respectively, can occur. Those biodistribution effects may even become the dominant factors over preferential proteolysis, which could be difficult to observe *in vivo*.

[0008] Thus, Conjugate compounds having peptide sequences providing enhanced exposure of released free cytotoxic compound to tumor tissue in comparison to normal tissue should exhibit reduced undesired toxicities due to the peptide sequences being overall less susceptible to proteolysis within normal tissue or cells thereof in comparison to those of the tumor and/or from improved pharmacokinetic properties for Conjugate compounds incorporating those peptide sequences that favor tumor tissue over normal tissue.

[0009] The Ligand Drug Conjugates of the present invention therefore have two levels of selectivity for targeted cells over non-targeted normal cells: (1) selective entry into targeted cells and (2) decreased exposure of normal tissue in comparison to tumor tissue to the Conjugate compound. From that second level of selectivity, reduction in normal tissue toxicities is expected to provide reduced adverse events associated with conventional targeted therapies.

SUMMARY

[0009a] In an aspect of the present disclosure, there is provided a Ligand Drug Conjugate composition represented by Formula **1**:

$$L\text{-}[LU\text{-}D']_p \qquad (\mathbf{1})$$

or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

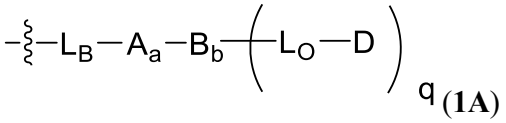
LU is a Linker Unit;

D' represents from 1 to 4 Drug Units (D) in each drug linker moiety of formula -LU-D'; and

subscript p is a number from 1 to 12, from 1 to 10 or from 1 to 8 or is 4 or 8,

wherein the Ligand Unit is from an antibody or an antigen-binding fragment of an antibody that is capable of selective binding to an antigen of tumor tissue for subsequent release of the Drug Unit(s) as free drug,

wherein the drug linker moiety of formula -LU-D' in each of the Ligand Drug Conjugate compounds of the composition has the structure of Formula **1A**:



(1A)

or a salt thereof,

wherein the wavy line indicates covalent attachment to L;

D is the Drug Unit;

L_B is a ligand covalent binding moiety;

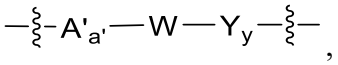
A is a first optional Stretcher Unit;

subscript a is 0 or 1, indicating the absence or presence of A, respectively;

B is an optional Branching Unit;

subscript b is 0 or 1, indicating the absence or presence of B, respectively;

L_O is a secondary linker moiety, wherein the secondary linker has the formula of;



,

wherein the wavy line adjacent to Y indicates the site of covalent attachment of L_O to the Drug Unit and the wavy line adjacent to A' indicates the site of covalent attachment to the remainder of the drug linker moiety;

A' is a second optional Stretcher Unit, which in the absence of B becomes a subunit of A,

subscript a′ is 0 or 1, indicating the absence or presence of A', respectively,

W is a Peptide Cleavable Unit, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

a first one of the amino acids P1, P2, or P3 is negatively charged;

a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and

a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine,

wherein the first one of the amino acids P1, P2, or P3 corresponds to any one of P1, P2, or P3, the second one of the amino acids P1, P2, or P3 corresponds to one of the two remaining amino acids P1, P2, or P3, and the third one of the amino acids P1, P2, or P3 corresponds to the last remaining amino acids P1, P2, or P3, wherein the P1 amino acid is a natural or unnatural amino acid having a side chain with at least one charged substituent or at least one uncharged substituent with a permanent electric dipole moment that is greater than that of -NH-C(O)NH_2;

provided that -P3-P2-P1- is not -Glu-Val-Cit- or -Asp-Val-Cit-;

Y is a self-immolative Spacer Unit;

subscript y is 0, 1 or 2 indicating the absence or presence of 1 or 2 of Y, respectively; and

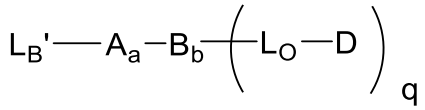
subscript q is an integer ranging from 1 to 4,

provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1; and

wherein the Ligand Drug Conjugate compounds of the composition have the structure of Formula **1** in which subscript p is replaced by subscript p', wherein subscript p' is an integer from 1 to 12, 1 to 10 or 1 to 8 or is 4 or 8.

[0009b] In another aspect of the present disclosure, there is provided a pharmaceutically acceptable formulation, wherein the formulation comprises an effective amount of a Ligand Drug Conjugate composition or an equivalent amount of a non-binding control Conjugate disclosed herein, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

[0009c] In a further aspect of the present disclosure, there is provided a Drug Linker compound of Formula **IA**:



(**IA**)

or a salt thereof, wherein

D is a Drug Unit;

L_B' is a ligand covalent binding precursor moiety;

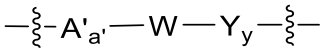
A is a first optional Stretcher Unit;

subscript a is 0 or 1, indicating the absence or presence of A, respectively;

B is an optional Branching Unit;

subscript b is 0 or 1, indicating the absence or presence of B, respectively;

L_O is a secondary linker moiety, wherein the secondary linker has the formula of;



wherein the wavy line adjacent to Y indicates the site of covalent attachment of L_O to the Drug Unit and the wavy line adjacent to A' indicates the site of covalent attachment to the remainder of the Drug Linker compound;

A' is a second optional Stretcher Unit, which in the absence of B becomes a subunit of A;

subscript a′ is 0 or 1, indicating the absence or presence of A', respectively,

W is a Peptide Cleavable Unit, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

a first one of the amino acids P1, P2, or P3 is negatively charged;

a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and

a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine,

wherein the first one of the amino acids P1, P2, or P3 corresponds to any one of P1, P2, or P3, the second one of the amino acids P1, P2, or P3 corresponds to one of the two remaining amino acids P1, P2, or P3, and the third one of the amino acids P1, P2, or P3 corresponds to the last remaining amino acids P1, P2, or P3, wherein the P1 amino acid is a natural or unnatural amino acid having a side chain with at least one charged substituent or at least one uncharged substituent with a permanent electric dipole moment that is greater than that of -NH-C(O)NH_2;

provided that -P3-P2-P1- is not -Glu-Val-Cit- or -Asp-Val-Cit-;

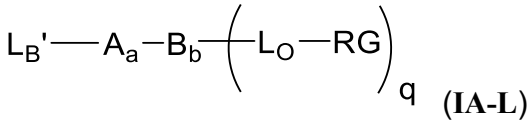
Y is a self-immolative Spacer Unit;

subscript y is 0, 1 or 2 indicating the absence or presence of 1 or 2 of Y, respectively; and

subscript q is an integer ranging from 1 to 4,

provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1.

[0009d] In another aspect of the present disclosure, there is provided a Linker compound of Formula **IA-L**:



(IA-L)

or a salt thereof, wherein

RG is a reactive group;

L_B' is a ligand covalent binding precursor moiety;

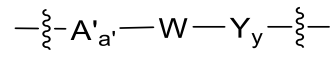
A is a first optional Stretcher Unit;

subscript a is 0 or 1, indicating the absence or presence of A, respectively;

B is an optional Branching Unit;

subscript b is 0 or 1, indicating the absence or presence of B, respectively;

L_O is a secondary linker moiety, wherein the secondary linker has the formula of;



wherein the wavy line adjacent to Y indicates the site of covalent attachment of L_O to the Drug Unit and the wavy line adjacent to A' indicates the site of covalent attachment to the remainder of the Drug Linker compound;

A' is a second optional Stretcher Unit, which in the absence of B becomes a subunit of A;

subscript a' is 0 or 1, indicating the absence or presence of A', respectively,

W is a Peptide Cleavable Unit, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

a first one of the amino acids P1, P2, or P3 is negatively charged;

a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and

a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine,

wherein the first one of the amino acids P1, P2, or P3 corresponds to any one of P1, P2, or P3, the second one of the amino acids P1, P2, or P3 corresponds to one of the two remaining amino acids P1, P2, or P3, and the third one of the amino acids P1, P2, or P3 corresponds to the last remaining amino acids P1, P2, or P3, wherein the P1 amino acid is a natural or unnatural amino acid having a side chain with at least one charged substituent or at least one uncharged substituent with a permanent electric dipole moment that is greater than that of -NH-C(O)NH_2;

provided that -P3-P2-P1- is not -Glu-Val-Cit- or -Asp-Val-Cit-;

Y is a self-immolative Spacer Unit;

subscript y is 0, 1 or 2 indicating the absence or presence of 1 or 2 of Y, respectively; and

subscript q is an integer ranging from 1 to 4,

provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1.

[0010] One principle example of the present disclosure provides a Ligand Drug Conjugate composition represented by Formula 1:



or a salt thereof, in particular a pharmaceutically acceptable salt, wherein

L is a Ligand Unit;

WHAT IS CLAIMED IS:

1. A Ligand Drug Conjugate composition represented by Formula 1:

$$L\text{-}[LU\text{-}D']_p \qquad (1)$$

or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

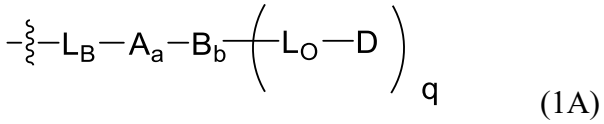
LU is a Linker Unit;

D' represents from 1 to 4 Drug Units (D) in each drug linker moiety of formula -LU-D'; and

subscript p is a number from 1 to 12, from 1 to 10 or from 1 to 8 or is 4 or 8,

wherein the Ligand Unit is from an antibody or an antigen-binding fragment of an antibody that is capable of selective binding to an antigen of tumor tissue for subsequent release of the Drug Unit(s) as free drug,

wherein the drug linker moiety of formula -LU-D' in each of the Ligand Drug Conjugate compounds of the composition has the structure of Formula 1A:



(1A)

or a salt thereof,

wherein the wavy line indicates covalent attachment to L;

D is the Drug Unit;

L_B is a ligand covalent binding moiety;

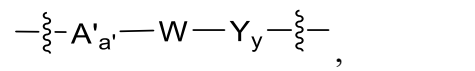
A is a first optional Stretcher Unit;

subscript a is 0 or 1, indicating the absence or presence of A, respectively;

B is an optional Branching Unit;

subscript b is 0 or 1, indicating the absence or presence of B, respectively;

L_O is a secondary linker moiety, wherein the secondary linker has the formula of;



,

wherein the wavy line adjacent to Y indicates the site of covalent attachment of L_O to the Drug Unit and the wavy line adjacent to A' indicates the site of covalent attachment to the remainder of the drug linker moiety;

A' is a second optional Stretcher Unit, which in the absence of B becomes a subunit of A,

subscript a' is 0 or 1, indicating the absence or presence of A', respectively,

W is a Peptide Cleavable Unit, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

a first one of the amino acids P1, P2, or P3 is negatively charged;

a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and

a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine,

wherein the first one of the amino acids P1, P2, or P3 corresponds to any one of P1, P2, or P3, the second one of the amino acids P1, P2, or P3 corresponds to one of the two remaining amino acids P1, P2, or P3, and the third one of the amino acids P1, P2, or P3 corresponds to the last remaining amino acids P1, P2, or P3, wherein the P1 amino acid is a natural or unnatural amino acid having a side chain with at least one charged substituent or at least one uncharged substituent with a permanent electric dipole moment that is greater than that of -NH-C(O)NH_2;

provided that -P3-P2-P1- is not -Glu-Val-Cit- or -Asp-Val-Cit-;

Y is a self-immolative Spacer Unit;

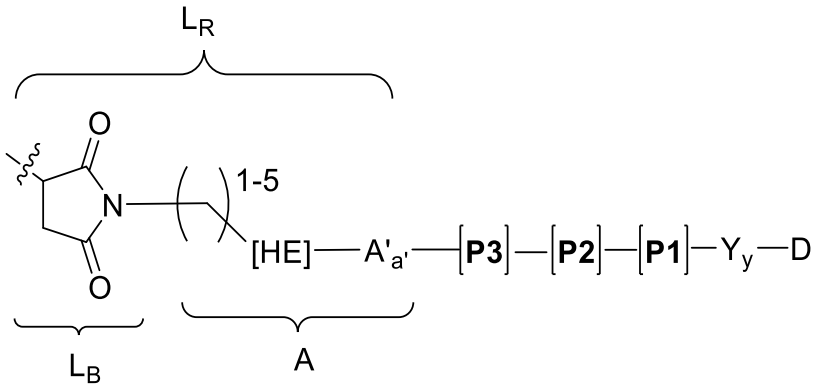
subscript y is 0, 1 or 2 indicating the absence or presence of 1 or 2 of Y, respectively; and

subscript q is an integer ranging from 1 to 4,

provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1; and

wherein the Ligand Drug Conjugate compounds of the composition have the structure of Formula 1 in which subscript p is replaced by subscript p', wherein subscript p' is an integer from 1 to 12, 1 to 10 or 1 to 8 or is 4 or 8.

2. The Ligand Drug Conjugate composition of claim 1, wherein the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition have drug linker moieties of Formula 1H:



(Formula 1H)

or pharmaceutically acceptable salts thereof, and optionally having a minority of Ligand Drug Conjugate compounds in which one or more of the drug linker moieties in each of such compounds has its succinimide ring in hydrolyzed form and wherein

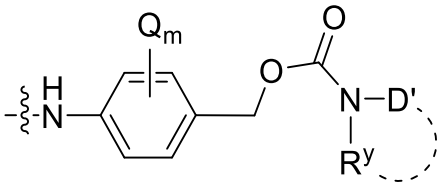
HE is a Hydrolysis Enhancing Unit;

A' is a subunit, when present, of the indicated first Stretcher Unit (A); subscript a' is 0 or 1, indicating the absence or presence of A'; and

the wavy line indicates the site of covalent binding to a sulfur atom of the Ligand Unit.

3. The Ligand Drug Conjugate composition of claim 2, or a pharmaceutically acceptable salt thereof, wherein HE is –C(=O).

4. The Ligand Drug Conjugate composition of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein -Y_y-D has the structure of:



wherein -N(R^y)D' represents D, wherein D' is the remainder of D;

the wavy line indicates the site of covalent attachment to P1;

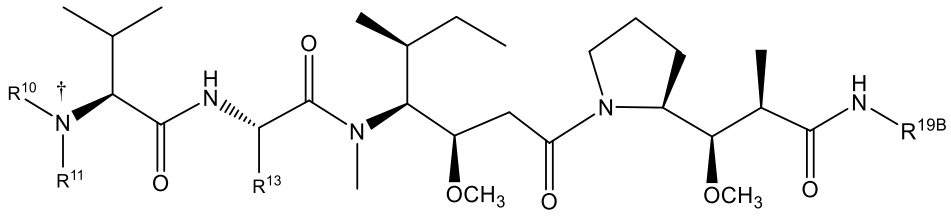
the dotted line indicates optional cyclization of R^y to D';

R^y is optionally substituted C_1-C_6 alkyl in absence of cyclization to D' or optionally substituted C_1-C_6 alkylene when cyclized to D';

each Q is independently selected from the group consisting of -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), halogen, nitro and cyano; and

subscript m is 0, 1 or 2.

5. The Ligand Drug Conjugate composition of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein D is a cytotoxic drug wherein the cytotoxic drug is a secondary amine-containing auristatin compound wherein the nitrogen atom of the secondary amine is the site of covalent attachment to the drug linker moiety and the secondary amine-containing auristatin compound has the structure of Formula $D_{F/E-3}$:



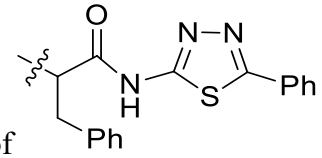
$D_{F/E-3}$

wherein the dagger indicates the site of covalent attachment of the nitrogen atom that provides the carbamate functional group;

one of R^{10} and R^{11} is hydrogen and the other is methyl;

R^{13} is isopropyl or $–CH_2$-$CH(CH_3)_2$; and

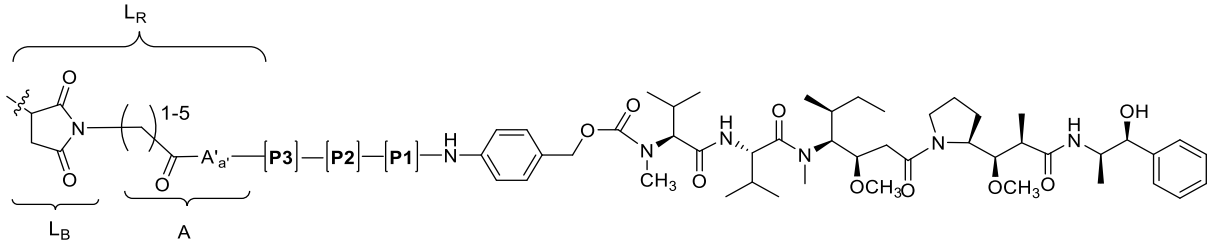
R^{19B} is $–CH(CH_3)$-CH(OH)-Ph, $–CH(CO_2H)$-CH(OH)-CH_3, $–CH(CO_2H)$-CH_2Ph, -CH(CH_2Ph)-2-thiazolyl, -CH(CH_2Ph)-2-pyridyl, -CH(CH_2-p-Cl-Ph), -CH(CO_2Me)-CH_2Ph, -CH(CO_2Me)-$CH_2CH_2SCH_3$, -CH($CH_2CH_2SCH_3$)C(=O)NH-quinol-3-yl, -CH(CH_2Ph)C(=O)NH-p-Cl-Ph, or

R^{19B} has the structure of 

, wherein the wavy line indicates covalent attachment to the remainder of the auristatin compound.

6. The Ligand Drug Conjugate composition of claim 5, or a pharmaceutically acceptable salt thereof, wherein the secondary amine-containing auristatin compound is monomethylauristatin E (MMAE) or monomethylauristatin F (MMAF).

7. The Ligand Drug Conjugate composition of claim 1, wherein subscript q is 1 and the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition have drug linker moieties of Formula 1H-MMAE:



(Formula 1H-MMAE)

or a pharmaceutically acceptable salt thereof, and optionally having a minority of Ligand Drug Conjugate compounds in which one or more of the drug linker moieties in each of such compounds has its the succinimide ring in hydrolyzed form and wherein:

subscript a' is 0, and A' is absent; and

the wavy line indicates the site of covalent binding to a sulfur atom of the Ligand Unit.

8. The Ligand Drug Conjugate composition of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

the P3 amino acid of the tripeptide is in the D-amino acid configuration;

one of the P2 and P1 amino acids has an aliphatic side chain with hydrophobicity lower than that of leucine; and

the other of the P2 and P1 amino acids is negatively charged.

9. The Ligand Drug Conjugate composition of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein the P3 amino acid is D-Leu or D-Ala.

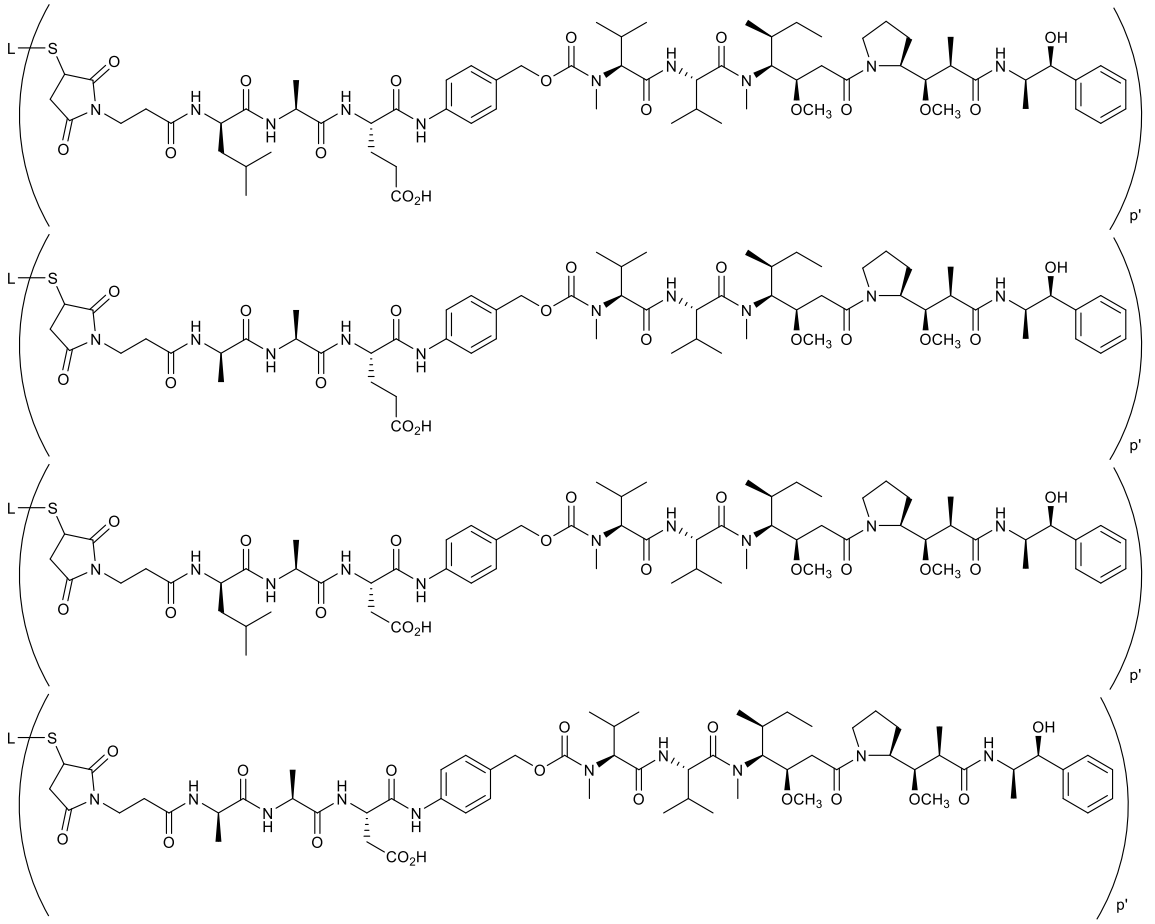
10. The Ligand Drug Conjugate composition of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein one of the P2 or P1 amino acid has an aliphatic side chain with hydrophobicity no greater than that of valine, and the other of the P2 or P1 amino acid is negatively charged at plasma physiological pH.

11. The Ligand Drug Conjugate composition of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein the P2 amino acid has an aliphatic side chain with hydrophobicity no greater than that of valine, and the P1 amino acid is negatively charged at plasma physiological pH.

12. The Ligand Drug Conjugate composition of any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein -P2-P1- is -Ala-Glu- or -Ala-Asp-.

13. The Ligand Drug Conjugate composition of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, wherein -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-.

14. The Ligand Drug Conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has the structure of:



,

,

, or

,

or a pharmaceutically acceptable salt thereof,

wherein L is a Ligand Unit, and subscript p' is an integer from 1 to 12.

15. The Ligand Drug Conjugate composition of any one of claims 1-14, or a pharmaceutically acceptable salt thereof, wherein L is an antibody Ligand Unit of an intact antibody or an antigen-binding fragment thereof.

16. The Ligand Drug Conjugate composition of claim 15, or a pharmaceutically acceptable salt thereof, wherein the intact antibody or fragment thereof is capable of selectively binding to a cancer cell antigen.

17. The Ligand Drug Conjugate composition of claim 15, or a pharmaceutically acceptable salt thereof, wherein the intact antibody is a chimeric, humanized or human antibody, wherein the antibody is capable of selectively binding to a cancer cell antigen or the antibody is a non-binding control antibody thereby defining a non-binding control Conjugate composition.

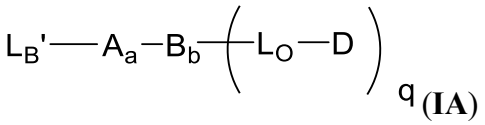
18. The Ligand Drug Conjugate composition of any one of claims 1-17, or a pharmaceutically acceptable salt thereof, wherein subscript p ranges from 2 to 12, or from 2 to 10, or from 2 to 8, or subscript p is 2, 4 or 8.

19. A pharmaceutically acceptable formulation, wherein the formulation comprises an effective amount of a Ligand Drug Conjugate composition or an equivalent amount of a non-binding control Conjugate of any one of claims 1-14, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

20. The pharmaceutically acceptable formulation of claim 19, or a pharmaceutically acceptable salt thereof, wherein the least one pharmaceutically acceptable excipient is a liquid carrier that provides a liquid formulation, wherein the liquid formulation is suitable for lyophilization or administration to a subject in need thereof.

21. The pharmaceutically acceptable formulation of claim 19, or a pharmaceutically acceptable salt thereof, wherein the formulation is a solid from lyophilization or a liquid formulation of claim 21, wherein the at least one excipient of the solid formulation is a lyoprotectant.

22. A Drug Linker compound of Formula IA:



(IA)

or a salt thereof, wherein

D is a Drug Unit;

L_B' is a ligand covalent binding precursor moiety;

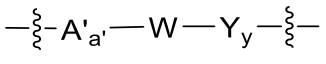
A is a first optional Stretcher Unit;

subscript a is 0 or 1, indicating the absence or presence of A, respectively;

B is an optional Branching Unit;

subscript b is 0 or 1, indicating the absence or presence of B, respectively;

L_O is a secondary linker moiety, wherein the secondary linker has the formula of;



wherein the wavy line adjacent to Y indicates the site of covalent attachment of L_O to the Drug Unit and the wavy line adjacent to A' indicates the site of covalent attachment to the remainder of the Drug Linker compound;

A' is a second optional Stretcher Unit, which in the absence of B becomes a subunit of A;

subscript a' is 0 or 1, indicating the absence or presence of A', respectively,

W is a Peptide Cleavable Unit, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

a first one of the amino acids P1, P2, or P3 is negatively charged;

a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and

a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine,

wherein the first one of the amino acids P1, P2, or P3 corresponds to any one of P1, P2, or P3, the second one of the amino acids P1, P2, or P3 corresponds to one of the two remaining amino acids P1, P2, or P3, and the third one of the amino acids P1, P2, or P3 corresponds to the last remaining amino acids P1, P2, or P3, wherein the P1 amino acid is a natural or unnatural amino acid having a side chain with at least one charged substituent or at least one uncharged substituent

with a permanent electric dipole moment that is greater than that of -NH-C(O)NH_2;

provided that -P3-P2-P1- is not -Glu-Val-Cit- or -Asp-Val-Cit-;

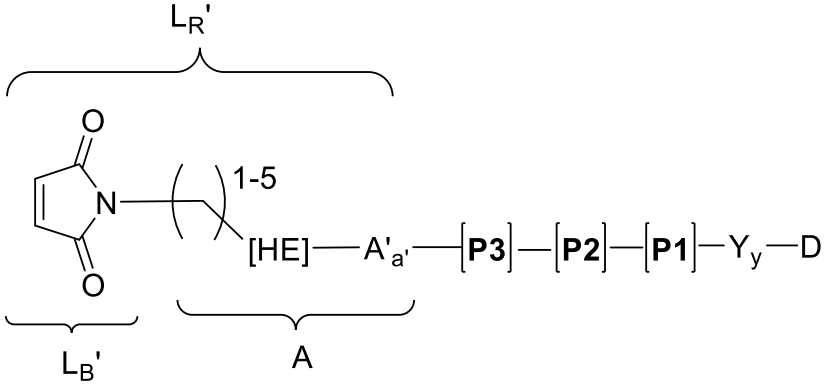
Y is a self-immolative Spacer Unit;

subscript y is 0, 1 or 2 indicating the absence or presence of 1 or 2 of Y, respectively; and

subscript q is an integer ranging from 1 to 4,

provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1.

23. The Drug Linker compound of claim 22, or a salt thereof, wherein the Drug Linker compound has the structure of Formula IH:



(Formula IH)

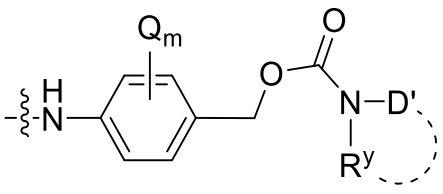
or salt thereof, wherein:

HE is a Hydrolysis Enhancing Unit; and

A' is a subunit, when present, of the indicated first Stretcher Unit (A); subscript a' is 0 or 1, indicating the absence or presence of A'.

24. The Drug Linker compound of 23, or a salt thereof, wherein HE is –C(=O).

25. The Drug Linker compound of any one of claims 22-24, or a salt thereof, wherein -Y_y-D has the structure of:



wherein -N(R^y)D' represents D, wherein D' is the remainder of D;

the wavy line indicates the site of covalent attachment to P1;

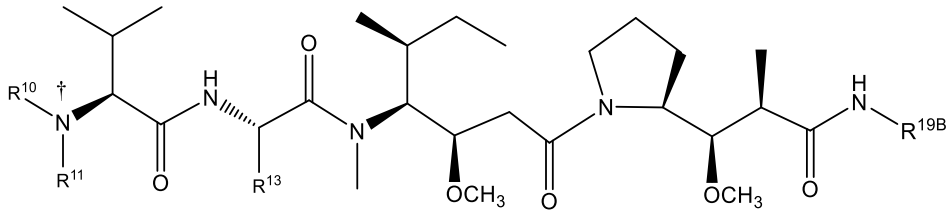
the dotted line indicates optional cyclization of R^y to D';

R^y is optionally substituted C_1-C_6 alkyl in absence of cyclization to D' or optionally substituted C_1-C_6 alkylene when cyclized to D';

each Q is independently selected from the group consisting of -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), halogen, nitro and cyano; and

subscript m is 0, 1 or 2.

26. The Drug Linker compound of any one of claims 22-25, or a salt thereof, wherein D is a cytotoxic drug wherein the cytotoxic drug is a secondary amine-containing auristatin compound wherein the nitrogen atom of the secondary amine is the site of covalent attachment to the drug linker moiety and the secondary amine-containing auristatin compound has the structure of Formula $D_{F/E-3}$:



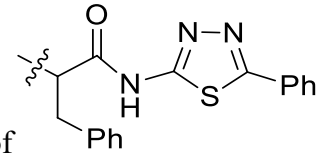
$D_{F/E-3}$

wherein the dagger indicates the site of covalent attachment of the nitrogen atom that provides the carbamate functional group;

one of R^{10} and R^{11} is hydrogen and the other is methyl;

R^{13} is isopropyl or –CH_2-$CH(CH_3)_2$; and

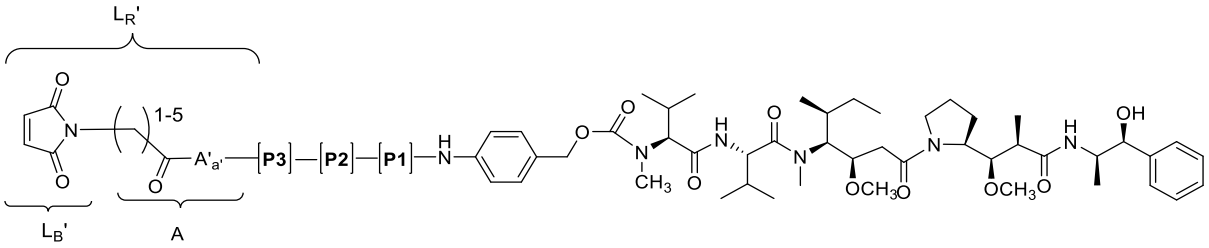
R^{19B} is –$CH(CH_3)$-CH(OH)-Ph, –$CH(CO_2H)$-CH(OH)-CH_3, –$CH(CO_2H)$-CH_2Ph, -CH(CH_2Ph)-2-thiazolyl, -CH(CH_2Ph)-2-pyridyl, -CH(CH_2-p-Cl-Ph), -CH(CO_2Me)-CH_2Ph, -CH(CO_2Me)-$CH_2CH_2SCH_3$, -CH($CH_2CH_2SCH_3$)C(=O)NH-quinol-3-yl, -CH(CH_2Ph)C(=O)NH-p-Cl-Ph, or

R^{19B} has the structure of 

, wherein the wavy line indicates covalent attachment to the remainder of the auristatin compound.

27. The Drug Linker compound of claim 26, or a salt thereof, wherein the secondary amine-containing auristatin compound is monomethylauristatin E (MMAE) or monomethylauristatin F (MMAF).

28. The Drug Linker compound of claim 22, wherein the Drug Linker compound has the structure of Formula IH-MMAE:



(Formula IH-MMAE)

or a salt thereof, wherein

subscript a' is 0, and A' is absent.

29. The Drug Linker compound of any one of claims 22-28, or a pharmaceutically acceptable salt thereof, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

the P3 amino acid of the tripeptide is in the D-amino acid configuration;

one of the P2 and P1 amino acids has an aliphatic side chain with hydrophobicity lower than that of leucine; and

the other of the P2 and P1 amino acids is negatively charged.

30. The Drug Linker compound of any one of claims 22-29. or a salt thereof, wherein the P3 amino acid is D-Leu or D-Ala.

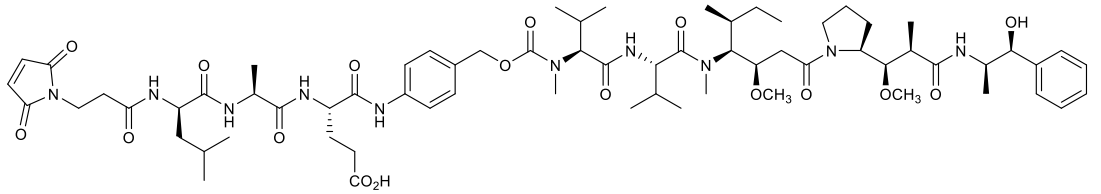
31. The Drug Linker compound of any one of claims 22-30, or a salt thereof, wherein one of the P2 or P1 amino acid has an aliphatic side chain with hydrophobicity no greater than that of valine, and the other of the P2 or P1 amino acid is negatively charged at plasma physiological pH.

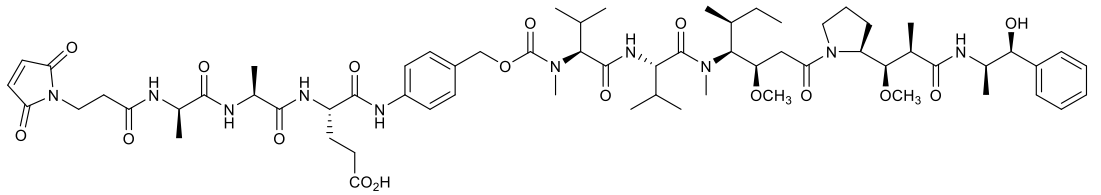
32. The Drug Linker compound of any one of claims 22-31, or a salt thereof, wherein the P2 amino acid has an aliphatic side chain with hydrophobicity no greater than that of valine, and the P1 amino acid is negatively charged at plasma physiological pH.

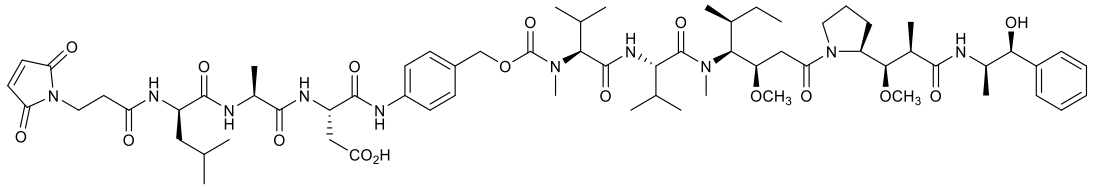
33. The Drug Linker compound of any one of claims 22-32, or a salt thereof, wherein -P2-P1- is -Ala-Glu- or -Ala-Asp-.

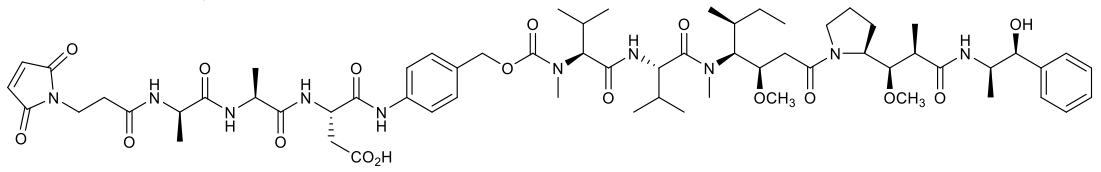
34. The Drug Linker compound of any one of claims 22-33, or a salt thereof, wherein -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-.

35. The Drug Linker compound of claim 22, or a salt thereof, wherein the Drug Linker compound has the structure of:


,

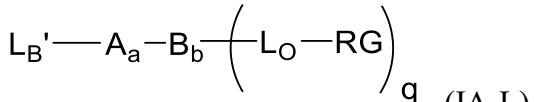

,


, or


,

or a salt thereof.

36. A Linker compound of Formula IA-L:


(IA-L)

or a salt thereof, wherein

RG is a reactive group;

L_B' is a ligand covalent binding precursor moiety;

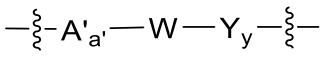
A is a first optional Stretcher Unit;

subscript a is 0 or 1, indicating the absence or presence of A, respectively;

B is an optional Branching Unit;

subscript b is 0 or 1, indicating the absence or presence of B, respectively;

L_O is a secondary linker moiety, wherein the secondary linker has the formula of;



wherein the wavy line adjacent to Y indicates the site of covalent attachment of L_O to the Drug Unit and the wavy line adjacent to A' indicates the site of covalent attachment to the remainder of the Drug Linker compound;

A' is a second optional Stretcher Unit, which in the absence of B becomes a subunit of A;

subscript a' is 0 or 1, indicating the absence or presence of A', respectively,

W is a Peptide Cleavable Unit, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

a first one of the amino acids P1, P2, or P3 is negatively charged;

a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and

a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine,

wherein the first one of the amino acids P1, P2, or P3 corresponds to any one of P1, P2, or P3, the second one of the amino acids P1, P2, or P3 corresponds to one of the two remaining amino acids P1, P2, or P3, and the third one of the amino acids P1, P2, or P3 corresponds to the last remaining amino acids P1, P2, or P3, wherein the P1 amino acid is a natural or unnatural amino acid having a side chain with at least one charged substituent or at least one uncharged substituent with a permanent electric dipole moment that is greater than that of -NH-C(O)NH_2;

provided that -P3-P2-P1- is not -Glu-Val-Cit- or -Asp-Val-Cit-;

Y is a self-immolative Spacer Unit;

subscript y is 0, 1 or 2 indicating the absence or presence of 1 or 2 of Y, respectively; and

subscript q is an integer ranging from 1 to 4,

provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1.

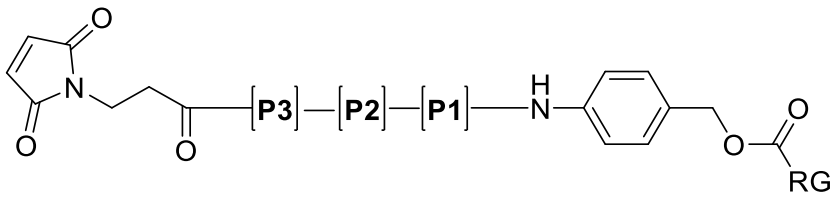
37. The Linker compound of claim 36, wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein:

the P3 amino acid of the tripeptide is in the D-amino acid configuration;

one of the P2 and P1 amino acids has an aliphatic side chain with hydrophobicity lower than that of leucine; and

the other of the P2 and P1 amino acids is negatively charged.

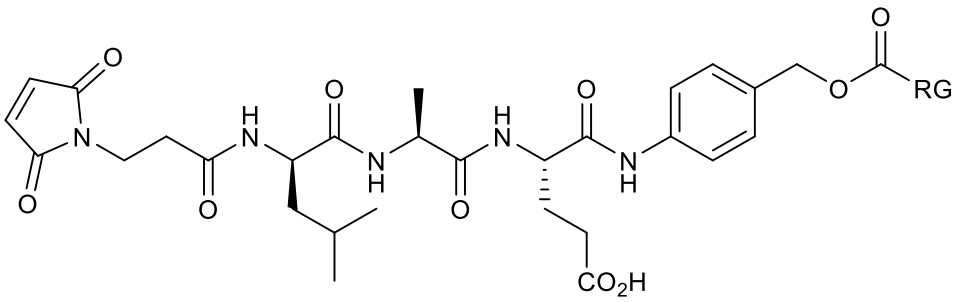
38. The Linker compound of claim 36, wherein the Linker compound has the structure of Formula IA-L-3:



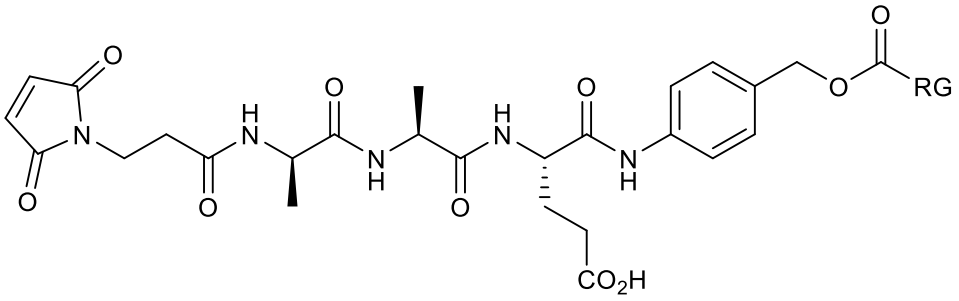
(IA-L-3),

or a salt thereof.

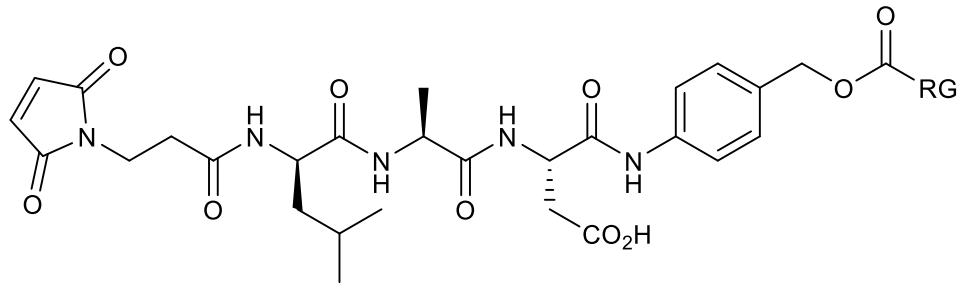
39. The Linker compound of claim 36, wherein the Linker compound has the structure of:



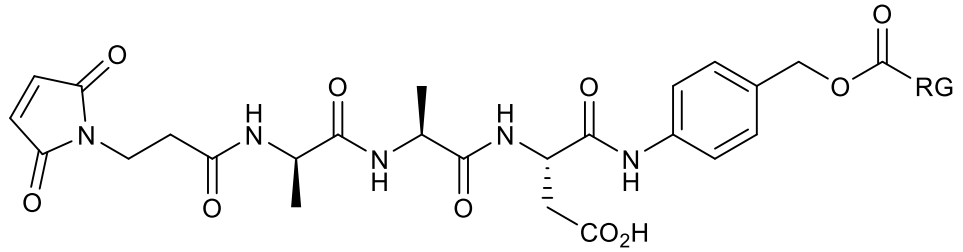
,



,



, or



,

or a salt thereof.