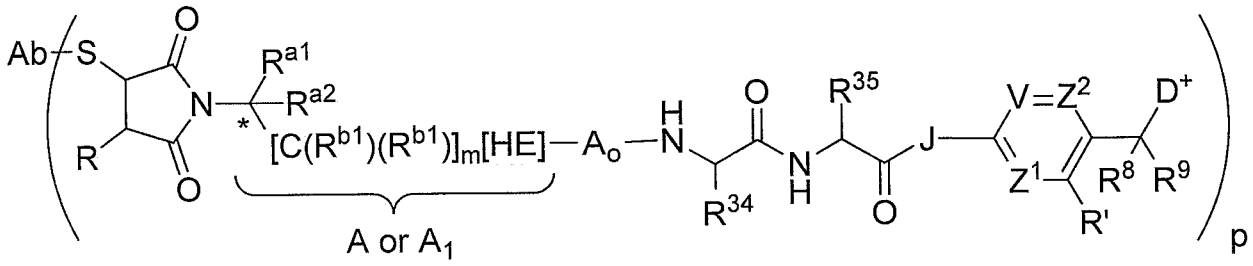
R^8 is hydrogen;

R^9 is hydrogen, optionally substituted C_1-C_6 alkyl or optionally substituted phenyl;

R^{45} is $-CO_2H$; and

subscript p is a number ranging from 1 to 8.

6. The LDC composition of claim 5, wherein the structure of the composition is represented by Formula 10:



(Formula 10)

wherein

S is a sulfur atom of the antibody Ligand Unit and the succinimide ring to which it is covalently attached is optionally in hydrolysed form;

the asterisk (*) designates chirality or absence thereof at the indicated carbon;

A_o is an optional subunit of A, wherein $-[C(R^{b1})(R^{b1})]_m$-[HE]- is A when A_o is absent and is A_1 when A_o is present so A becomes $-A_1-A_o-$;

R is –H;

R^{a1} is –H or a basic unit (BU), in which the succinimide ring is in hydrolyzed form, wherein BU has the structure of $-CH_2-N(R^{22})(R^{23})$, wherein R^{22} and R^{23} independently are hydrogen, methyl or ethyl or both together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl;

R^{a2} is hydrogen;

subscript m is an integer ranging from 0 to 5 when HE is present or from 1 to 5 when HE is absent;

each R^{b1} independently is hydrogen or optionally substituted C_1-C_6 alkyl;

HE is absent or is –C(=O)-;

R^{34} is methyl, isopropyl or $-CH(OH)CH_3$;

R^{35} is $-(CH_2)_3NH(C=O)NH_2$, or $-(CH_2)_2CO_2H$;

J is –NH-;

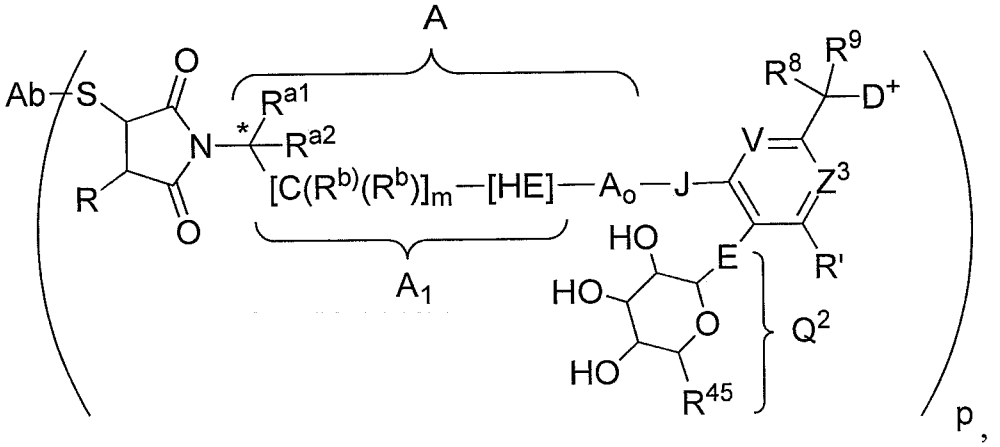
R' is hydrogen or an electron donating group;

R^8 is hydrogen; and

R^9 is hydrogen or methyl,

or

wherein the structure of the composition is represented by Formula 12:



(Formula 12)

wherein

S is a sulfur atom of the antibody Ligand Unit and the succinimide ring to which it is covalently attached is optionally in hydrolysed form;

the asterisk (*) designates chirality or absence thereof at the indicated carbon atom;

A_1 and A_O are independently selected subunits of A, wherein A_O is an optional subunit of A, wherein–$[C(R^{b1})(R^{b1})]_m$-[HE]- is A when A_O is absent and is A_1 when A_O is present so that A becomes A_1-A_O; wherein A_O when present corresponds in structure to an amine-containing acid bonded to J through the C-terminal carbonyl of the amine-containing acid;

R is hydrogen;

R' is hydrogen or an electron withdrawing group;

R^{a1} is hydrogen or a basic unit (BU) in which the succinimide ring is in hydrolyzed form, wherein BU has the structure of $–CH_2$-$N(R^{22})(R^{23})$, or a an acid addition salt thereof, wherein R^{22} and R^{23} independently are hydrogen, methyl or ethyl or both together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl;

R^{a2} is hydrogen;

subscript m is an integer ranging from 0 to 5 when HE is present or 1 to 5 when HE is absent;

each R^{b1} independently is hydrogen or optionally substituted C_1-C_6 alkyl;

HE is absent or is –C(=O)-;

R^{45} is $–CO_2H$;

E is –O-;

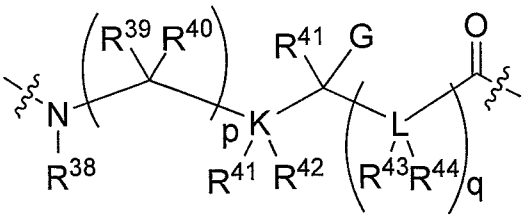
J is –NH-;

R^8 is hydrogen;

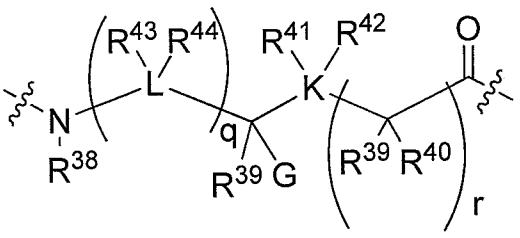
R^9 is hydrogen or methyl; and

subscript p is a number ranging from 1 to 8.

7. The LDC composition of claim 6, wherein A_O, when present, has the structure of Formula 13 or Formula 14:



(Formula 13)



(Formula 14)

wherein the wavy line to the carbonyl moiety of either structure represents the point of attachment of A_O to W and wherein the wavy line to the amino moiety of either structure represents the point of attachment of A_O to A_1,

wherein K and L independently are C, N, O or S, provided that when K or L is O or S, R^{41} and R^{42} to K or R^{43} and R^{44} to L are absent, and when K or L is N, one of R^{41}, R^{42} to K or one of R^{43}, R^{44} to L is absent, and provided that no two adjacent L are independently selected as N, O, or S;

wherein subscript q is an integer ranging from 0 to 12, and subscript r is an integer ranging from 1 to 12;

wherein G is hydrogen, optionally substituted C_1-C_6 alkyl, -OH, -OR^G, -CO_2H, or -CO_2R^G, wherein R^G is C_1-C_6 alkyl, aryl or heteroaryl, optionally substituted, or R^{PR},

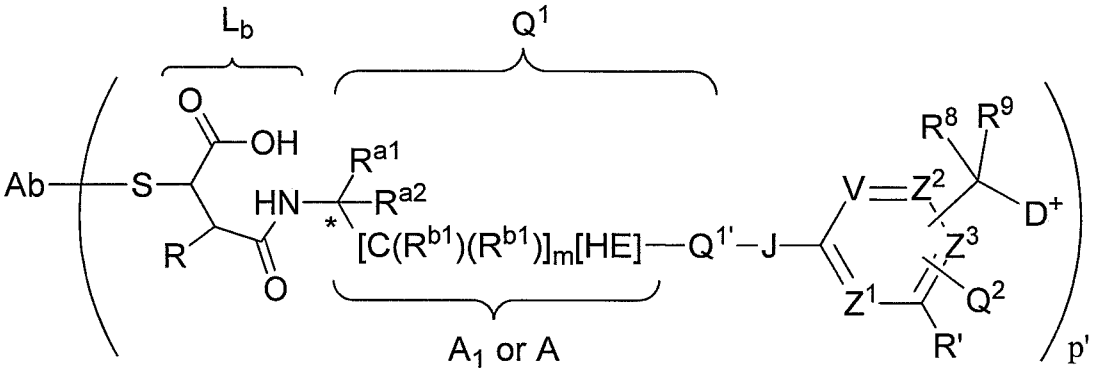
wherein R^{PR} is a suitable protecting group, -NH_2, or -$N(R^G)(R^{PG})$, wherein R^G independently selected is as previously defined or both R^G together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl or both R^{PR} together form a suitable protecting group;

wherein R^{38} is hydrogen or optionally substituted C_1-C_6 alkyl; R^{39}-R^{44} independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted, or optionally substituted heteroaryl, or both R^{39}, R^{40} together with the carbon to which they are attached define a C_3-C_6 cycloalkyl, or R^{41}, R^{42} together with K to which they are attached when K is C, or R^{43}, R^{44} together with L to which they are attached when L is C, define a C_3-C_6 cycloalkyl, or R^{40} and R^{41}, or R^{40} and R^{43}, or R^{41} and R^{43} together with the carbon or heteroatom to which they are attached and atoms intervening between those carbon and/or heteroatoms define a 5- or 6-membered cycloalkyl or heterocycloalkyl, or

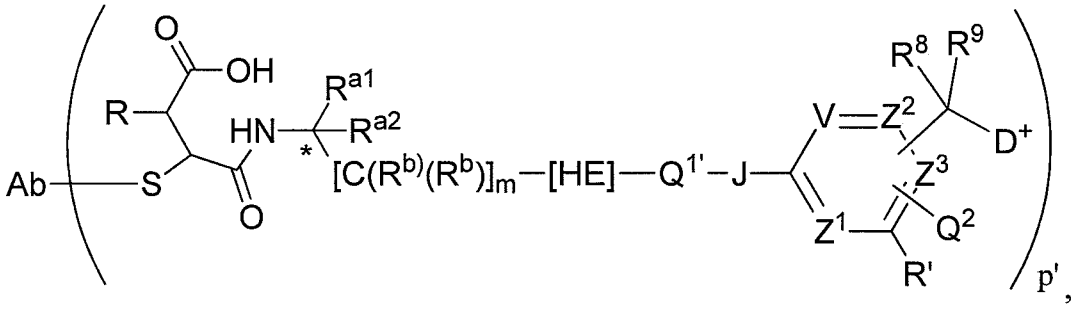
wherein A_O has a structure corresponding to alpha-amino, beta-amino or another amine-containing acid; and

wherein the indicated starred (*) carbon is predominantly in the same absolute configuration as the alpha carbon of an L-amino acid when that indicated carbon has chirality.

8. The LDC composition of claim 3, wherein a Ligand Drug Conjugate compound of the composition has the structure of Formula 16A or Formula 16B:



(Formula 16A)



(Formula 16B)

wherein Ab is the antibody Ligand Unit;

S is a sulfur atom of the antibody Ligand Unit;

the asterisk (*) designates chirality or absence thereof at the indicated carbon atom carbon;

$Q^{1'}$ is A_O-W_w, wherein A_O is an optional subunit of A so that -$Q^{1'}$- is –W_w- when A_O is absent, or is –A_O-W_w- when A_O is present,

wherein –[$C(R^b)(R^b)]_m$-[HE]- becomes A when A_O is absent or is A_1 when A_o is present, and

wherein subscript w is 1 when Q^2 is absent or subscript w is 0 so that W is absent and Q^2 is present;

R is hydrogen;

R^{a1} is –H or BU wherein BU has the structure of $–CH_2-N(R^{22})(R^{23})$, or an acid addition salt thereof, wherein R^{22} and R^{23} independently are hydrogen or methyl or both together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl;

R^{a2} is hydrogen;

subscript m is an integer ranging from 0 to 5 when HE is present or from 1 to 5 when HE is absent;

each R^{b1} independently is hydrogen or optionally substituted C_1-C_6 alkyl;

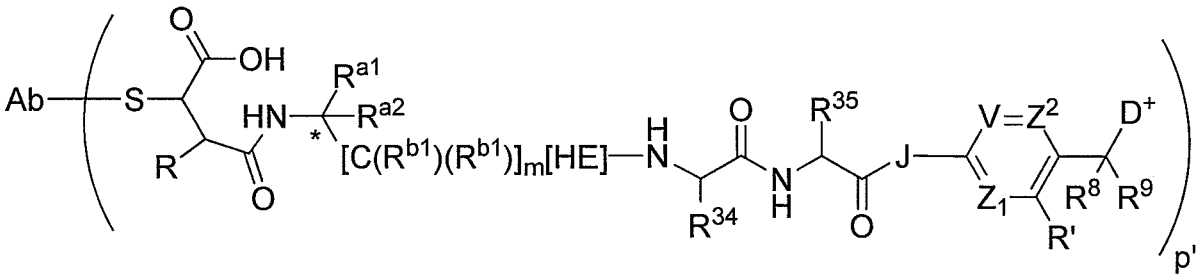
HE is absent or is –C(=O)-;

J is –O- or –NH-;

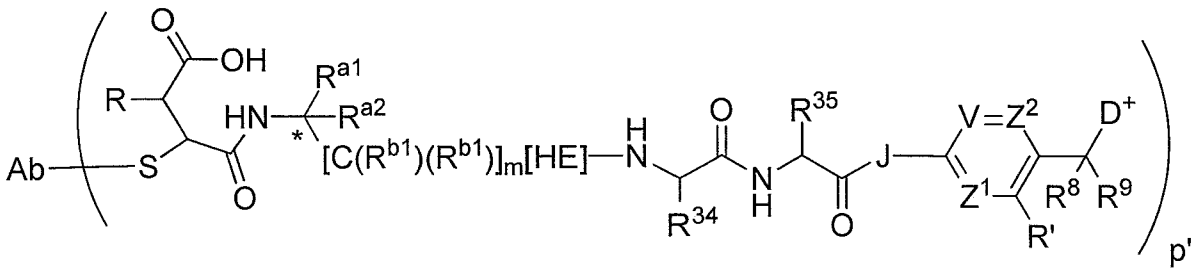
Q^2 when present is W'-E, wherein E is –O- or –NH-; and

subscript p' is an integer ranging from 1 to 8.

9. The LDC composition of claim 8, wherein a Ligand Drug Conjugate compound of the composition has the structure of Formula 17A or Formula 17B:



(Formula 17A)



(Formula 17B)

wherein

J is –NH-;

R is hydrogen;

R^{a1} is –H or BU, wherein BU has the structure of $–CH_2-N(R^{22})(R^{23})$, or an acid addition salt thereof, wherein R^{22} and R^{23} independently are hydrogen or methyl or both together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl;

R^{a2} is hydrogen;

subscript m is an integer ranging from 0 to 5 when HE is present or from 1 to 5 when HE is absent;

each R^{b1} independently is hydrogen or optionally substituted C_1-C_6 alkyl;

HE is absent or is –C(=O)-;

J is –O- or –NH;

one of V, Z^1 is $=C(R^{24})$-, wherein R^{24} is hydrogen, -Cl or $–NO_2$, and the other V, Z^1 and Z^2 are $=CH_2$-;

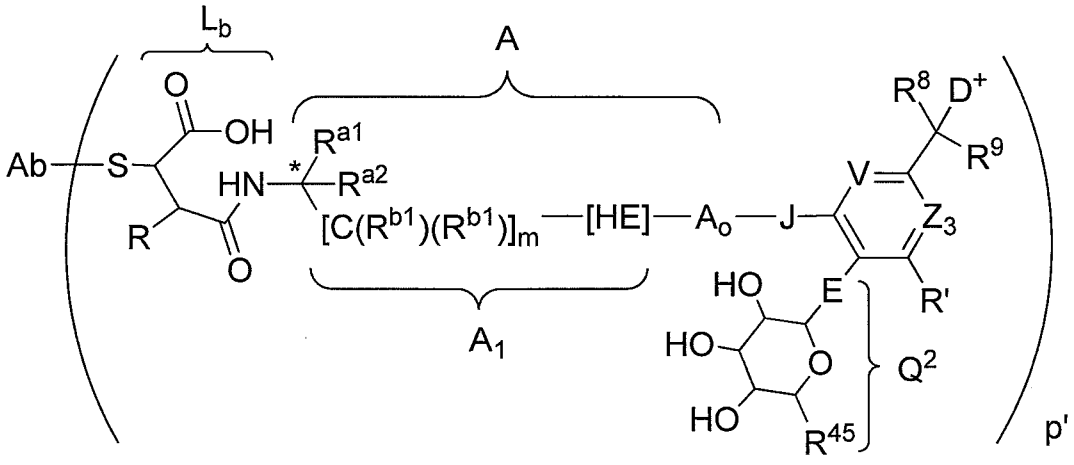
R^8 is hydrogen;

R^9 is hydrogen or methyl; and

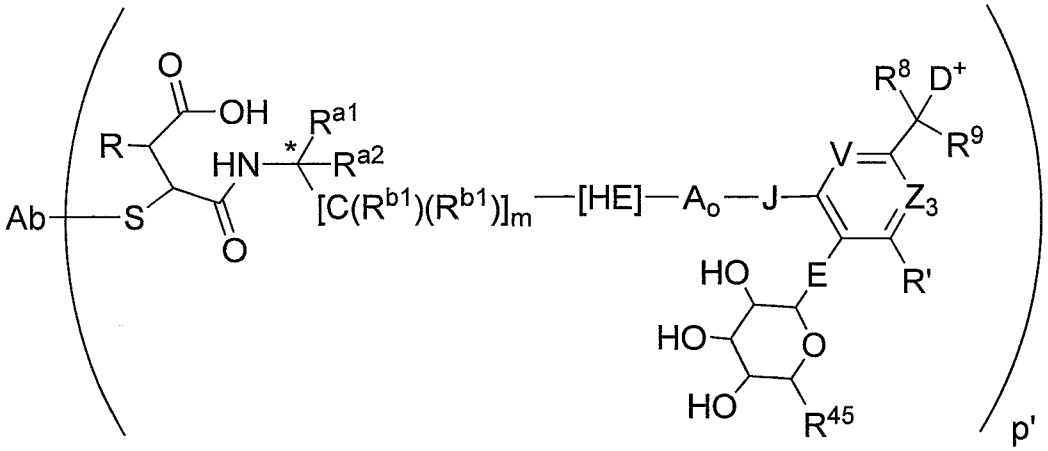
subscript p' is an integer ranging from 1 to 8,

or

a Ligand Drug Conjugate compound of the composition independently has the structure of Formula 19A or Formula 19B:



(Formula 19A)



(Formula 19B)

wherein

A_O is an optional subunit of A, wherein the $-[C(R^{b1})(R^{b1})]_m$-[HE]- moiety is A when A_O is absent or the moiety is A_1 when A_O is present so that A becomes $-A_1-A_O-$;

R is –H;

R^{a1} is –H or a Basic Unit (BU), wherein BU has the structure of $-CH_2-N(R^{22})(R^{23})$, or an acid addition salt thereof, wherein R^{22} independently are hydrogen or methyl or R^{22} both together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl;

R^{a2} is hydrogen;

subscript m is an integer ranging from 0 to 5 when HE is present or 1 to 5 when HE is absent;

each R^{b1} independently is hydrogen or optionally substituted C_1-C_6 alkyl;

HE is absent or is –C(=O)-;

R^{45} is $-CO_2H$;

E is –O-;

J is –NH-;

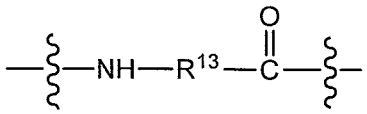
V and Z^3 are each $=CH_2$-;

R^8 is hydrogen; and

R^9 is hydrogen or methyl; and

subscript p' is an integer ranging from 1 to 8.

10. The LDC composition of claim 9, wherein A_O, when present, has the structure of:



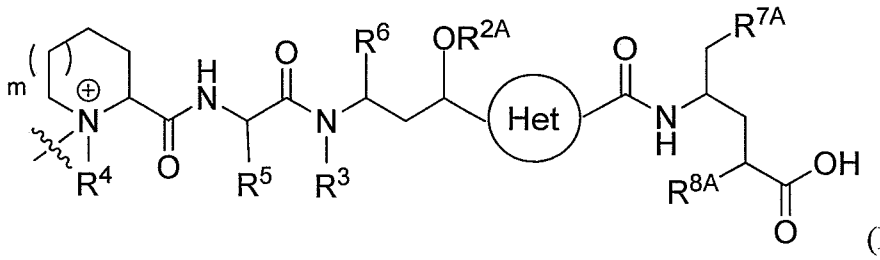
wherein R^{13} is -C_1-C_{10} alkylene-, -C_3-C_8carbocyclo-, -arylene-, -C_1-C_{30}heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10}alkylene-, -C_1-C_{10} alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -$(CH_2CH_2O)_{1-10}(-CH_2)_{1-3}$-, or -$(CH_2CH_2NH)_{1-10}(-CH_2)_{1-3}$-,

or wherein A_O has a structure corresponding to alpha-amino or beta-amino acid; and

wherein the indicated starred (*) carbon of Formula 19A or Formula 19B is predominantly in the same absolute configuration as the alpha carbon of an L-amino acid when that indicated carbon has chirality.

11. The LDC composition of claim 1, wherein $-D^+$ is a quaternized tertiary amine-containing tubulin disrupting agent.

12. The LDC composition of claim 11, wherein the quaternized tertiary amine-containing tubulin disrupting agent $-D^+$ is a quaternized tubulysin Drug Unit having the structure of Formula D_{G-1}':



(Formula D_{G-1}')

wherein

the circle represents a 5-membered nitrogen-containing heteroaryl and wherein the indicated required substituents to that heteroaryl are in a 1,3-relationship with each other with optional substitutions at the remaining positions;

subscript m is 0 or 1;

R^{2A} is hydrogen or optionally substituted alkyl or R^{2A} along with the oxygen atom to which it is attached defines an O-linked substituent other than -OH;

R^3 is hydrogen or optionally substituted alkyl;

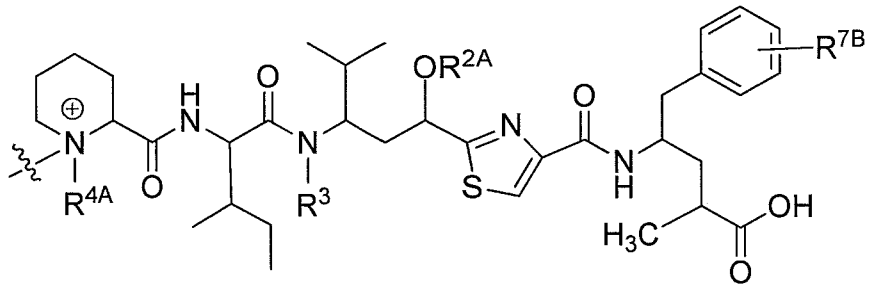
R^4, R^5 and R^6 are optionally substituted alkyl, independently selected;

R^{7A} is optionally substituted aryl or optionally substituted heteroaryl; and

R^{8A} is hydrogen or optionally substituted alkyl,

wherein the wavy line indicates covalent bonding of D^+ to the remainder of the composition or compound structure.

13. The LDC composition of claim 11 wherein the quaternized tertiary amine-containing tubulin disrupting agent $-D^+$ is a quaternized tubulysin Drug Unit having the structure of:



,

wherein

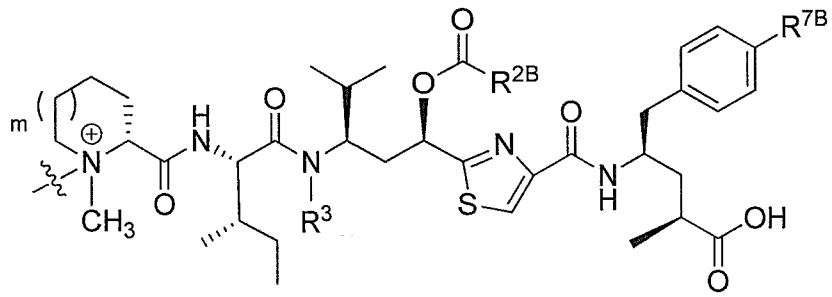
R^{4A} is methyl;

R^3 is H, methyl, ethyl, propyl, $-CH_2-OC(O)R^{3A}$, $-CH2CH(R^{3B})C(O)R^{3A}$ or $-CH(R^{3B})C(O)NHR^{3A}$, wherein R^{3A} is C_1-C_6 alkyl and R^{3B} is H or C_1-C_6 alkyl, independently selected from R^{3A};

$-OR^{2A}$ is an O-linked substituent selected from the group consisting of $-OR^{2B}$, $-OC(O)R^{2B}$ and $-OC(O)N(R^{2B})(R^{2C})$, wherein R^{2B} and R^{2C} are independently selected from the group consisting of H, C_1-C_6 alkyl and C_2-C_6 alkenyl; and

the R^{7B} substituent is absent or is –OH.

14. The LDC composition of claim 13 wherein the quaternized tubulysin Drug Unit $-D^+$ has the structure of:



wherein subscript m is 1;

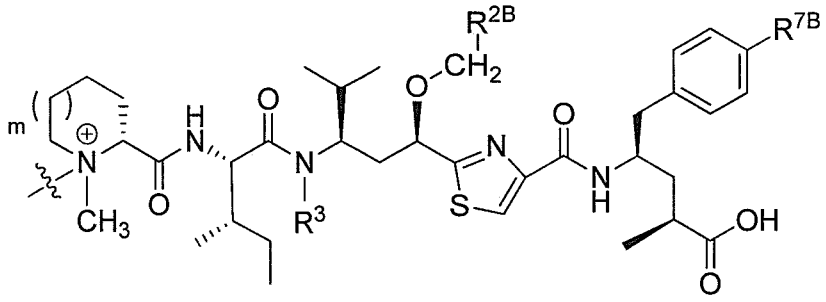
$-OC(O)R^{2B}$ is $-OC(O)CH_3$, $-OC(O)CH_2CH_3$, $-OC(O)CH(CH_3)_2$, $-OC(O)C(CH_3)_3$, or $-OC(O)CH=CH_2$;

R^3 is methyl, ethyl or propyl; and

the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen, or is –OH,

or

$-D^+$ has the structure of:



wherein

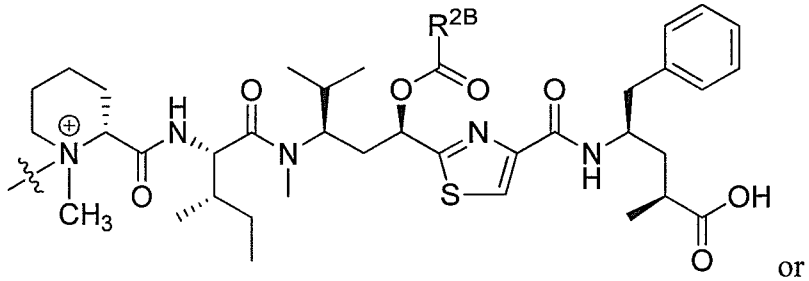
subscript m is 1;

$-OCH_2R^{2B}$ is $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$ or $-OCH_2OCH_3$; and

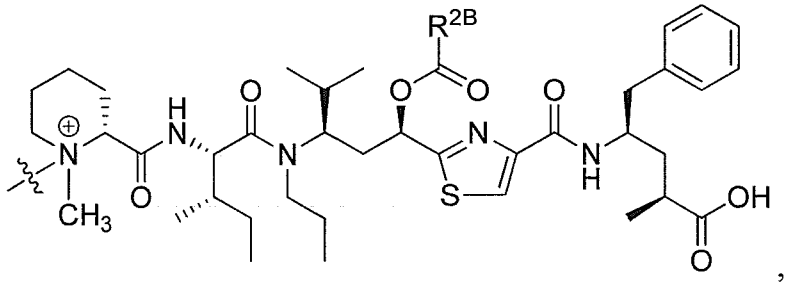
R^3 is methyl, ethyl or propyl; and

the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen, or is –OH.

15. The LDC composition of claim 14, wherein the quaternized tubulysin Drug Unit – D^+ has the structure of:



or



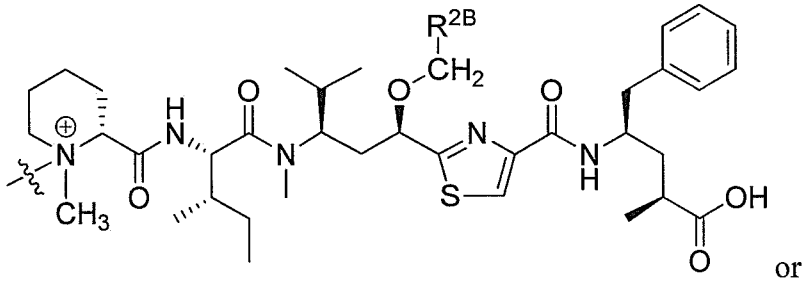
,

wherein

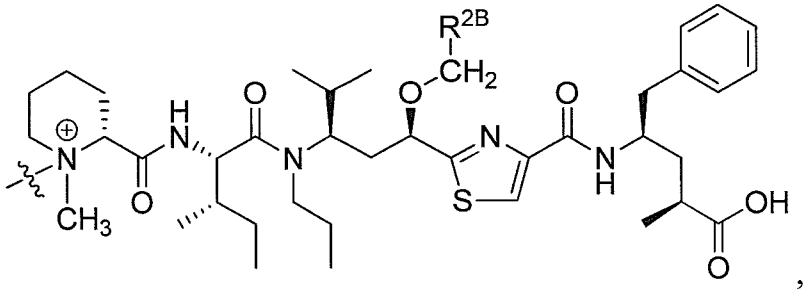
R^{2B} is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$,

or

$-D^+$ has the structure of:



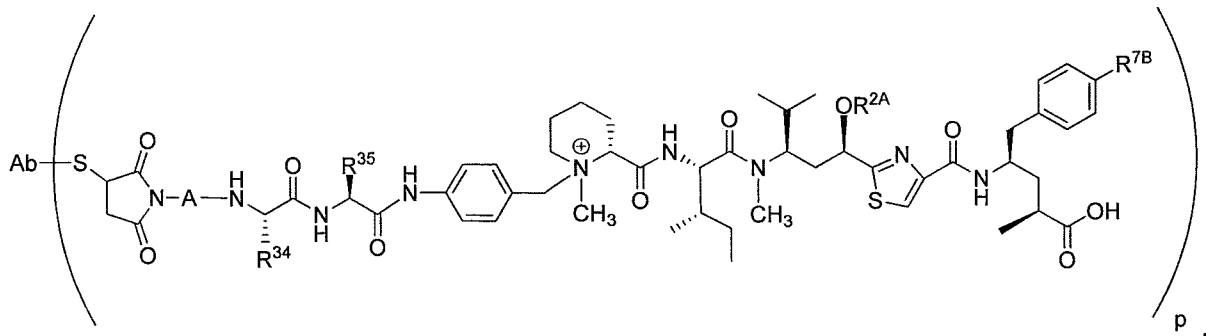
or



,

wherein R^{2B} is hydrogen, methyl or $-OCH_3$ so that $-OCH_2R^{2B}$ is a methyl, ethyl, or methoxymethyl ether O-linked substituent.

16. The LDC composition of claim 1 wherein the composition is represented by the structure of:



p ,

wherein

Ab is the antibody Ligand Unit;

S is a sulfur atom of the antibody Ligand Unit and the succinimide ring to which it is covalently attached is optionally in hydrolysed form;

R^{34} is isopropyl and R^{35} is $-CH_3$, isopropyl, $-CH_2CH_2CH_2NH(C=O)NH_2$ or $-CH_2CH_2CO_2H$;

the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen, or is $-OH$;

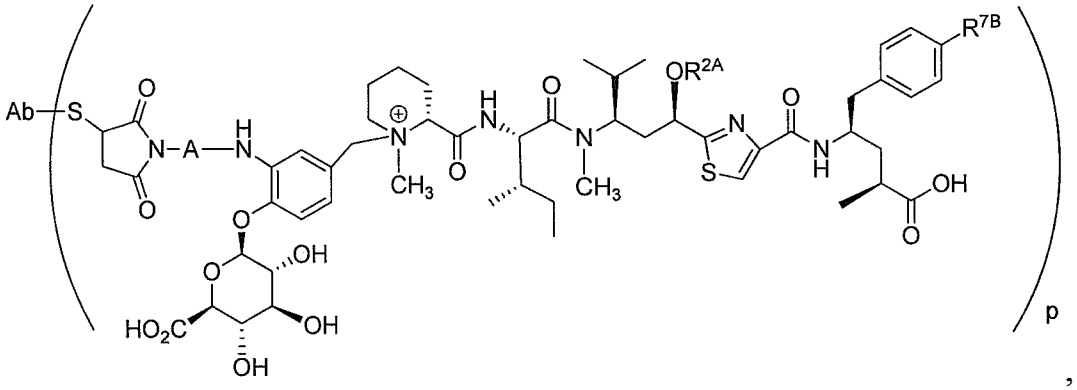
R^{2A} is lower alkyl, $-C(=O)R^{2B}$ or $-C(=O)NHR^{2B}$, wherein R^{2B} is lower alkyl;

subscript p is a number ranging from 1 to 8; and

A is $-CH_2(CH_2)_4(C=O)-$ or $-CH_2(CH_2)_4(C=O)NHCH_2CH_2(C=O)-$,

or

wherein the composition is represented by the structure of:



,

wherein

Ab is the antibody Ligand Unit and the succinimide ring to which it is covalently attached is optionally in hydrolysed form;

S is a sulfur atom of the antibody Ligand Unit;

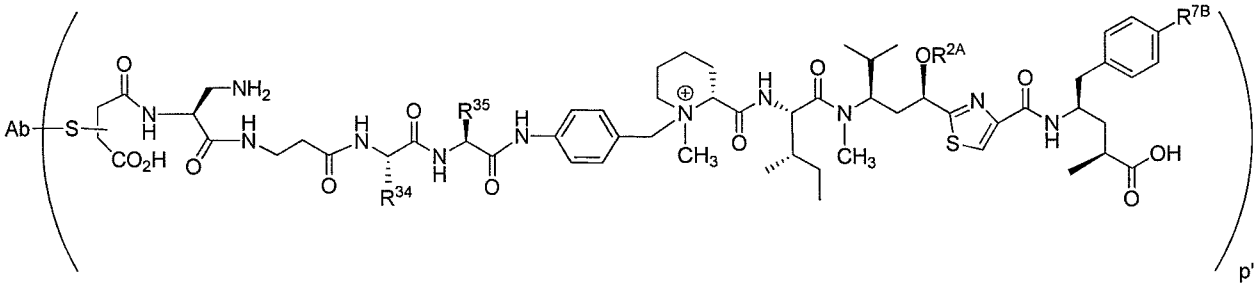
the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen, or is –OH;

R^{2A} is C_1-C_6 alkyl, $-CH_2OR^{2B}$ $-C(=O)R^{2B}$ or $-C(=O)NHR^{2B}$, wherein R^{2B} is C_1-C_6 alkyl or C_2-C_6 alkenyl;

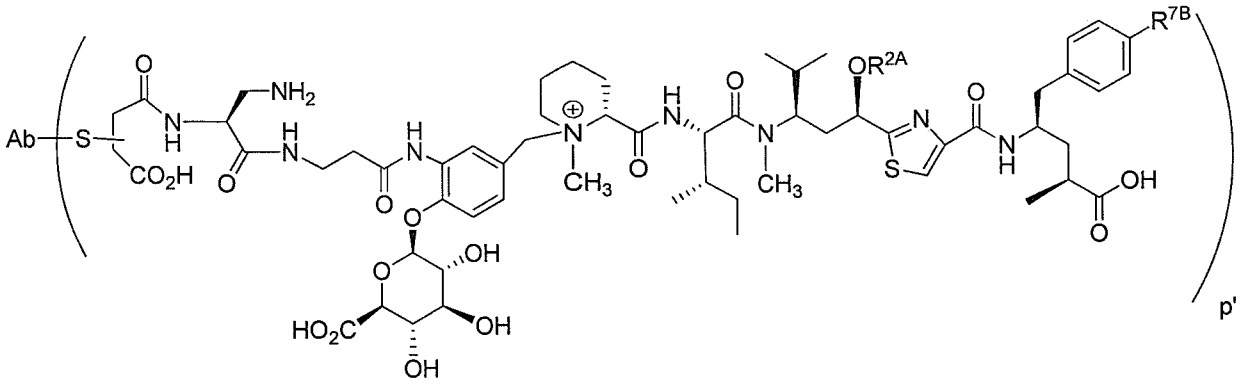
subscript p is a number ranging from 1 to 8; and

A is $-CH_2(CH_2)_4(C=O)-$ or $-CH_2(CH_2)_4(C=O)NHCH_2CH_2(C=O)-$.

17. The LDC composition of claim 1, wherein the Ligand Drug Conjugate compounds of the composition are represented by the structure of:



or



wherein

Ab is the antibody Ligand Unit;

S is a sulfur atom of the antibody Ligand Unit;

the Ab-S- moiety is bonded to the carbon α or β to the carboxylic acid;

subscript p' is an integer ranging from 1 to 8;

the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen, or is –OH;

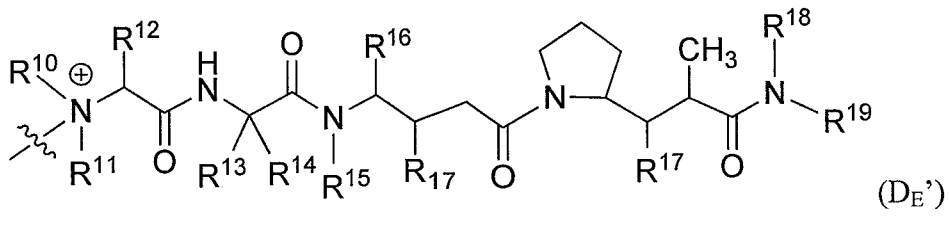
R^{34} is isopropyl and R^{35} is $–CH_3$, isopropyl, $–CH_2CH_2CH_2NH(C=O)NH_2$ or $–CH_2CH_2CO_2H$; and

R^{2A} is $–C(O)CH_3$, methyl, ethyl or propyl.

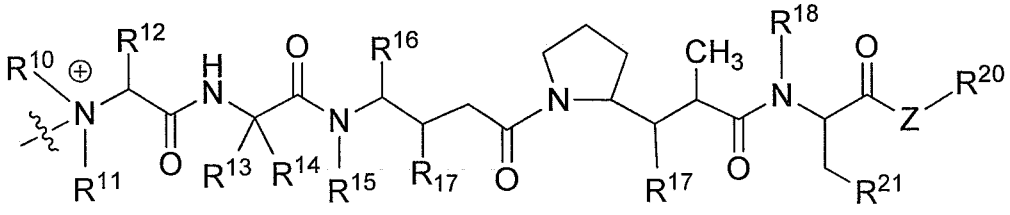
18. The LDC composition of claim 11, wherein the quaternized tertiary amine-containing tubulin disrupting agent–D^+ is a

quaternized dolastatin 10 or quaternized dolastatin 15, or

quaternized auristatin having the structure of D_E' or D_F':



(D_E')



(D_F')

wherein

R^{10} and R^{11} are independently C_1-C_8 alkyl;

R^{12} is hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, aryl, -X^1-aryl, -X^1-(C_3-C_8 cycloalkyl), C_3-C_8 heterocycle or -X^1-(C_3-C_8 heterocycle);

R^{13} is hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, aryl, -X^1-aryl, -X^1-(C_3-C_8 cycloalkyl), C_3-C_8 heterocycle or -X^1-(C_3-C_8 heterocycle);

R^{14} is hydrogen or methyl, or

R^{13} and R^{14} taken together with the carbon atom to which they are attached define a C_3-C_8 cycloalkyl;

R^{15} is hydrogen or C_1-C_8 alkyl;

R^{16} is hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, aryl, -X^1-aryl, -X^1-(C_3-C_8 cycloalkyl), C_3-C_8 heterocycle or -X^1-(C_3-C_8 heterocycle);

R^{17} independently are hydrogen, -OH, C_1-C_8 alkyl, C_3-C_8 cycloalkyl or O-(C_1-C_8 alkyl);

R^{18} independently are hydrogen or C_1-C_8 alkyl;

R^{19} is $-C(R^{19A})_2-C(R^{19A})_2$–aryl, $-C(R^{19A})_2-C(R^{19A})_2-$($C_3$-$C_8$ heterocycle) or $-C(R^{19A})_2-C(R^{19A})_2-$($C_3$-$C_8$ cycloalkyl); wherein R^{19A} is hydrogen, C_1-C_8 alkyl or –OH;

R^{20} is hydrogen, C_1-C_{20} alkyl, aryl, C_3-C_8 heterocycle, -$(R^{47}O)_m$-R^{48}, or -$(R^{47}O)_m$-$CH(R^{49})_2$;

R^{21} is aryl or C_3-C_8 heterocycle;

subscript m is an integer ranging from 1-1000;

R^{47} is C_2-C_8 alkyl;

R^{48} is hydrogen or C_1-C_8 alkyl;

R^{49} independently are -COOH, $-(CH_2)_n$-$N(R^{50})_2$, $-(CH_2)_n$-SO_3H, or $-(CH_2)_n$-SO_3-C_1-C_8 alkyl;

R^{50} independently are C_1-C_8 alkyl or $-(CH_2)_n$-COOH;

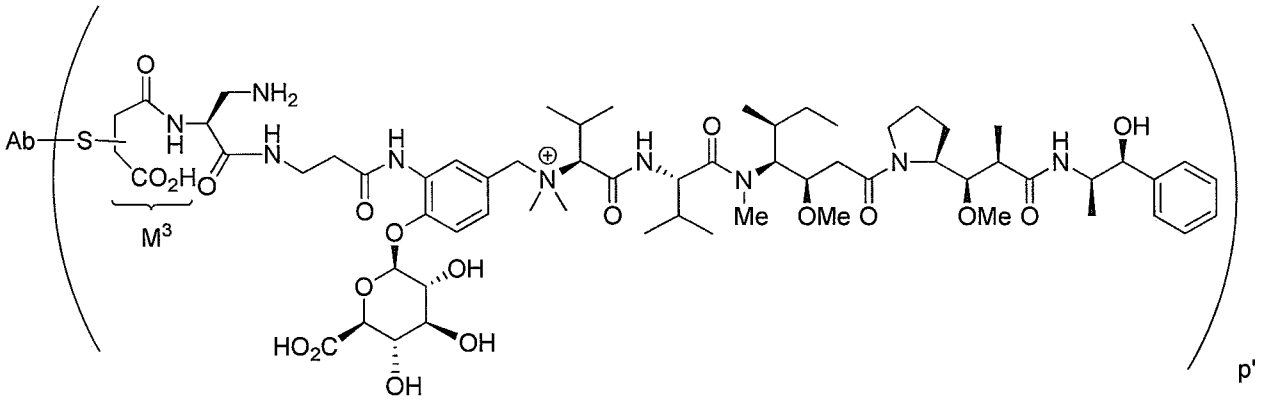
Z is O, S, NH, or NR^{46}, wherein R^{46} is C_1-C_8 alkyl;

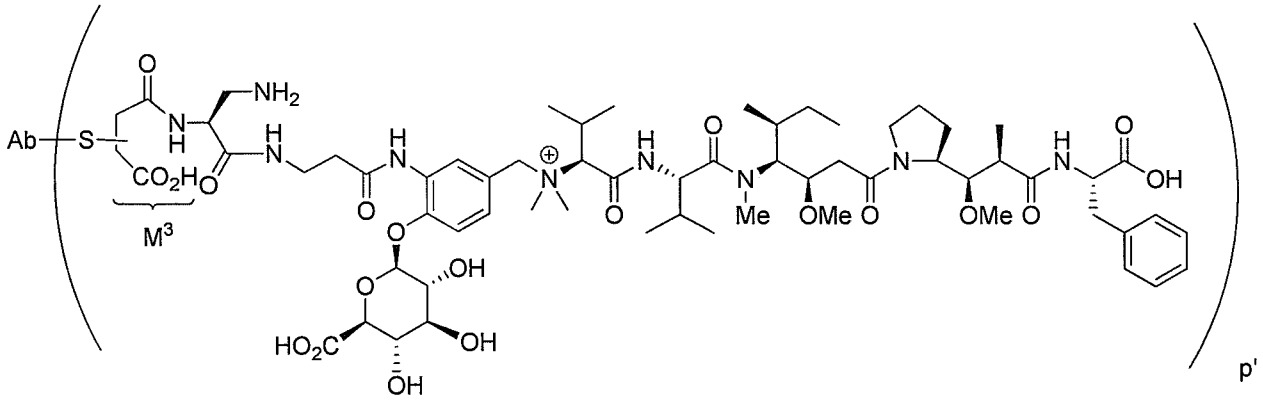
X^1 is C_1-C_{10} alkylene;

subscript n is an integer ranging from 0 to 6; and

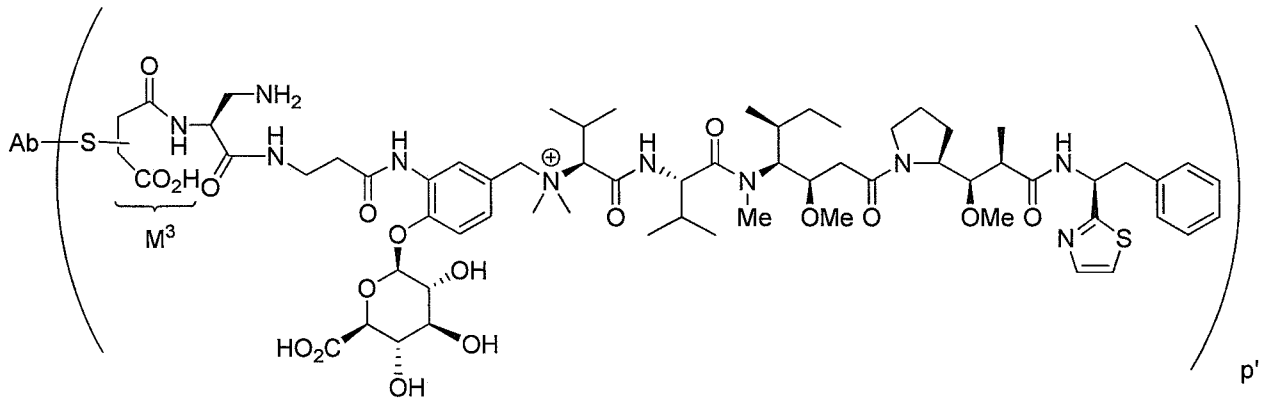
the wavy line indicates covalent bonding of D^+ to the remainder of the composition structure.

19. The LDC composition of claim 18 wherein the Ligand Drug Conjugate compounds of the composition are represented by the structure of:





or



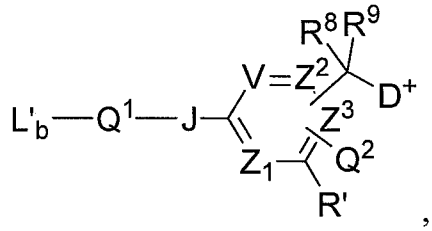
wherein Ab is the antibody Ligand Unit;

S is a sulfur atom of the antibody Ligand Unit;

the Ab-S- moiety is bonded to the carbon α or β to the M^3 carboxylic acid; and

subscript p' is an integer ranging from 1 to 8.

20. A Drug-Linker compound, wherein the Drug Linker compound has the structure of Formula I:



(Formula I)

wherein

L'_b is a ligand covalent binding moiety precursor;

Q^1 is A_a-W_w, wherein A is an optional Stretcher unit so that subscript a is 0 when A is absent or 1 when A is present and is optionally comprised of two, three or four subunits;

Q^2 is $W'_{w'}$-E-, wherein Q^2, when present, is bonded to V, Z^1, Z^2 or Z^3;

W_w and $W'_{w'}$ are Cleavable units, wherein

W_w of Q^1 is capable of selective cleavage by an intracellular or regulatory protease in comparison to serum proteases, or by glutathione through disulfide exchange, or is more reactive to hydrolysis under more acidic conditions present in lysosomes in comparison to physiological pH of serum,

W'-E of Q^2 provides a glycosidic bond cleavable by a glycosidase located intracellularly, and

subscript w is 0 or 1 so that W is absent when subscript w is 0 or W is present when subscript w is 1, and subscript subscript w' is 0 or 1, wherein W'-E is absent when subscript w' is 0 or W'-E is present when subscript w' is 1, and wherein w + w' is 1 so that one and only one of W, W' is present;

V, Z^1, Z^2 and Z^3 are $=C(R^{24})$-, wherein R^{24} is hydrogen or alkyl, alkenyl or alkynyl, optionally substituted, or halogen, $-NO_2$, -CN or other electron withdrawing group, an electron donating group, $-Q^2$, or $-C(R^8)(R^9)-D^+$, wherein at least one of V, Z^1, Z^2 and Z^3 is $=C(R^{24})$- when subscript w is 1, and at least two of V, Z^1, Z^2 and Z^3 are $=C(R^{24})$- when subscript w' is 1,

provided that when subscript w is 1, Q^2 is absent and one and only one R^{24} is $-C(R^8)(R^9)-D^+$ so that $-C(R^8)(R^9)-D^+$ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})$- and the Q^1-J- and $-C(R^8)(R^9)-D^+$ substituents are *ortho* or *para* to each other,

provided that when subscript w' is 1, one and only one R^{24} is $-C(R^8)(R^9)-D^+$ so that $-C(R^8)(R^9)-D^+$ is bonded to one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})-$ and one and only one other R^{24} is Q^2 so that Q^2 is bonded to another one of V, Z^1, Z^2, Z^3 when that variable group is $=C(R^{24})-$, and the Q^2 and $-C(R^8)(R^9)-D^+$ substituents are *ortho* or *para* to each other;

one of R^8 and R^9 is hydrogen and the other is hydrogen, alkyl, alkenyl or alkynyl, optionally substituted, or aryl or heteroaryl, optionally substituted;

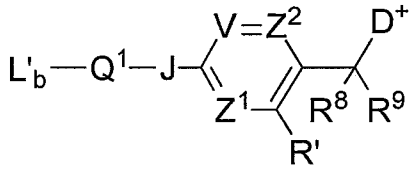
R' is hydrogen or is halogen, $-NO_2$, -CN or other electron withdrawing group, or is an electron donating group;

E and J independently are –O-, -S- or $-N(R^{33})-$, wherein R^{33} is hydrogen or optionally substituted alkyl;

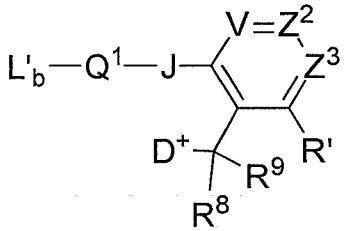
D^+ represents a structure of a quaternized tertiary amine-containing drug, wherein the tertiary amine-containing drug is quaternized at the nitrogen atom of its tertiary amine and is cytotoxic or cytostatic towards mammalian cells,

wherein said protease cleavage, disulfide exchange, acid hydrolysis or glycosidase cleavage results in expulsion of free tertiary amine-containing drug (D) from the Drug-Linker Compound, or a Ligand Drug Conjugate compound or N-acetyl-cysteine Conjugate derived therefrom.

21. The Drug Linker compound of claim 20, wherein the Drug Linker compound has the structure of Formula IIA or Formula IIB:

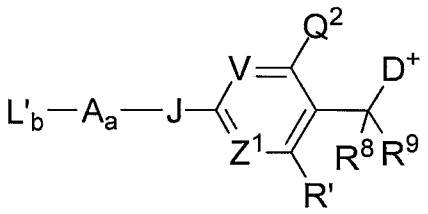


(Formula IIA)

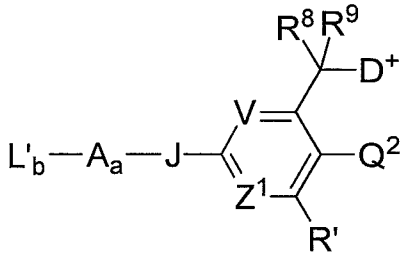


(Formula IIB), or

wherein the Drug Linker compound has the structure of Formula IIIA or Formula IIIB:

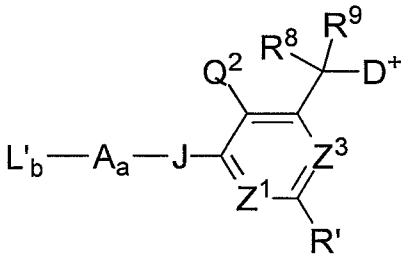


(Formula IIIA)

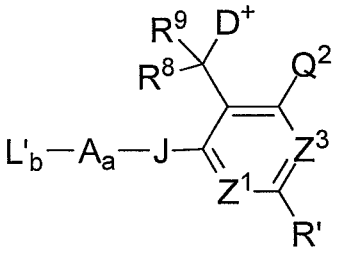


(Formula IIIB), or

wherein the Drug Linker compound has the structure of Formula IIIC or Formula IIID:

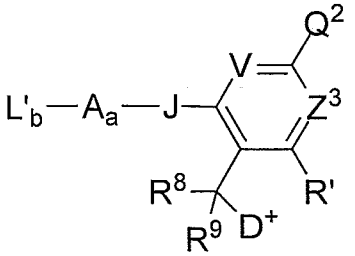


(Formula IIIC)

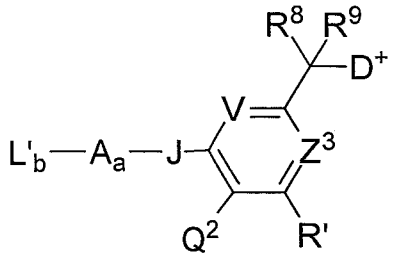


(Formula IIID), or

wherein the Drug Linker compound has the structure of Formula IIIE or Formula IIIF:



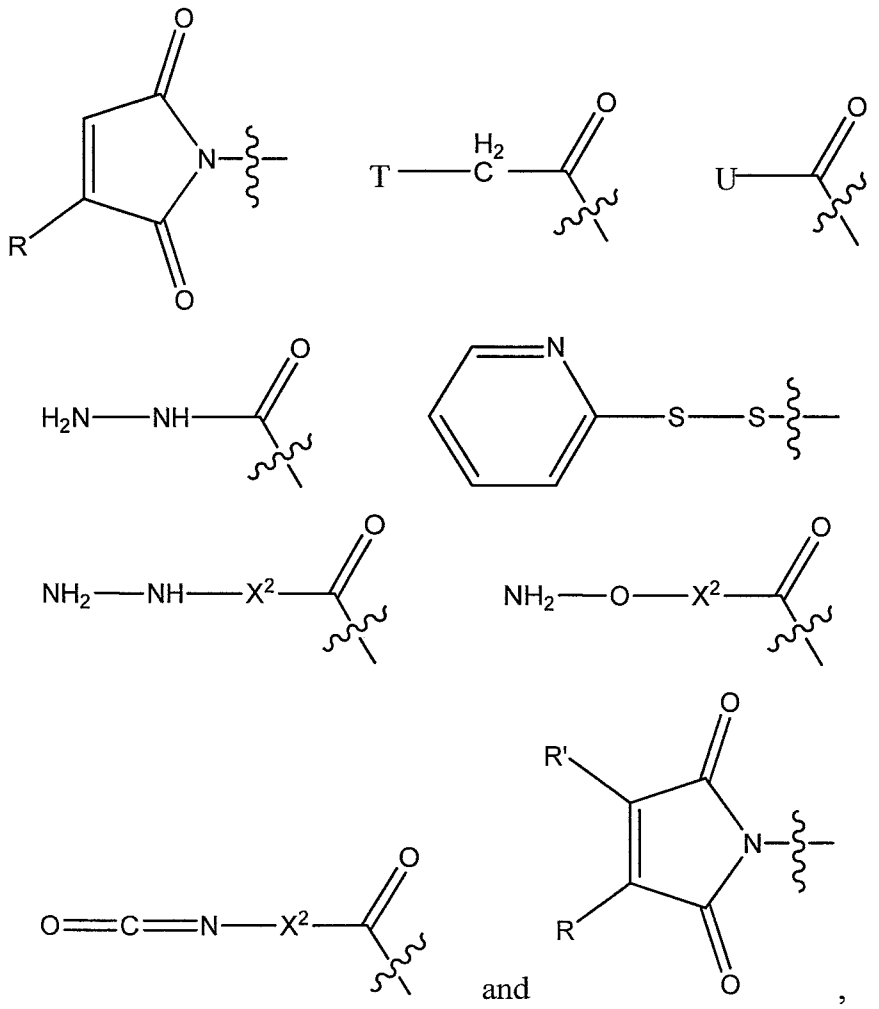
(Formula IIIE)



(Formula IIIF),

and

wherein L'$_b$- has a structure selected from the group consisting of:



and

,

wherein

the wavy line indicates covalent attachment to A if subscript a is 1 or to J when subscript a is 0;

R is hydrogen or C_1-C_6 optionally substituted alkyl;

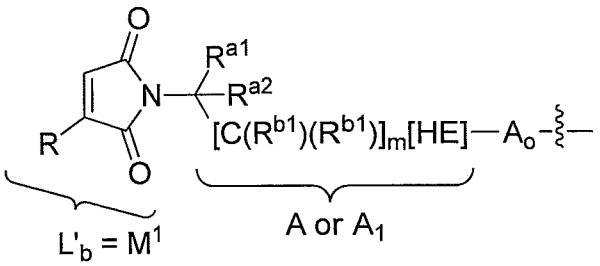
R' is hydrogen or halogen or R and R' are independently selected halogen;

T is –Cl, -Br, -I, -O-mesyl or –O-tosyl or other sulfonate leaving group;

U is –F, –Cl, -Br, -I, -O-N-succinimide, -O-(4-nitrophenyl), -O-pentafluorophenyl, -O-tetrafluorophenyl or –O-C(=O)-OR^{57}; wherein R^{57} is C_1-C_6 alkyl or aryl; and

X^2 is C_{1-10} alkylene, C_3-C_8-carbocycle,-O-(C_1-C_6 alkyl), -arylene-, C_1-C_{10} alkylene-arylene, -arylene-C_1-C_{10} alkylene, -C_1-C_{10} alkylene-(C_3-C_6-carbocycle)-, -(C_3-C_8 carbocycle)-C_1-C_{10} alkylene-, C_3-C_8-heterocycle, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -C_3-C_8-heterocyclo)-C_1-C_{10} alkylene, -$(CH_2CH_2O)_u$, or –$CH_2CH_2O)_u$-CH_2-, wherein subscript u is an integer ranging from 1 to 10.

22. The Drug-Linker compound of claim 20, wherein subscript a is 1 so that A in Q^1 is bonded to L'$_b$ of Formula I and L_b'-A is of general formula M^1-A_1-A_O-, wherein M^1-A^1-A_O- has the structure of Formula VIII:



(Formula VIII)

wherein

A_O is an optional subunit of A, wherein –$[C(R^{b1})(R^{b1})]_m$-[HE]- is A when A_O is absent and is A_1 when A_O is present so that A becomes -A_1-A_O-;

R and R^{a2} independently are hydrogen or methyl;

R^{a1} is hydrogen, methyl, ethyl or a Basic Unit (BU);

HE is an optional Hydrolysis Enhancer (HE) unit;

subscript m is an integer ranging from 0 to 6;

each R^{b1} independently is hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted aryl or optionally substituted heteroaryl, or two R^{b1} together with the carbon(s) to which they are attached define a C_3-C_6 cycloalkyl or one R^{b1} and HE together with the carbon atom to which they are attached define a 5- or 6-membered cycloalkyl or a 5- or 6-membered heterocycloalkyl and the other R^{b1} is hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted aryl or optionally substituted heteroaryl;

BU has the structure of –$[C(R^1)(R^1)]$-$[C(R^2)(R^2)]_n$-$N(R^{22})(R^{23})$, or an acid addition salt thereof,

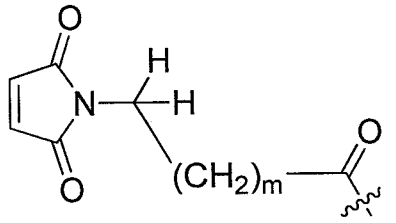
wherein subscript n is 0, 1, 2 or 3;

each R^1 independently is hydrogen or lower alkyl or two R^1 together with the carbon to which they are attached define a C_3-C_6 cycloalkyl, and each R^2 independently is hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted aryl or optionally substituted heteroaryl, or two R^2 together with the carbon(s) to which they are attached and any intervening carbons define a C_3-C_6 cycloalkyl, or one R^1 and one R^2 together with the carbons to which they are attached and any intervening carbons define a 5- or 6-membered cycloalkyl and the remaining R^1 and R^2 are as defined;

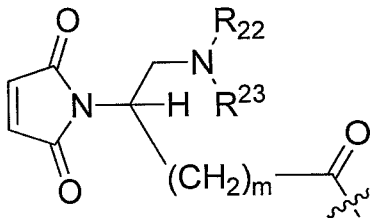
R^{22} and R^{23} independently are hydrogen or optionally substituted C_1-C_6 alkyl or together with the nitrogen to which they are attached define a 5- or 6-membered heterocycloalkyl; and

the wavy line indicates covalent bonding of A (or A_O) to the remainder of the Formula VIII structure.

23. The Drug-Linker compound of claim 22, wherein M^1-A^1-A_O- of Formula VIII has the structure of



,



or an acid addition salt thereof,

wherein

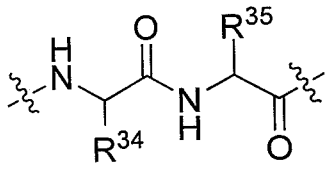
subscript m is 0 or 4; and

R^{22} and R^{23} are each hydrogen or one of R^{22}, R^{23} is hydrogen and the other is –C(O)Ot-Bu.

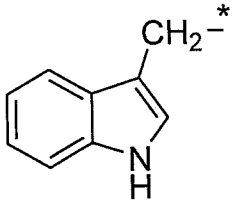
24. The Drug-Linker compound of claim 21, wherein W of Q^1 is comprised or consists of a peptide moiety having a peptide bond to J that is selectively cleavable by an

intracellular or regulatory protease in comparison to serum proteases wherein action of the regulatory protease on W causes release of free tertiary amine-containing drug (D) from the Drug-Linker Compound or a Ligand Drug Conjugate compound or N-acetyl-cysteine Conjugate derived therefrom, or wherein W' of Q^2 is a glycoside-bonded carbohydrate, wherein the glycoside bond W'-E of Q^2 provides for a cleavage site for a glycosidase located intracellularly wherein action of the glycosidase on W'-E causes release of tertiary amine-containing drug (D) from the Drug-Linker Compound or a Ligand Drug Conjugate compound or N-acetyl-cysteine Conjugate derived therefrom.

25. The Drug-Linker compound of claim 24, wherein the peptide moiety of W is comprised or consists of a dipeptide moiety having the structure of Formula VI:



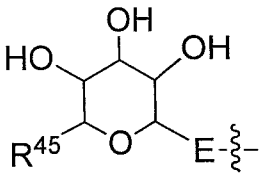
(Formula VI),

wherein R^{34} is benzyl, methyl, isopropyl, isobutyl, sec-butyl, $-CH(OH)CH_3$ or has the structure of 

, wherein the asterisk indicates covalent bonding to the dipeptide backbone; and R^{35} is methyl, $-(CH_2)_4-NH_2$, $-(CH_2)_3NH(C=O)NH_2$, $-(CH_2)_3NH(C=NH)NH_2$, or $-(CH_2)_2CO_2H$,

wherein the wavy line to the dipeptide's C-terminus indicates covalent bonding to J of the arylene moiety of Formula IIA or IIB and the wavy line to the dipeptide's N-terminus indicates covalent bonding to the remainder of W, if any such remainder is present, or to A, or a subunit thereof, when subscript a is 1 or to L_b when subscript a is 0, and wherein the dipeptide's bond to J is cleavable by an intracellular or regulatory protease, and

wherein W' in Q^2 is a carbohydrate moiety that is glycoside-bonded to E, wherein the glycosidic bond is cleavable by an intracellular glycosidase, and wherein W'-E has the structure of Formula VII:

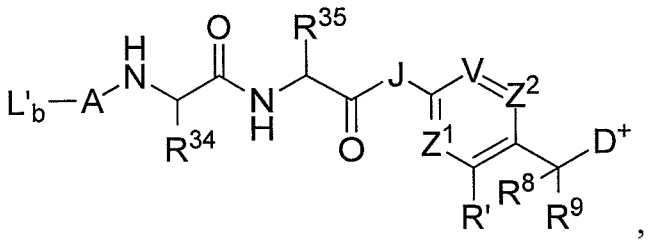


(Formula VII),

wherein the wavy line represents E bonded to one of V, Z^1, Z^2, or Z^3 when that variable group is $=C(R^{24})$, so that R^{24} represents a covalent bond to E, wherein E is –O-, -S- , or $–N(R^{33})$-, wherein R^{33} is hydrogen or methyl; and

wherein R^{45} is $–CH_2OH$ or $–CO_2H$.

26. The Drug-Linker compound of claim 25, wherein the Drug Linker compound has the structure of Formula IX:



(Formula IX)

wherein

R' is hydrogen or an electron donating group;

R^8 is hydrogen;

R^9 is hydrogen, optionally substituted C_1-C_6 alkyl, or optionally substituted phenyl;

R^{34} is methyl, isopropyl or $-CH(OH)CH_3$;

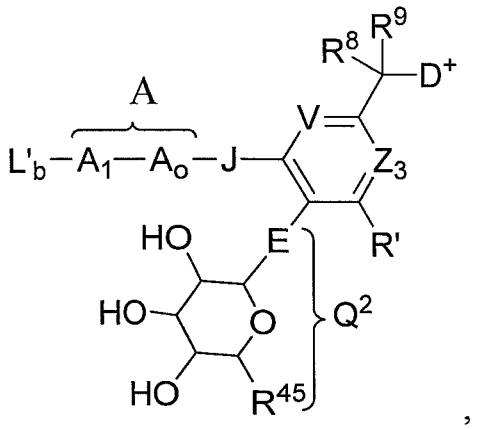
R^{35} is methyl, $-(CH_2)_3NH(C=O)NH_2$ or $-(CH_2)_2CO_2H$;

J is $–N(R^{33})$-, wherein R^{33} is hydrogen or methyl; and

V, Z^2 and Z^1 are each =CH-,

or

the Drug Linker compound has the structure of Formula XI:



(Formula XI)

wherein

A_1 and A_O are independently selected subunits of A, wherein A_O is an optional subunit of A so that A_1 becomes A when A_O is absent and A is $-A_1-A_O-$ when A_O is present;

E is –O- or –NH-;

J is $-N(R^{33})-$, wherein R^{33} is hydrogen or methyl;

V, Z^2 and Z^3 are each =CH-;

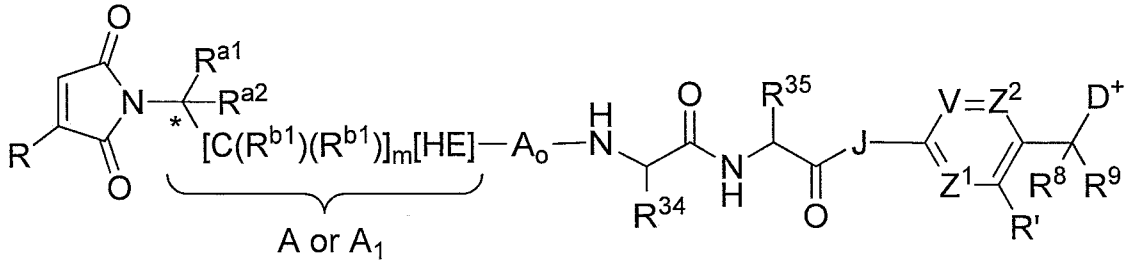
R' is hydrogen or an electron withdrawing group;

R^8 is hydrogen;

R^9 is hydrogen, optionally substituted C_1-C_6 alkyl or optionally substituted phenyl; and

R^{45} is $-CO_2H$ or $-CH_2OH$.

27. The Drug-Linker compound of claim 26, wherein the Drug Linker compound has the structure of Formula X:



(Formula X)

wherein

the asterisk (*) designates chirality or absence thereof at the indicated carbon atom;

A_O is an optional subunit of A, wherein $-[C(R^{b1})(R^{b1})]_m$-[HE]- is A when A_O is absent and is A_1 when A_O is present so that A becomes A_1-A_O;

R is –H;

R^{a1} is –H or a Basic Unit (BU), wherein BU has the structure of $-CH_2$-$N(R^{22})(R^{23})$, or an acid addition salt thereof, wherein R^{22} and R^{23} independently are hydrogen, methyl or ethyl or both together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl;

R^{a2} is hydrogen;

subscript m is an integer ranging from 0 to 4;

each R^{b1} independently is hydrogen or optionally substituted C_1-C_6 alkyl;

HE is absent or is –C(=O)-;

R^{34} is methyl, isopropyl or $-CH(OH)CH_3$;

R^{35} is $-(CH_2)_3NH(C=O)NH_2$, or $-(CH_2)_2CO_2H$;

J is –NH-;

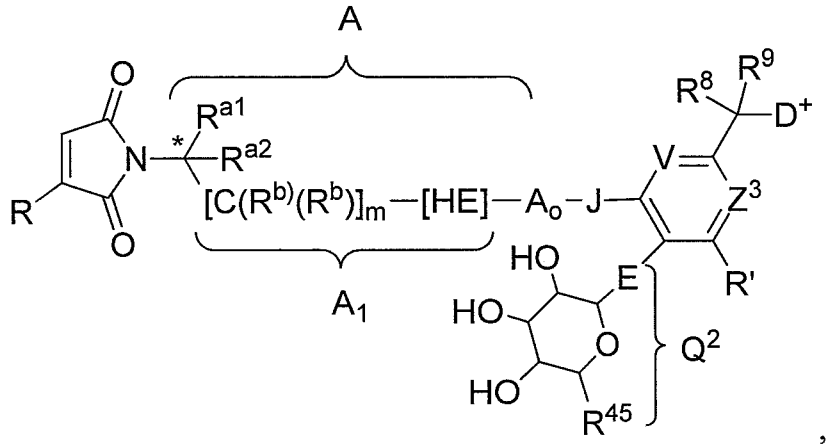
R' is hydrogen or an electron donating group;

R^8 is hydrogen; and

R^9 is hydrogen or methyl,

or

wherein the compound has the structure of Formula XII:



(Formula XII)

wherein

the asterisk (*) designates chirality or absence thereof at the indicated carbon atom;

A_1 and A_O are independently selected subunits of A, wherein A_O is an optional subunit of A, wherein $-[C(R^{b1})(R^{b1})]_m$-[HE]- is A when A_o is absent and is A_1 when A_O is

present so that A becomes A_1-A_O; wherein A_O when present corresponds in structure to an amine-containing acid bonded to J through the C-terminal carbonyl of the amine-containing acid;

R is hydrogen;

R' is hydrogen or an electron withdrawing group;

R^{a1} is hydrogen or a basic unit (BU) wherein BU has the structure of $-CH_2-N(R^{22})(R^{23})$, or an acid addition salt thereof, wherein R^{22} and R^{23} independently are hydrogen, methyl or ethyl or both together with the nitrogen atom to which they are attached define a 5- or 6-membered heterocycloalkyl;

R^{a2} is hydrogen;

subscript m is an integer ranging from 1 to 5;

each R^{b1} independently is hydrogen or optionally substituted C_1-C_6 alkyl;

HE is absent or is –C(=O)-;

R^{45} is $-CO_2H$ or $-CH_2OH$;

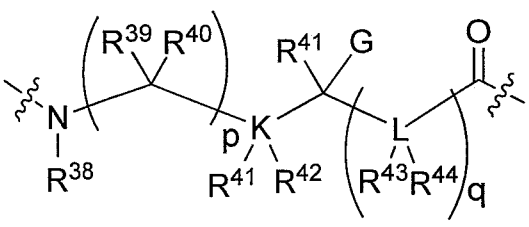
E is –O-;

J is –NH-;

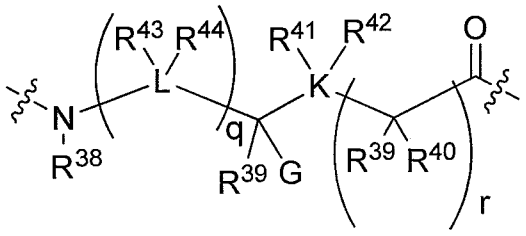
R^8 is hydrogen; and

R^9 is hydrogen or methyl.

28. The Drug-Linker compound of claim 27, wherein A_O, when present, has the structure of Formula XIII or Formula XIV:



(Formula XIII)



(Formula XIV)

wherein the wavy line to the carbonyl moiety of either structure represents the point of attachment of A_O to W and wherein the wavy line to the amino moiety of either structure represents the point of attachment of A_O to A_1,

wherein K and L independently are C, N, O or S, provided that when K or L is O or S, R^{41} and R^{42} to K or R^{43} and R^{44} to L are absent, and when K or L is N, one of R^{41}, R^{42} to K

or one of R^{43}, R^{44} to L is absent, and provided that no two adjacent L are independently selected as N, O, or S;

wherein subscript q is an integer ranging from 0 to 12, and subscript r is an integer ranging from 1 to 12;

wherein G is hydrogen, optionally substituted C_1-C_6 alkyl, -OH, -OR^G, -CO_2H, or -CO_2R^G, wherein R^G is C_1-C_6 alkyl, aryl or heteroaryl, optionally substituted, or R^{PR}, wherein R^{PR} is a suitable protecting group, -NH_2, or -$N(R^G)(R^{PG})$, wherein R^G independently selected is as previously defined or both R^G together with the nitrogen to which they are attached define a 5- or 6-membered heterocycloalkyl or both R^{PR} together form a suitable protecting group;

wherein R^{38} is hydrogen or optionally substituted C_1-C_6 alkyl;

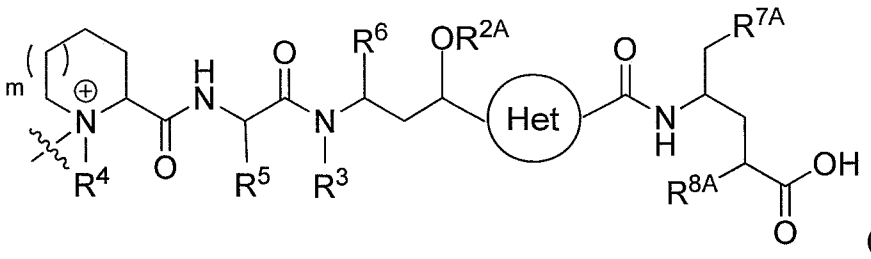
R^{39}-R^{44} independently are hydrogen, optionally substituted C_1-C_6 alkyl, or optionally substituted heteroaryl, or both R^{39}, R^{40} together with the carbon to which they are attached define a C_3-C_6 cycloalkyl, or R^{41}, R^{42} together with K to which they are attached when K is C, or R^{43}, R^{44} together with L to which they are attached when L is C, define a C_3-C_6 cycloalkyl, or R^{40} and R^{41}, or R^{40} and R^{43}, or R^{41} and R^{43} together with the carbon or heteroatom to which they are attached and atoms intervening between those carbon and/or heteroatoms define a 5- or 6-membered cycloalkyl or heterocycloalkyl, or

wherein A_O has a structure corresponding to alpha-amino, beta-amino or another amine-containing acid; and

wherein the indicated starred (*) carbon is predominantly in the same absolute configuration as the alpha carbon of an L-amino acid when that indicated carbon has chirality.

29. The Drug-Linker compound of claim 20, wherein $-D^+$ is a quaternized tertiary amine-containing tubulin disrupting agent.

30. The Drug-Linker compound of claim 29, wherein the quaternized tertiary amine containing tubulin disrupting agent $-D^+$ is a quaternized tubulysin Drug Unit having the structure of Formula D_{G-1}'



(Formula D_{G-1}')

wherein the circle represents a 5-membered nitrogen-heteroaryl and wherein the indicated required substituents to that heteroaryl are in a 1,3-relationship with each other with optional substitution at the remaining positions;

R^{2A} is hydrogen or optionally substituted alkyl or R^{2A} along with the oxygen atom to which it is attached defines an O-linked substituent other than -OH;

R^3 is hydrogen or optionally substituted alkyl;

R^4, R^{4B}, R^5 and R^6 are optionally substituted alkyl, independently selected;

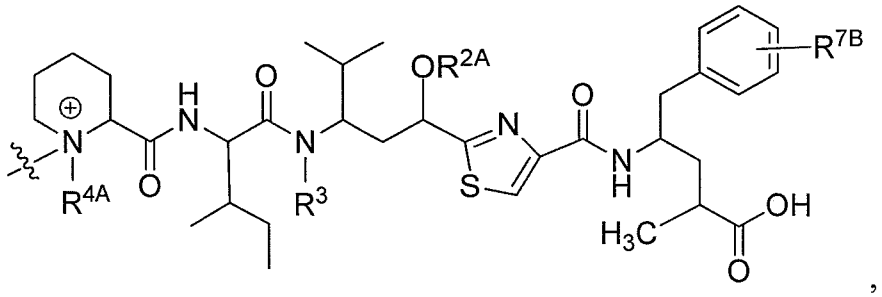
R^{7A} is optionally substituted aryl or optionally substituted heteroaryl;

R^{8A} is hydrogen or optionally substituted alkyl;

and subscript m is 0 or 1; and

wherein the wavy line indicates covalent bonding of D^+ to the remainder of the Drug-Linker compound structure.

31. The Drug-Linker compound of claim 29, wherein the quaternized tertiary amine containing tubulin disrupting agent $-D^+$ is a quaternized tubulysin Drug Unit having the structure of:



,

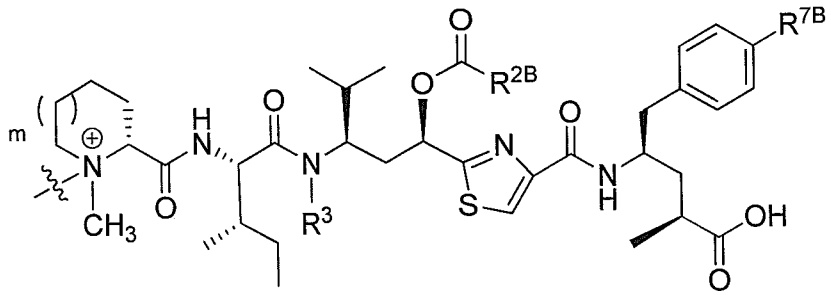
wherein R^{4A} is methyl;

R^3 is H, methyl, ethyl, propyl, $-CH_2-OC(O)R^{3A}$, $-CH_2CH(R^{3B})C(O)R^{3A}$ or $-CH(R^{3B})C(O)NHR^{3A}$, wherein R^{3A} is C_1-C_6 alkyl and R^{3B} is H or C_1-C_6 alkyl, independently selected from R^{3A}; and

$-OR^{2A}$ is an O-linked substituent selected from the group consisting of $-OR^{2B}$, $-OC(O)R^{2B}$ and $-OC(O)N(R^{2B})(R^{2C})$, wherein R^{2B} and R^{2C} are independently selected from the group consisting of H, C_1-C_6 alkyl and C_2-C_6 alkenyl; and

the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen, or is –OH.

32. The Drug-Linker compound of claim 31, wherein the quaternized tubulysin Drug Unit $-D^+$ has the structure of:



wherein

subscript m is 1;

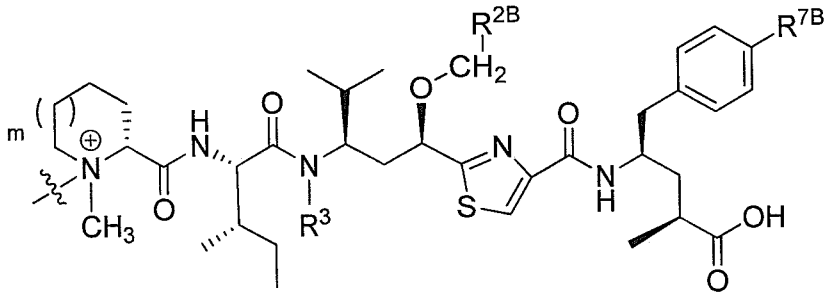
$-OC(O)R^{2B}$ is $-OC(O)CH_3$, $-OC(O)CH_2CH_3$, $-OC(O)CH(CH_3)_2$, $-OC(O)C(CH_3)_3$, or $-OC(O)CH=CH_2$;

R^3 is methyl, ethyl or propyl; and

the R^{7B} substituent is absent or is –OH,

or

wherein the quaternized tubulysin Drug Unit $-D^+$ has the structure of:



wherein

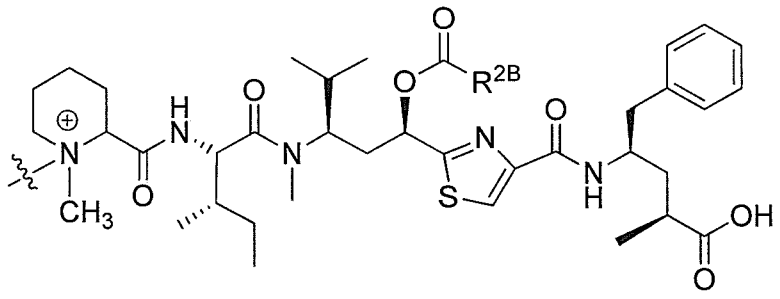
subscript m is 1;

$-OCH_2R^{2B}$ is $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$ or $-OCH_2OCH_3$;

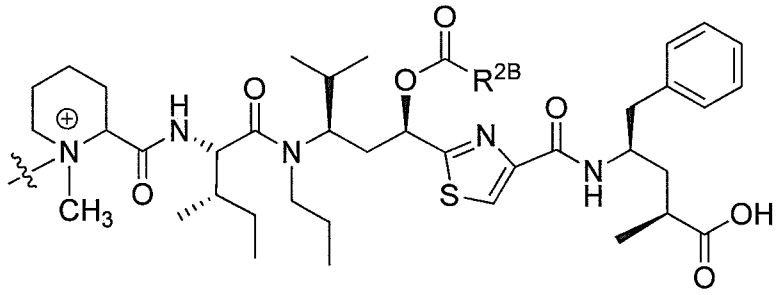
R^3 is methyl, ethyl or propyl; and

the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen, or is –OH.

33. The Drug-Linker compound of claim 31, wherein the quaternized tubulysin Drug Unit $-D^+$ has the structure of:



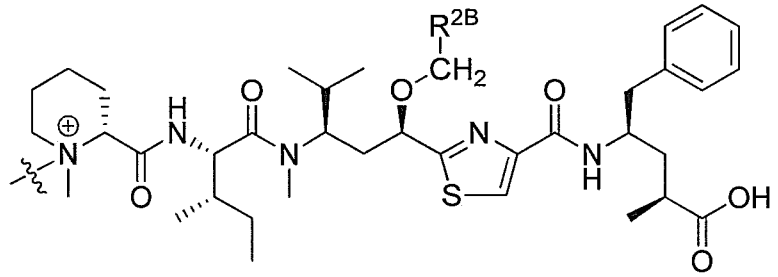
, or



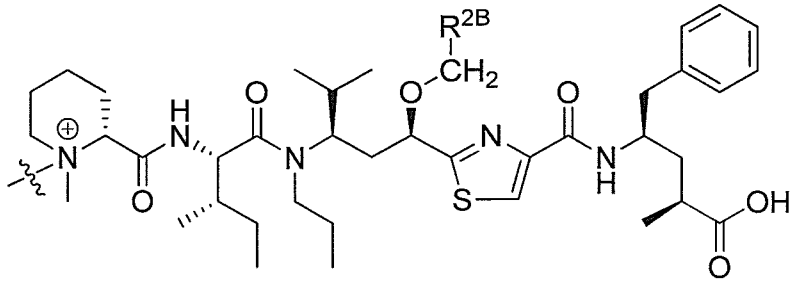
wherein

R^{2B} is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, or

$-D^+$ has the structure of:



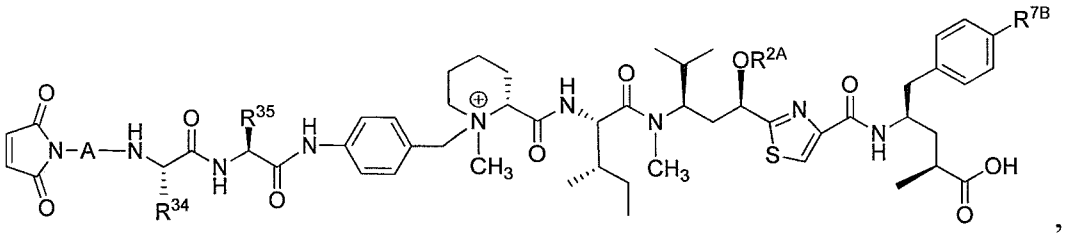
or



,

wherein R^{2B} is hydrogen, methyl or $-OCH_3$ so that $-OCH_2R^{2B}$ is a methyl, ethyl or methoxymethyl ether substituent.

34. The Drug-Linker compound of claim 20, wherein the Drug Linker compound has the structure of:



,

wherein

R^{34} is isopropyl and R^{35} is $-CH_3$, isopropyl, $-CH_2CH_2CH_2NH(C=O)NH_2$ or $-CH_2CH_2CO_2H$;

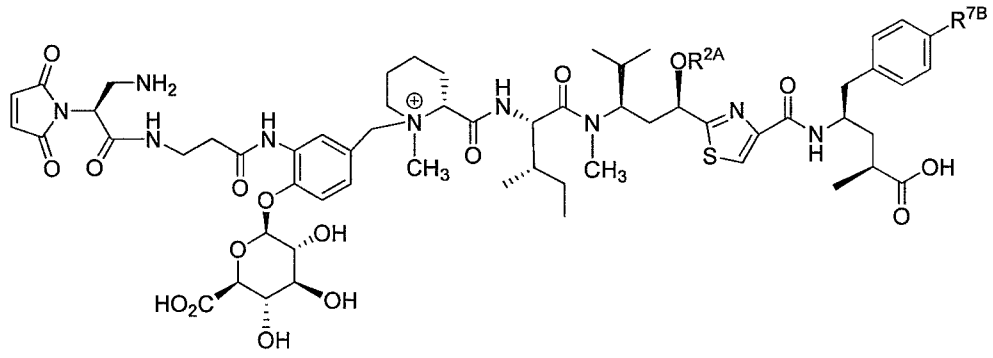
the R^{7B} substituent is absent, so that R^{7B} is replaced by hydrogen or is –OH; and

R^{2A} is lower alkyl, $-C(=O)R^{2B}$ or $-C(=O)NHR^{2B}$, wherein R^{2B} is lower alkyl; and

A is $-CH_2(CH_2)_4(C=O)-$ or $-CH_2(CH_2)_4(C=O)NHCH_2CH_2(C=O)-$,

or

wherein the compound has the structure of:



wherein

the R^{7B} substituent is absent or is –OH; and

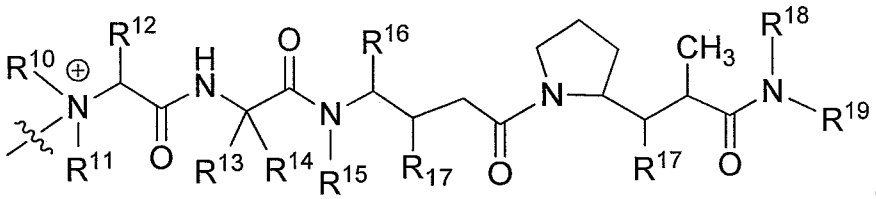
R^{2A} is C_1-C_6 alkyl, C_2-C_6 alkenyl, $-CH_2OR^{2B}$, $-C(=O)R^{2B}$ or $-C(=O)NHR^{2B}$, wherein R^{2B} is hydrogen, or C_1-C_6 alkyl.

35. The Drug Linker compound of claim 34, wherein R^{2A} is $-C(O)CH_3$, methyl, ethyl or propyl.

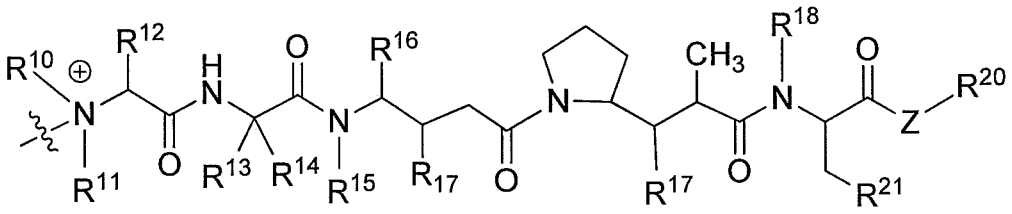
36. The Drug-Linker compound of claim 29, wherein the quaternized amine-containing tubulin disrupting agent $-D^+$ is a

quaternized dolastatin 10 or dolastatin 15, or

quaternized auristatin having the structure of D_E' or D_F':



(D_E')



(D_F')

wherein

R^{10} and R^{11} are independently C_1-C_8 alkyl;

R^{12} is hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, aryl, -X^1-aryl, -X^1-(C_3-C_8 cycloalkyl), C_3-C_8 heterocycle or -X^1-(C_3-C_8 heterocycle);

R^{13} is hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, aryl, -X^1-aryl, -X^1-(C_3-C_8 cycloalkyl), C_3-C_8 heterocycle or -X^1-(C_3-C_8 heterocycle);

R^{14} is hydrogen or methyl;

or R^{13} and R^{14} taken together with the carbon to which they are attached define a C_3-C_8 cycloalkyl;

R^{15} is hydrogen or C_1-C_8 alkyl;

R^{16} is hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, aryl, -X^1-aryl, -X^1-(C_3-C_8 cycloalkyl), C_3-C_8 heterocycle or -X^1-(C_3-C_8 heterocycle);

R^{17} independently are hydrogen, -OH, C_1-C_8 alkyl, C_3-C_8 cycloalkyl or O-(C_1-C_8 alkyl);

R^{18} is hydrogen or C_1-C_8 alkyl;

R^{19} is $-C(R^{19A})_2-C(R^{19A})_2-$aryl, $-C(R^{19A})_2-C(R^{19A})_2-$($C_3$-$C_8$ heterocycle) or $-C(R^{19A})_2-C(R^{19A})_2-$($C_3$-$C_8$ cycloalkyl); wherein R^{19A} is hydrogen, C_1-C_8 alkyl or –OH;

R^{20} is hydrogen, C_1-C_{20} alkyl, aryl, C_3-C_8 heterocycle, -$(R^{47}O)_m$-R^{48}, or -$(R^{47}O)_m$-$CH(R^{49})_2$;

R^{21} is aryl or C_3-C_8 heterocycle;

subscript m is an integer ranging from 1-1000;

R^{47} is C_2-C_8 alkyl;

R^{48} is hydrogen or C_1-C_8 alkyl;

R^{49} independently are -COOH, $-(CH_2)_n-N(R^{50})_2$, $-(CH_2)_n-SO_3H$, or $-(CH_2)_n-SO_3-C_1$-C_8 alkyl;

R^{50} independently are C_1-C_8 alkyl or $-(CH_2)_n$-COOH;

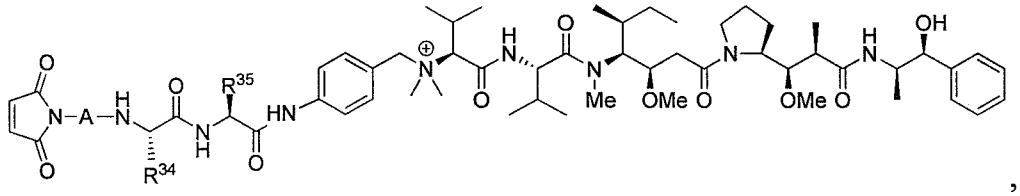
Z is O, S, NH, or NR^{46}, wherein R^{46} is C_1-C_8 alkyl;

X^1 is C_1-C_{10} alkylene; and

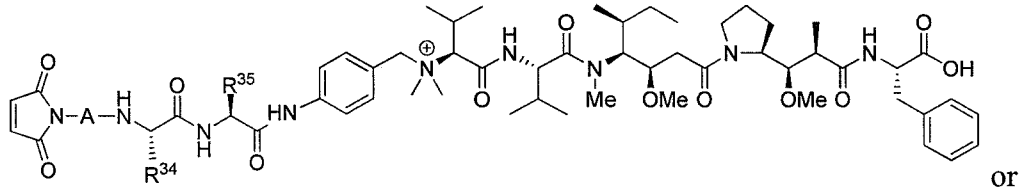
subscript n is an integer ranging from 0 to 6;

wherein the wavy line indicates covalent bonding of D^+ to the remainder of the Drug-Linker compound.

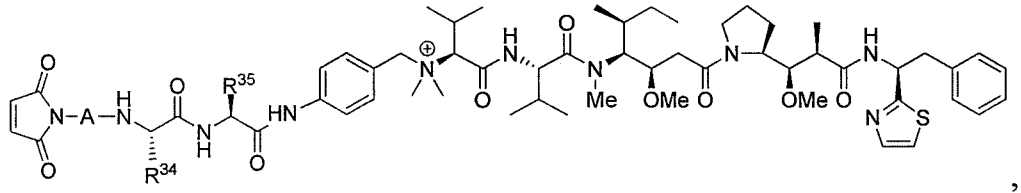
37. The Drug-Linker compound of claim 36, wherein the Drug Linker compound has the structure of:



,



or



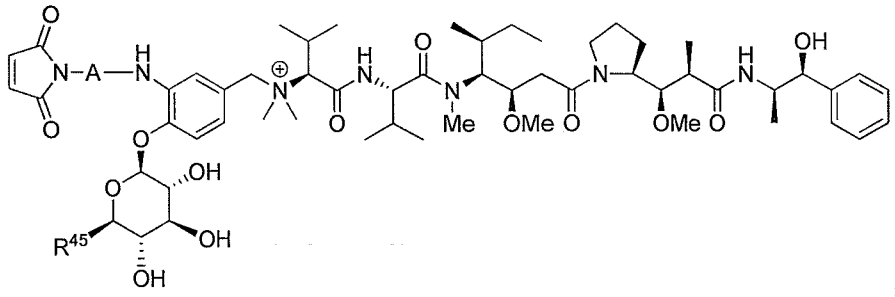
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wherein

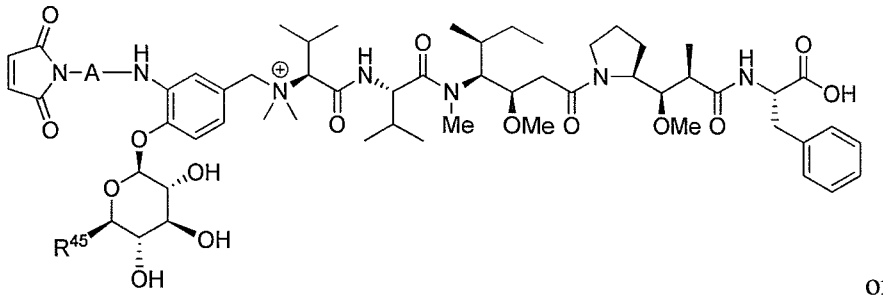
R^{34} is isopropyl and R^{35} is $-CH_3$, $-CH_2CH_2COOH$ or $-CH_2CH_2CH_2NH(C=O)NH_2$,

or

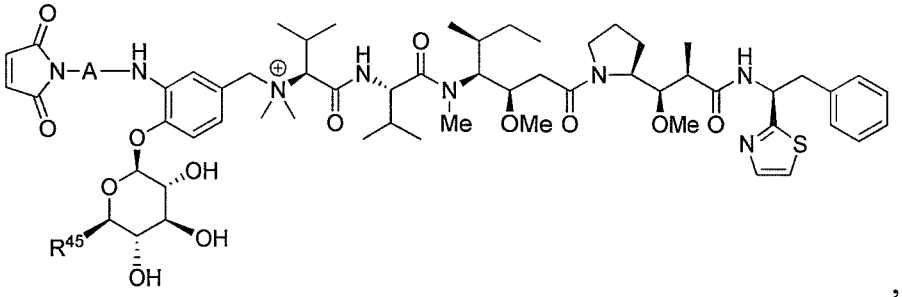
wherein the Drug Linker compound has the structure of:



,



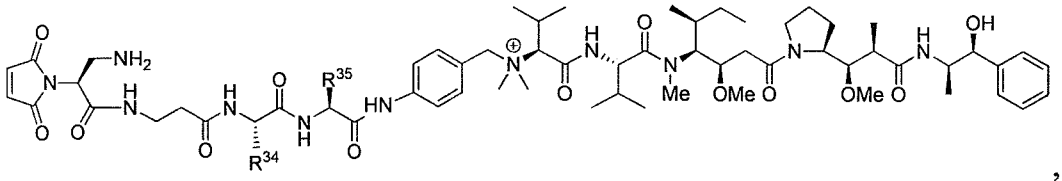
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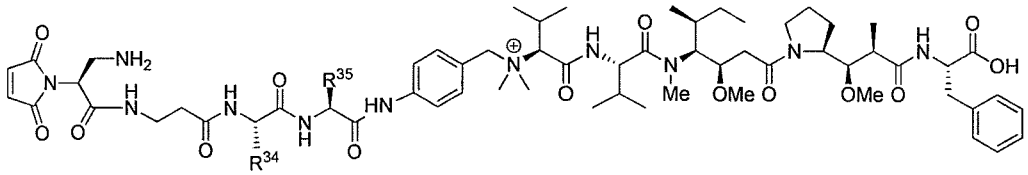
,

wherein R^{45} is $-CO_2H$ or CH_2OH.

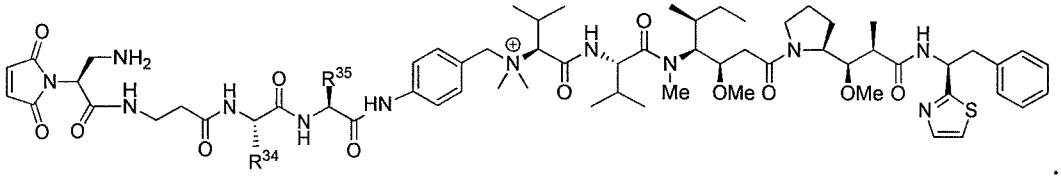
38. The Drug-Linker compound of claim 36, wherein the Drug Linker compound has the structure of:



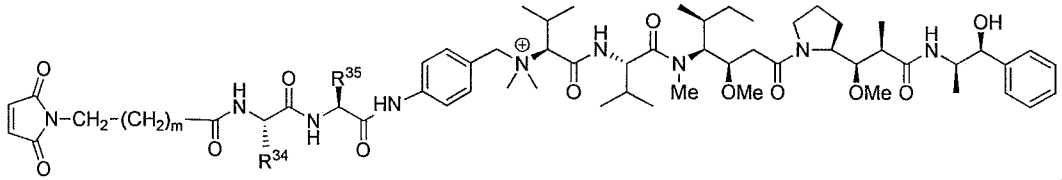
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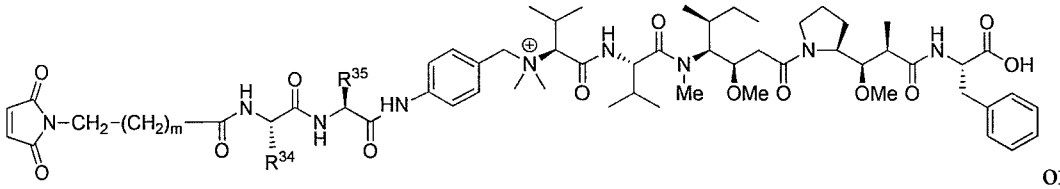
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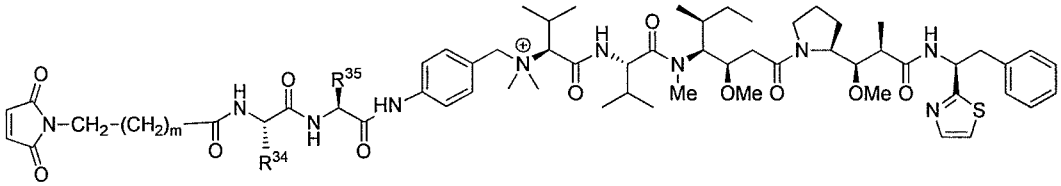
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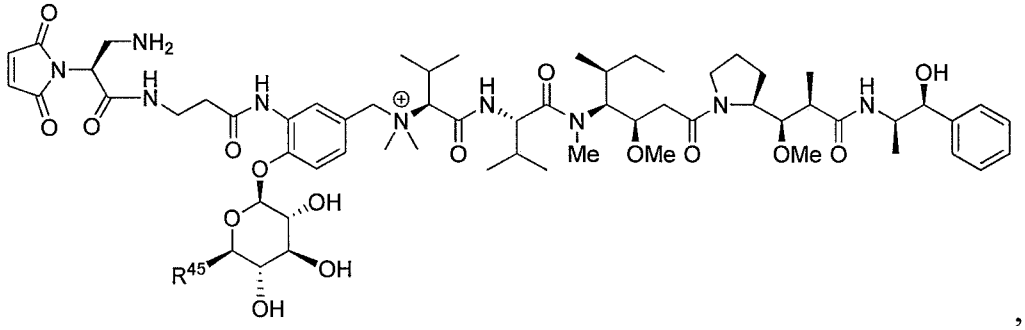


or

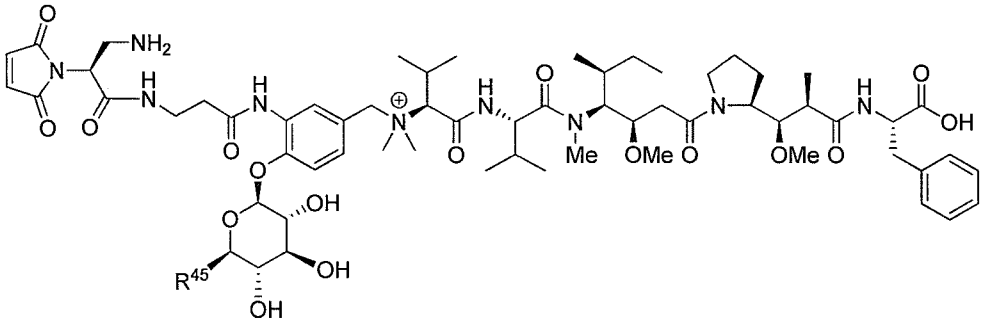


wherein the subscript m is 4.

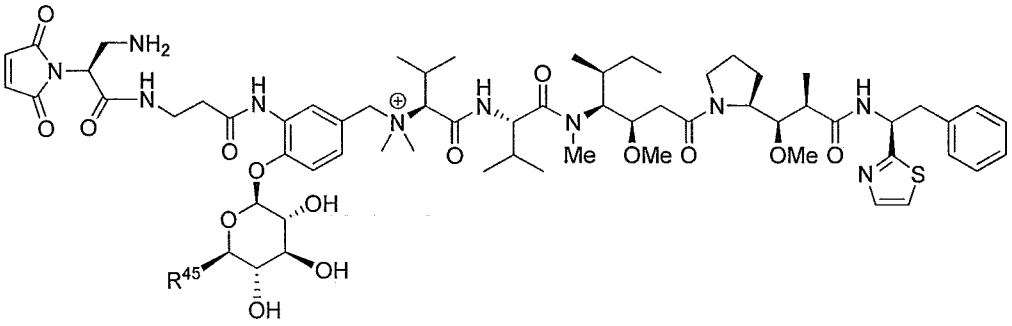
39. The Drug-Linker compound of claim 36, wherein the Drug Linker compound has the structure of:



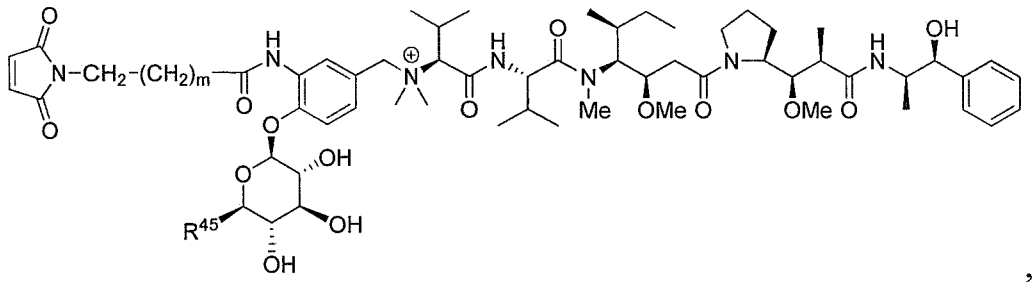
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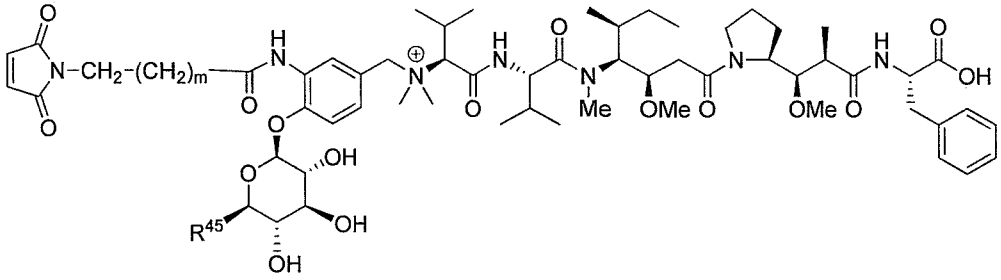
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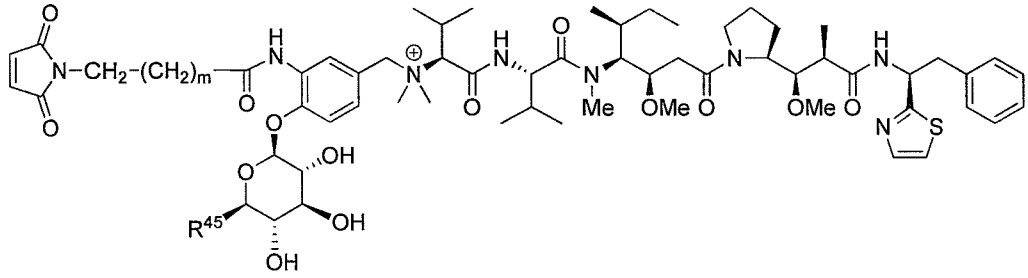
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,



or



wherein R^{45} is $-CO_2H$ or $-CH_2OH$; and subscript m is 4.

5