tolerability to the Conjugate is improved while retaining the efficacy of the traditional dipeptide-based Conjugates in treating cancer in a mammalian subject. That difference in exposure may result from greater selectivity for proteolysis of Ligand Drug Conjugates having the selectivity conferring peptide sequences within tumor tissue over proteolysis within normal tissue in comparison to proteolysis of the traditional dipeptide-based Conjugate. Because altering the peptide sequence may also affect the physiochemical properties of the Conjugate compound, greater exposure from improved biodistribution into tumor tissue and not normal tissue and/or improved disposition once distributed into these tissues, which preferentially retains the Conjugate compound in tumor tissue and/or preferentially eliminates the Conjugate compound from normal tissue, respectively, can occur. Those biodistribution effects may even become the dominant factors over preferential proteolysis, which could be difficult to observe *in vivo*.

[0009] 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.

[0010] 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

[0010a] In a first 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;

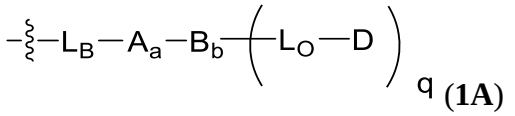
LU is a Linker Unit;

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 about 4 or about 8,

wherein the Ligand Unit is from an antibody or an antigen-binding fragment of an antibody, wherein the antibody or the antigen-binding fragment 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, wherein the Drug Unit is a camptothecin;

L_B is a ligand covalent binding moiety;

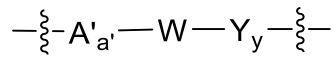
A is a first optional Stretcher Unit;

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 of L_O to the remainder of the drug linker moiety;

A’ is a second optional Stretcher Unit, which when present and 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 comprises 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 or is serine;

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

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

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,

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

each Y when present 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,

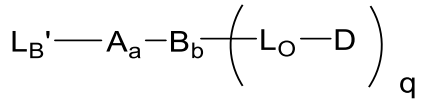
provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1; and

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.

[0010b] 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 disclosed herein and at least one pharmaceutically acceptable excipient.

[0010c] In yet another aspect of the present disclosure, there is provided a use of the Ligand Drug Conjugate composition disclosed herein or the pharmaceutically acceptable formulation disclosed herein, in the manufacture of a medicament for the treatment of cancer.

[0010d] 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, wherein the Drug Unit is a camptothecin;

L_B' is a ligand covalent binding precursor moiety;

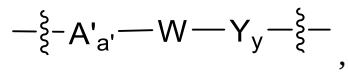
A is a first optional Stretcher Unit;

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 of L_O to the remainder of the Drug Linker compound;

A' is a second optional Stretcher Unit, which when present and 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 comprises 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 or is serine;

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

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

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,

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

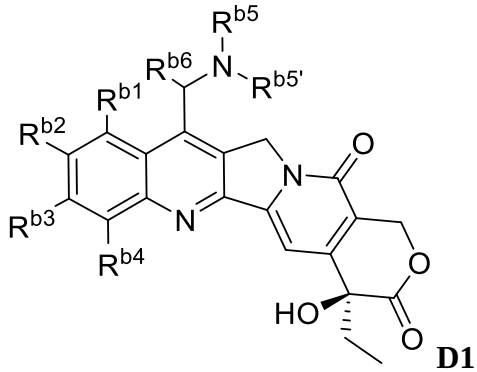
each Y when present is a self-immolative Spacer Unit;

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, and

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

[0010e] In another aspect of the present disclosure, there is provided a compound of formula D1



D1

or a salt thereof, wherein

R^{b1} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, (C_6-C_{12} aryl)-C_2-C_8 alkenyl-, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminoalkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_6-C_{12} aryl-C(O)-, C_6-C_{12} aryl-O-C(O)-NR^a-, C_6-C_{12} aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, C_1-C_8 haloalkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-$S(O)_2$-, C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminolkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-NR^a-, C_1-C_8 alkyl-NR^a-C(O)O-, C_1-C_8 alkyl-OC(O)-NR^a-, C_6-C_{12} aryl-C(O)-, C_6-C_{12} aryl-O-C(O)-NR^a-, C_6-C_{12} aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and $R^{b5'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl-, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl-, NH_2-SO_2-C_1-C_8 alkyl-, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; or

$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkyl-S(O)$_2$-, C_1-C_6 alkyl-C(O)-, C_1-C_6 aminoalkyl-C(O)-, and C_1-C_6 hydroxyalkyl-C(O)-.

[0010f] In yet another aspect of the present disclosure, there is provided a Ligand Drug Conjugate composition disclosed herein or the pharmaceutically acceptable formulation disclosed herein, for use in therapy.

[0011] One principle example of the present disclosure provides a Ligand Drug Conjugate composition represented by Formula 1:

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

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

L is a Ligand Unit;

LU is a Linker Unit; and

composition in which the peptide sequence of its Peptide Cleavable Unit is the dipeptide -valine-citrulline- or -valine-alanine-;

wherein the tumor and normal tissues are of rodent species and wherein the Formula 1 composition provides said improved exposure selectivity demonstrated by:

retaining efficacy in a tumor xenograft model of the comparator Ligand-Drug Conjugate conjugate composition when administered at the same effective amount and dose schedule previously determined for the comparator Ligand-Drug Conjugate conjugate composition, and

showing a reduction in plasma concentration of the free cytotoxic compound released from the Ligand Drug Conjugate compounds of the composition, and/or preservation of normal cells in tissue when administered at the same effective amount and dose schedule as in the tumor xenograft model to a non-tumor bearing rodent in comparison to the equivalent (e.g., same) administration of the comparator Ligand-Drug Conjugate composition in which the Ligand Units of both conjugate compositions are replaced by a non-binding antibody,

wherein cytotoxicity to cells in human tissue of the same type as the normal cells in the tissue of the non-tumor bearing rodent is responsible at least in part to an adverse event in a human subject to whom is administered a therapeutically effective amount of the comparator conjugate composition;

Y is a self-immolative Spacer Unit; and

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

subscript q is an integer ranging from 1 to 4 or 1 to 3,

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

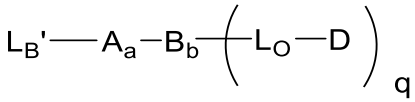
wherein the Ligand Drug Conjugate compounds of the composition have the structure of Formula **1** in which subscript p is replaced by subscript p', wherein subscript p' is an integer from 1 to 12, 1 to 10 or 1 to 8 or is 4 or 8.

[0012] A related principle example provides for a Drug Linker compound of Formula **I**:

$$LU'\text{-}(D') \qquad (\mathbf{I})$$

[0013] or a salt thereof, in particular a pharmaceutically acceptable salt thereof, wherein LU' is capable of providing a covalent bond between L and LU of Formula **1**, and therefore is sometimes referred to as a Linker Unit precursor; and D' represents from 1 to 4

Drug Units, wherein the Drug Linker compound is further defined by the structure of Formula **IA**:



(**IA**)

[0014] wherein L_B' is capable of transformation to L_B of Formula **1A** thereby forming a covalent bond to L of Formula **1**, and therefore is sometimes referred to a ligand covalent binding precursor moiety, and the remaining variable groups of Formula **IA** are as defined for Formula **1A**.

[0015] In some examples, provided herein is 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;

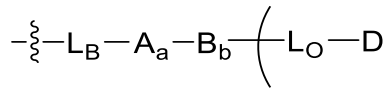
LU is a Linker Unit;

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 about 4 or about 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, in particular a pharmaceutically acceptable salt,

wherein the wavy line indicates covalent attachment to L;

D is the Drug Unit;

L_B is a ligand covalent binding moiety;

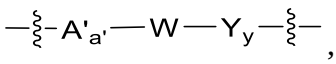
A is a first optional Stretcher Unit;

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 comprises 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 or is serine;

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

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

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,

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,

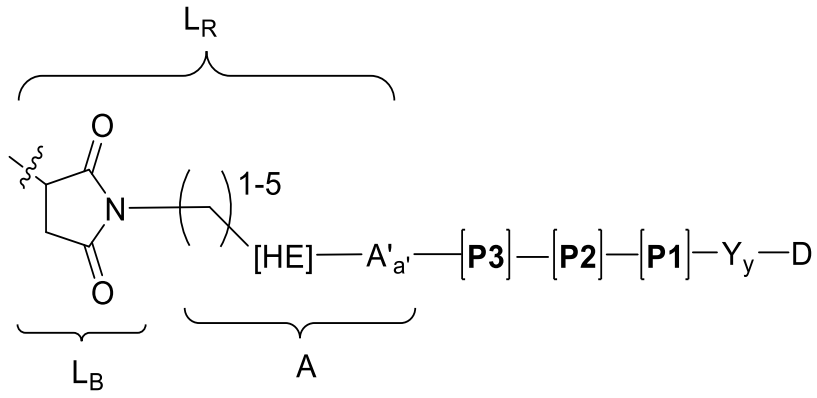
provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1; and

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 independently an integer from 1 to 12, 1 to 10 or 1 to 8 or is 4 or 8.

[0016] In some examples, 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.

[0017] In some examples, provided herein is the Ligand Drug Conjugate composition of Formula **1**, wherein the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition predominately 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

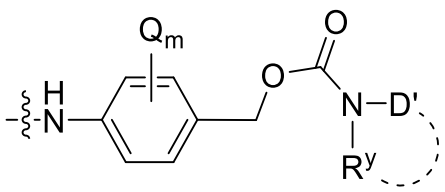
HE is a Hydrolysis Enhancing Unit;

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.

[0018] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition wherein HE is –(C=O).

[0019] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition 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;

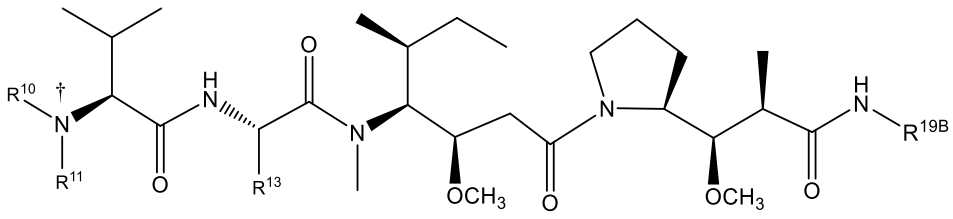
the dotted line indicates optional cyclization of R^y to D';

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.

[0020] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition 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 **$D_{F/E-3}$**:



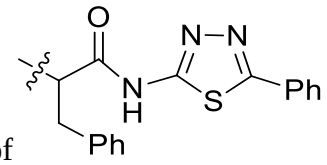
$D_{F/E-3}$

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

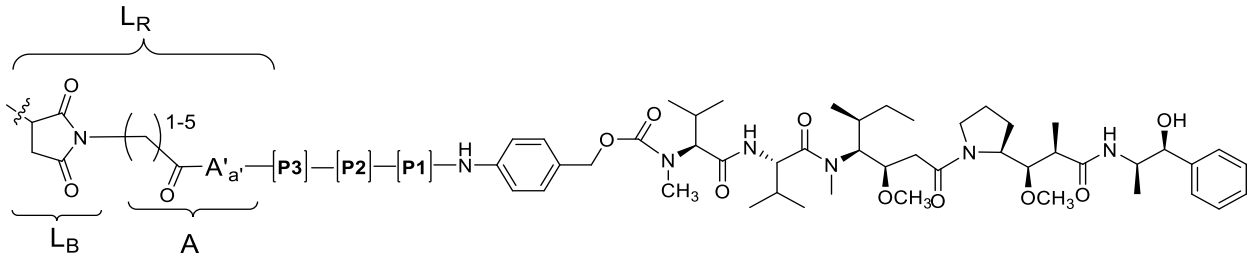
R^{19B} is $–CH(CH_3)$-CH(OH)-Ph, $–CH(CO_2H)$-CH(OH)-CH_3, $–CH(CO_2H)$-CH_2Ph, -CH(CH_2Ph)-2-thiazolyl, -CH(CH_2Ph)-2-pyridyl, -CH(CH_2-p-Cl-Ph), -CH(CO_2Me)-CH_2Ph, -CH(CO_2Me)-$CH_2CH_2SCH_3$, -CH($CH_2CH_2SCH_3$)C(=O)NH-quinol-3-yl, -CH(CH_2Ph)C(=O)NH-p-Cl-Ph, or

R^{19B} has the structure of 

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

[0021] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition wherein the secondary amine-containing auristatin compound is monomethylauristatin E (MMAE) or monomethylauristatin F (MMAF).

[0022] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition wherein subscript q is 1 and the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition predominately have drug linker moieties of Formula 1H-MMAE:



(Formula 1H-MMAE)

or a pharmaceutical 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:

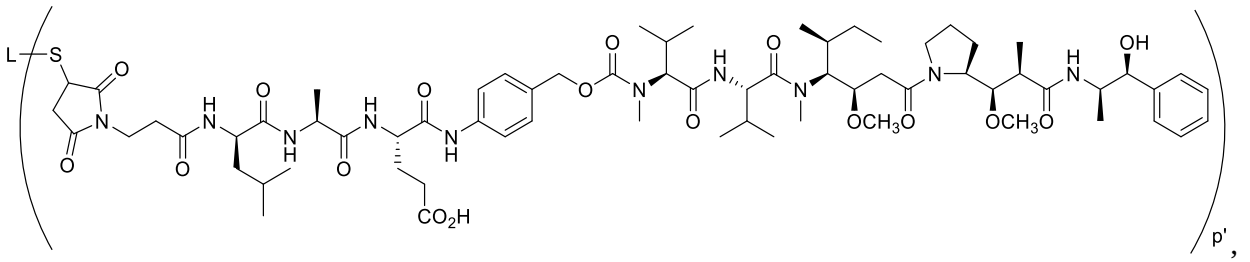
subscript a' is 0, and A' is absent; and

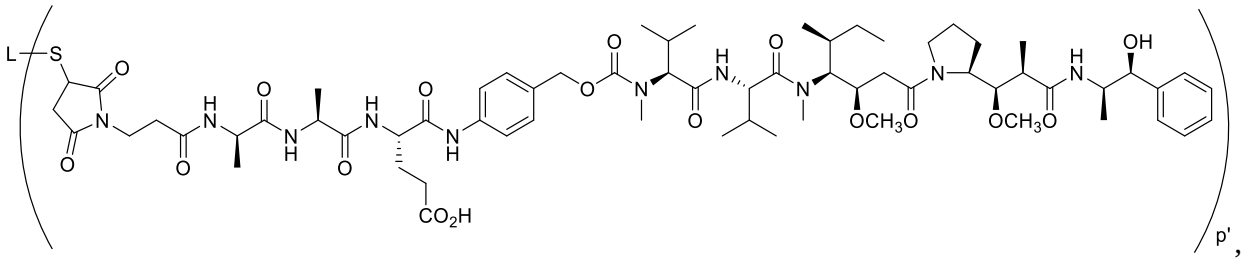
the wavy line indicates the site of covalent binding to a sulfur atom of the Ligand Unit.

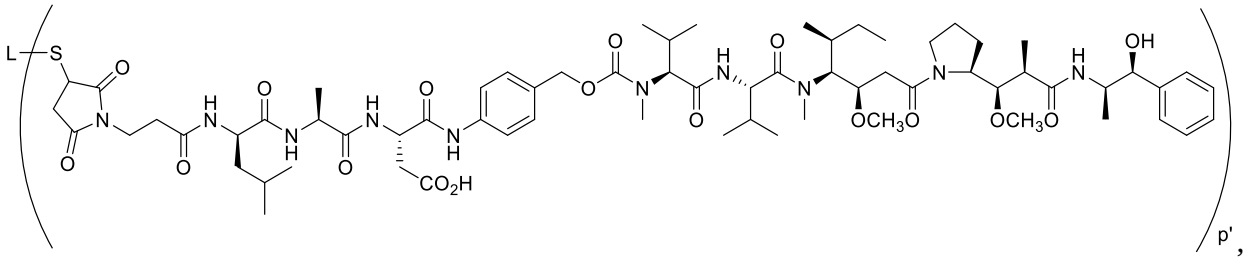
[0023] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition wherein the Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein: the P3 amino acid of the 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. In some examples, the P3 amino acid is D-Leu or D-Ala. Ins ome examples, 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. In some examples, 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. In some examples, -P2-P1- is -Ala-Glu- or -Ala-Asp-. In some examples, -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-. In some examples, the P3 amino acid is D-Leu or D-Ala, the P2 amino acid is Ala, Glu, or Asp, and the P1 amino acid is Ala, Glu, or Asp.

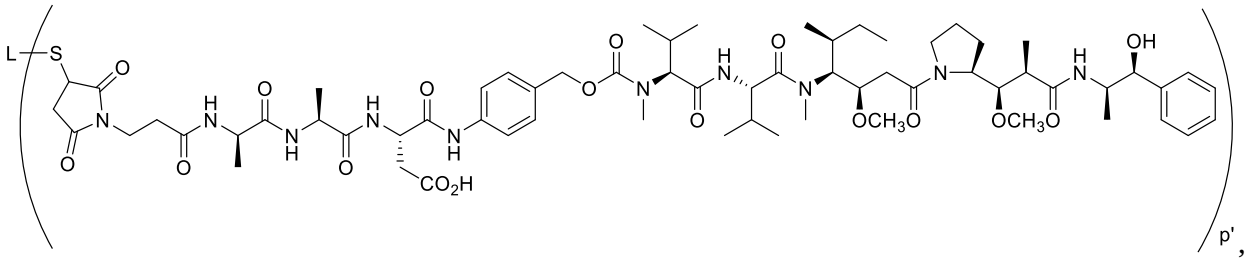
[0024] In some examples, provided herein is the Ligand Drug Conjugate composition wherein the compound has the structure of:







or



or a pharmaceutically acceptable salt thereof,

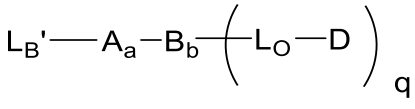
wherein L is a Ligand Unit, and subscript p’ is an integer from 1 to 24.

[0025] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition wherein L is an antibody Ligand Unit of an intact antibody or an antigen-binding fragment thereof. In some examples, the intact antibody or fragment thereof is capable of selectively binding to a cancer cell antigen. In some examples, 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.

[0026] In some examples, which may be combined with any of the preceding examples, provided herein is the Ligand Drug Conjugate composition wherein subscript p ranges from about 2 to about 12, or from about 2 to about 10, or from about 2 to about 8, in particular subscript p is about 2, about 4 or about 8.

[0027] In some examples, which may be combined with any of the preceding examples, provided herein are pharmaceutically acceptable formulations, wherein the formulation comprises an effective amount of a Ligand Drug Conjugate composition or an equivalent amount of a non-binding control Conjugate described herein and at least one pharmaceutically acceptable excipient. In some examples, 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. In some examples, the formulation is a solid from lyophilization or a liquid formulation described herein, wherein the at least one excipient of the solid formulation is a lyoprotectant.

[0028] In some examples, provided herein is 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;

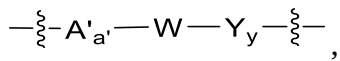
A is a first optional Stretcher Unit;

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 comprises 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 or is serine;

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

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

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,

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

Y is a self-immolative Spacer Unit;

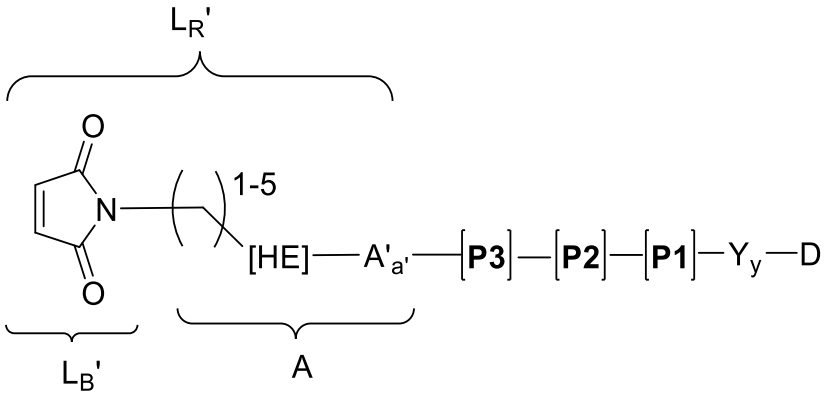
subscript y is 0, 1 or 2 indicating the absence or presence of 1 or 2 of Y, respectively; and

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.

[0029] In some examples, 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.

[0030] In some examples, provided herein is the Drug Linker compound of Formula **IA,** wherein the Drug Linker compound has the structure of Formula IH:



(Formula IH)

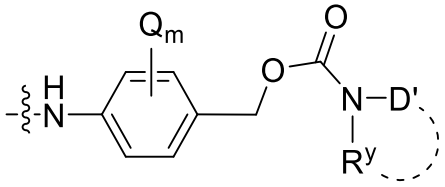
or salt thereof, wherein:

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'.

[0031] In some examples, which may be combined with any of the preceding examples, provided herein is the Drug Linker compound wherein HE is –(C=O).

[0032] In some examples, which may be combined with any of the preceding examples, provided herein is the Drug Linker compound 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;

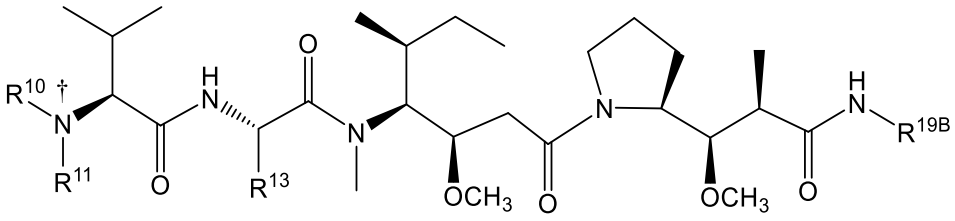
the dotted line indicates optional cyclization of R^y to D';

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.

[0033] In some examples, which may be combined with any of the preceding examples, provided herein is the Drug Linker compound 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 **$D_{F/E-3}$**:



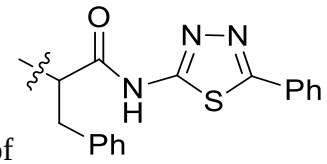
$D_{F/E-3}$

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;

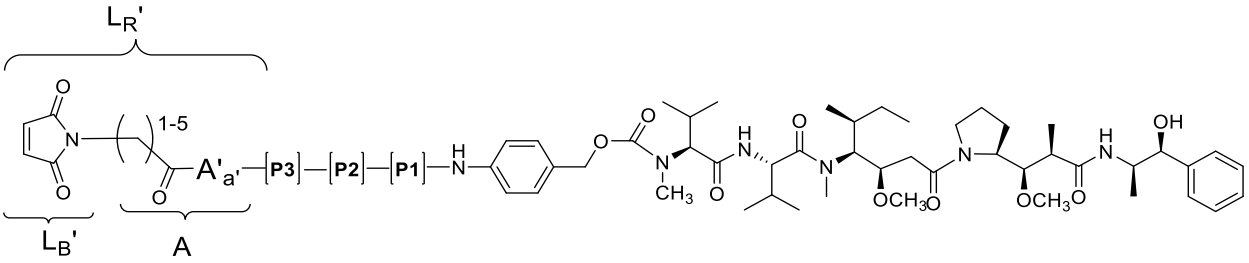
R^{13} is isopropyl or $–CH_2$-$CH(CH_3)_2$; and

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.

[0034] In some examples, which may be combined with any of the preceding examples, provided herein is the Drug Linker compound wherein the secondary amine-containing auristatin compound is monomethylauristatin E (MMAE) or monomethylauristatin F (MMAF).

[0035] In some examples, which may be combined with any of the preceding examples, provided herein is the Drug Linker compound wherein the Drug Linker compound has the structure of Formula IH-MMAE:



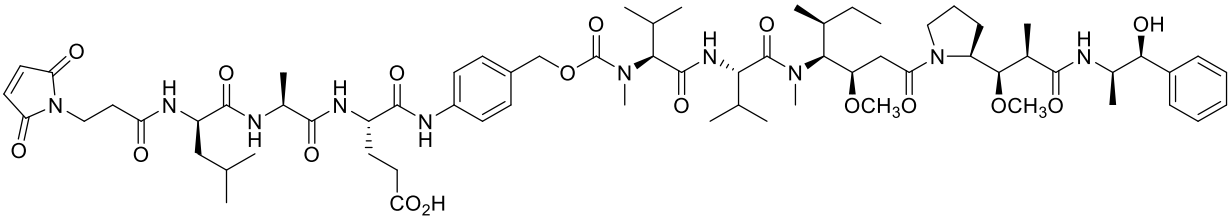
(Formula IH-MMAE)

or a salt thereof, wherein

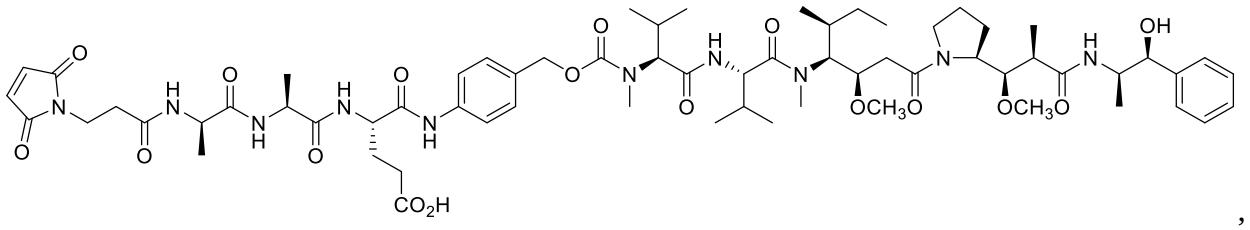
subscript a' is 0, and A' is absent.

[0036] In some examples, which may be combined with any of the preceding examples, provided herein is the Drug Linker compound 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. In some examples, the P3 amino acid is D-Leu or D-Ala. In some examples, 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. In some examples, 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. In some examples, -P2-P1- is -Ala-Glu- or -Ala-Asp-. In some examples, -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-. In some examples, the P3 amino acid is D-Leu or D-Ala, the P2 amino acid is Ala, Glu, or Asp, and the P1 amino acid is Ala, Glu, or Asp.

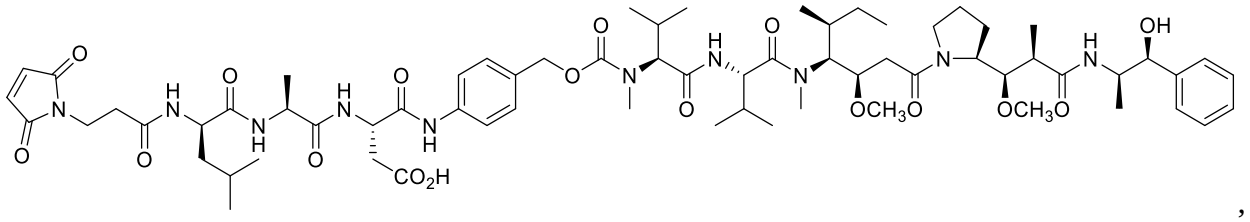
[0037] In some examples, provided herein is the Drug Linker compound wherein the Drug Linker compound has the structure of:



,

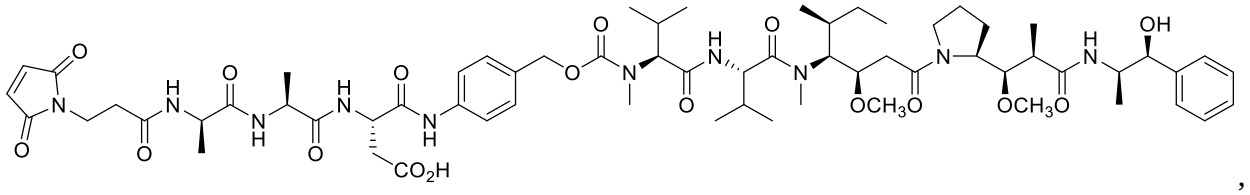


,



,

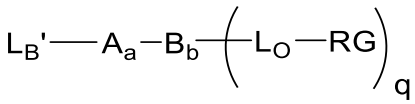
or



,

or a salt thereof.

[0038] In some examples, provided herein is 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;

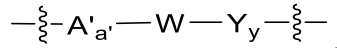
A is a first optional Stretcher Unit;

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 comprises 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 or is serine;

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

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

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,

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

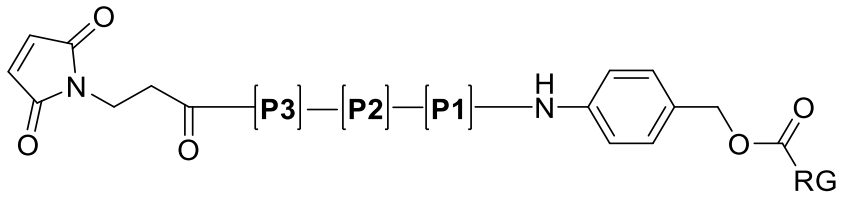
subscript q is an integer ranging from 1 to 4,

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

[0039] In some examples, 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.

[0040] In some examples, provided herein is the Linker compound, 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.

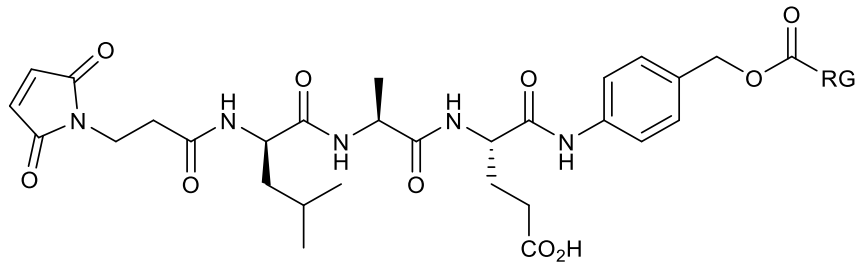
[0041] In some examples, provide herein is the Linker compound wherein the Linker compound has the structure of Formula **IA-L-3**:



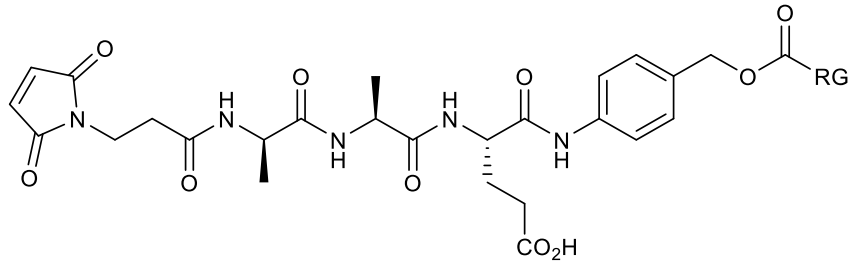
(**IA-L-3**),

or a salt thereof.

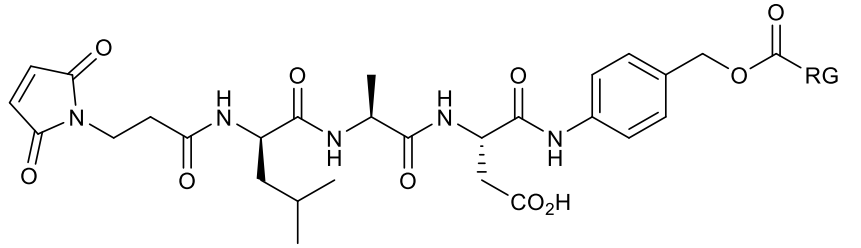
[0042] In some examples, provided herein is a Linker comound wherein the Linker compound has the structure of:



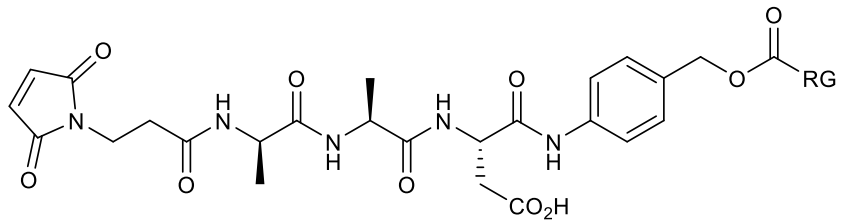
,



,



, or



,

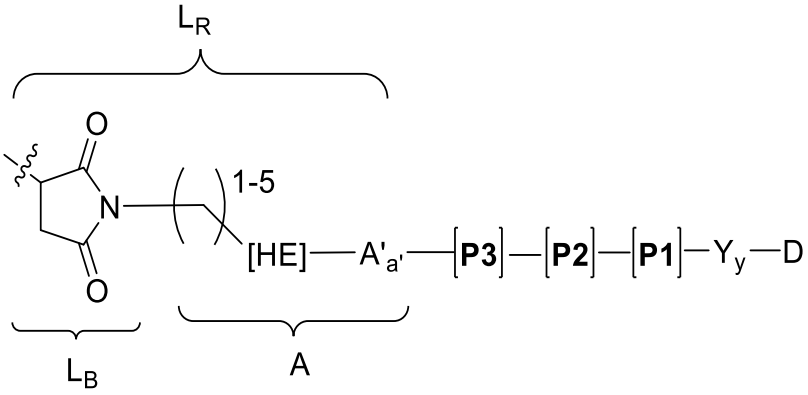
or a salt thereof.

[0043] In another example provided is a Ligand Drug Conjugate composition represented by Formula **1**:

Glu-Val-Cit- or -Asp-Val-Cit-; each Y when present 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. In some examples, W is a Peptide Cleavable Unit, wherein the Peptide Cleavable Unit comprises a tripeptide having the sequence -P3-P2-P1-, wherein one of the amino acids is negatively charged, another of the amino acids has a aliphatic side chain with hydrophobicity no greater than that of leucine and the remaining amino acid has hydrophobicity lower than that of leucine. In some examples, protease action upon the Peptide Cleavable Unit is capable of releasing D as the free drug.

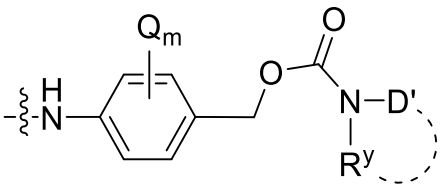
[0044] In some examples, a first one of the amino acids P1, P2, or P3 is negatively charged; a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine.

[0045] In some examples, the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition predominately have drug linker moieties of Formula 1H:

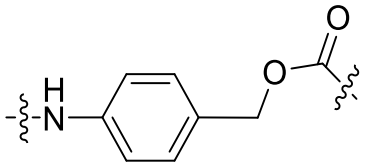


(Formula 1H)

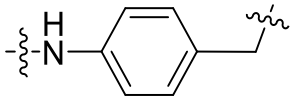
or pharmaceutically acceptable salts thereof, and optionally having a minority of Ligand Drug Conjugate compounds in which one or more of the drug linker moieties in each of such compounds has its succinimide ring in hydrolyzed form and wherein HE is a Hydrolysis Enhancing Unit; A' is a subunit, when present, of the indicated first Stretcher Unit (A); subscript a' is 0 or 1, indicating the absence or presence of A', respectively; and the wavy line indicates the site of covalent binding to a sulfur atom of the Ligand Unit. In some examples, HE is –C(=O). -Y_y-D has the structure of:



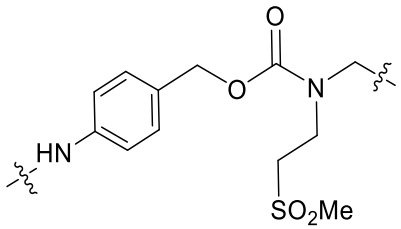
wherein -N(R^y)D' represents D, wherein D' is the remainder of D; the wavy line indicates the site of covalent attachment to P1; the dotted line indicates optional cyclization of R^y to D'; R^y is optionally substituted C_1-C_6 alkyl in absence of cyclization to D' or optionally substituted C_1-C_6 alkylene when cyclized to D'; each Q, when present, 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. In some examples, Y_y- has the structure of:



wherein the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to an oxygen, nitrogen, or sulfur atom of D to form a carbonate, carbamate, or thiocarbamate functional group that is shared between D and Y, or to a secondary nitrogen atom to form a carbamate that is shared between D and Y, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1. In some examples, Y_y- has the structure of:



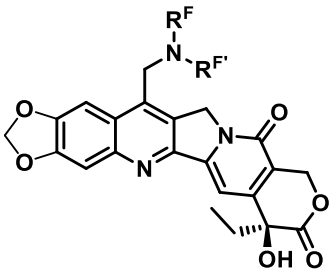
wherein the wavy line adjacent to the methylene carbon atom indicates the site of covalent attachment to a tertiary amine of D, such that -Y_y- is attached to D by way of a quaternized nitrogen atom that is part D, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1. In some examples, Y_y- has the structure of:



wherein the wavy line adjacent to the carbon atom of the methylene carbamate moiety indicates the site of covalent attachment to an oxygen atom of D to form a methylene alkoxy

carbamate moiety that is shared between D and Y and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1.

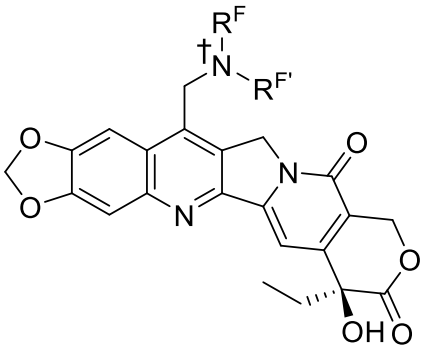
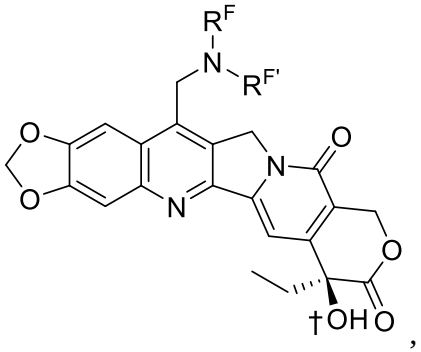
[0046] In some examples, D incorporates the structure of a camptothecin having a structure of



CPT6,

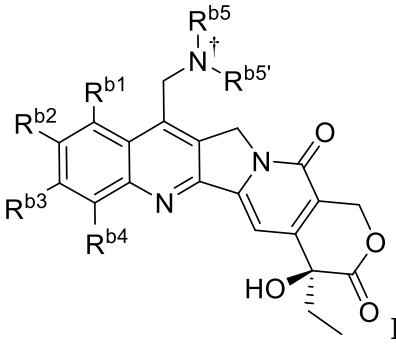
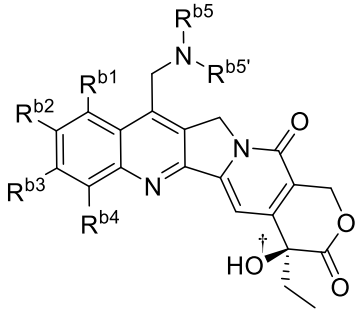
or a pharmaceutically acceptable salt thereof, wherein each R^F and $R^{F'}$ is independently selected from the group consisting of -H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl, or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; wherein the cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^F and $R^{F'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$.

[0047] In some examples, D has a formula of

wherein the dagger represents the point of covalent attachment of D to the secondary linker of the drug linker moiety. In some examples, R^F is selected from the group consisting of C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl. In some examples, $R^{F'}$ is -H. In some examples, $R^{F'}$ is methyl. In some examples, R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl.

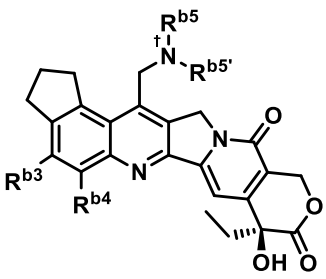
[0048] In some examples, D has a formula selected from the group consisting of


D_{2a}, and

$D2_b$,

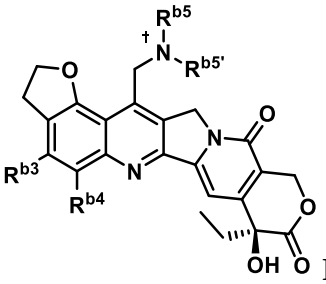
or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to the secondary linker of the drug linker moiety, R^{b1} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, (C_6-C_{12} aryl)-C_2-C_6 alkenyl- optionally substituted with -OR^a, -OR^a, -NHR^a, and -SR^a, or is combined with R^{b2} or R^{b5} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; R^{b2} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -NHR^a, and -SR^a, or is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; R^{b3} is selected from the group consisting of H, halogen, C_1-C_6

alkyl, C_1-C_6 haloalkyl, -OR^a, -NHR^a, and -SR^a, or is combined with R^{b2} or R^{b4} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; R^{b4} is selected from the group consisting of H or halogen, or is combined with R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; each R^{b5} and $R^{b5'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl-, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl-, NH_2-SO_2-C_1-C_8 alkyl-, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; or $R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$; and each R^a is independently selected from the group consisting of H, C_1-C_6 alkyl, and C_1-C_6 haloalkyl.

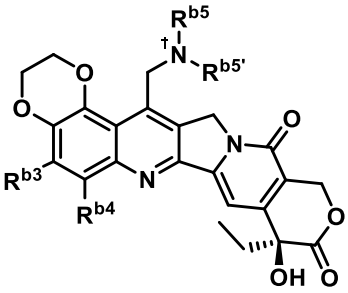
[0049] In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is halogen. In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is C_1-C_6 alkyl. In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is -OR^a, and R^a is H or C_1-C_6 alkyl. In some examples, R^{b5} and $R^{b5'}$ are each H. In some examples, D has a formula selected from the group consisting of



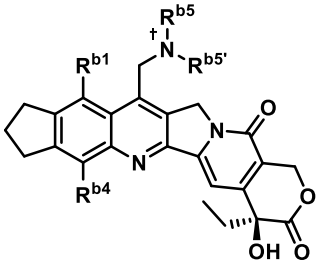
D_{1a}-I,



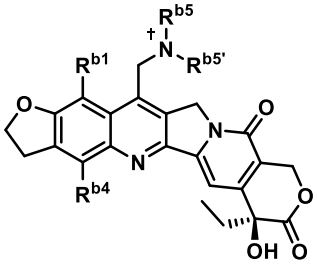
D_{1a}-II,



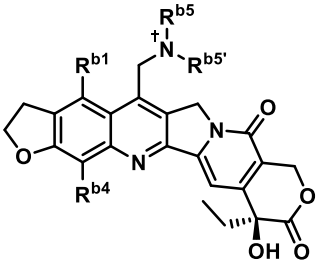
D_{1a}-III,



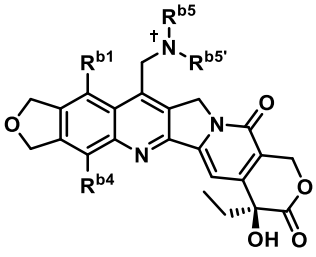
D_{1a}-IV,



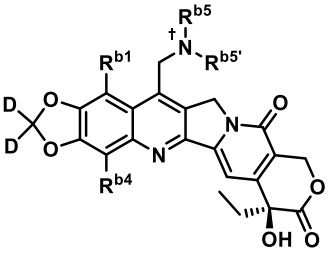
D_{1a}-V,



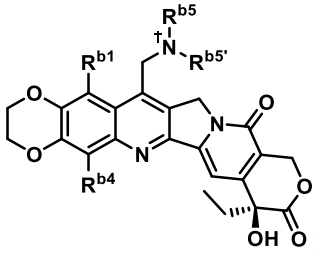
D_{1a}-VI,



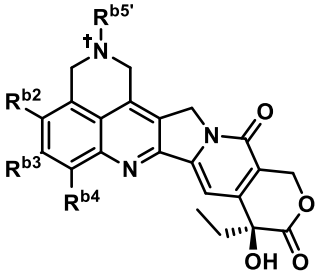
D_{1a}-VII,



D_{1a}-VIII,

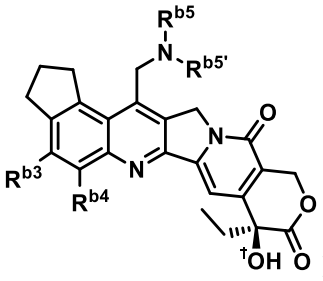


D_{1a}-IX , and

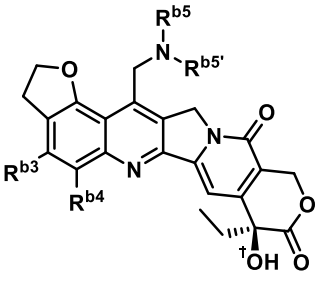


D_{1a}-X.

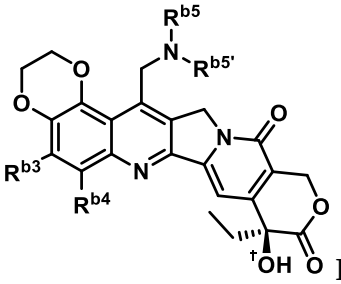
[0050] In some examples, D has a formula selected from the group consisting of



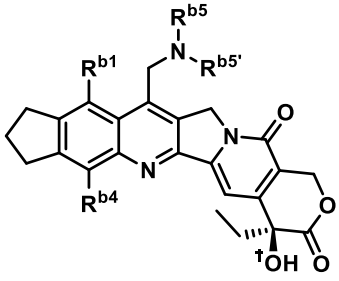
D_{1b}-I,



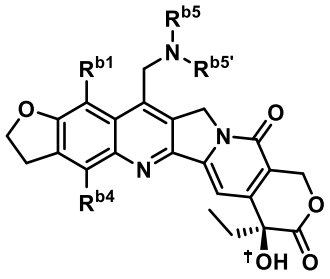
D_{1b}-II,



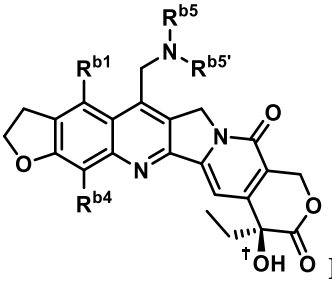
D_{1b}-III,



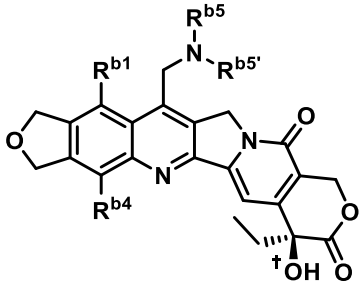
D_{1b}-IV,



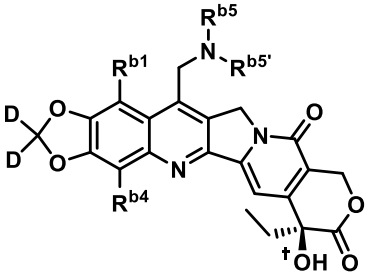
D_{1b}-V,



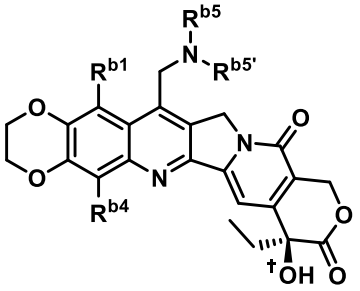
D_{1b}-VI,



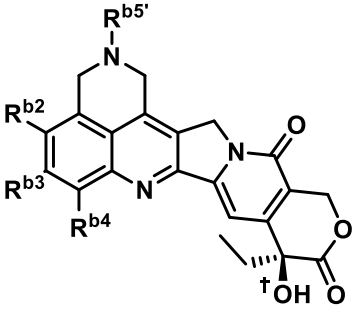
D_{1b}-VII,



D_{1b}-VIII,

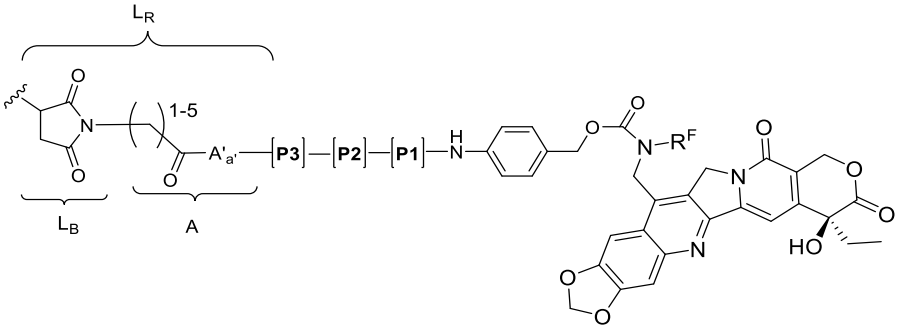


D_{1b}-IX , and

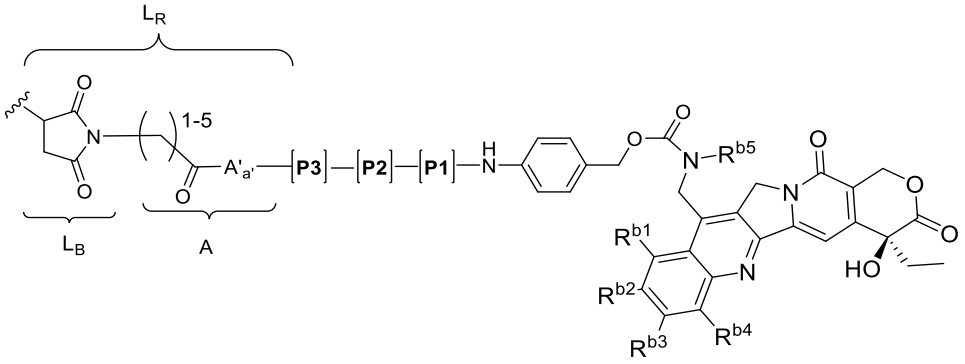


D_{1b}-X.

[0051] In some examples, subscript q is 1 and the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition predominately have drug linker moieties of:

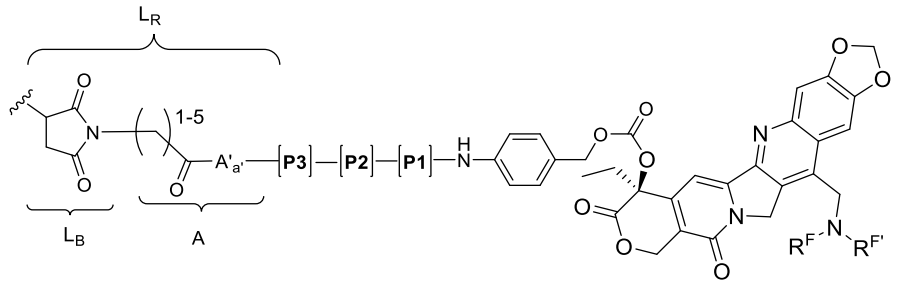


or

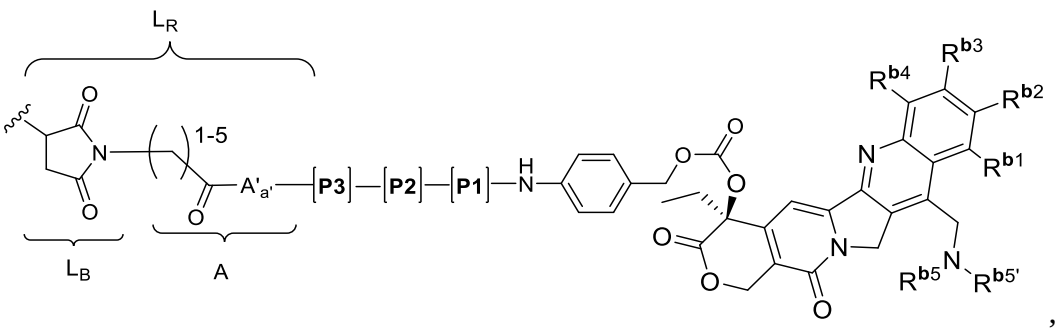


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or a pharmaceutical acceptable salt thereof, and optionally having a minority of Ligand Drug Conjugate compounds in which one or more of the drug linker moieties in each of such compounds has the succinimide ring in hydrolyzed form, and wherein: subscript a' is 0, and A' is absent; and the wavy line indicates the site of covalent attachment to a sulfur atom of the Ligand Unit. In some examples, subscript q is 1 and the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition predominately have drug linker moieties of:



or



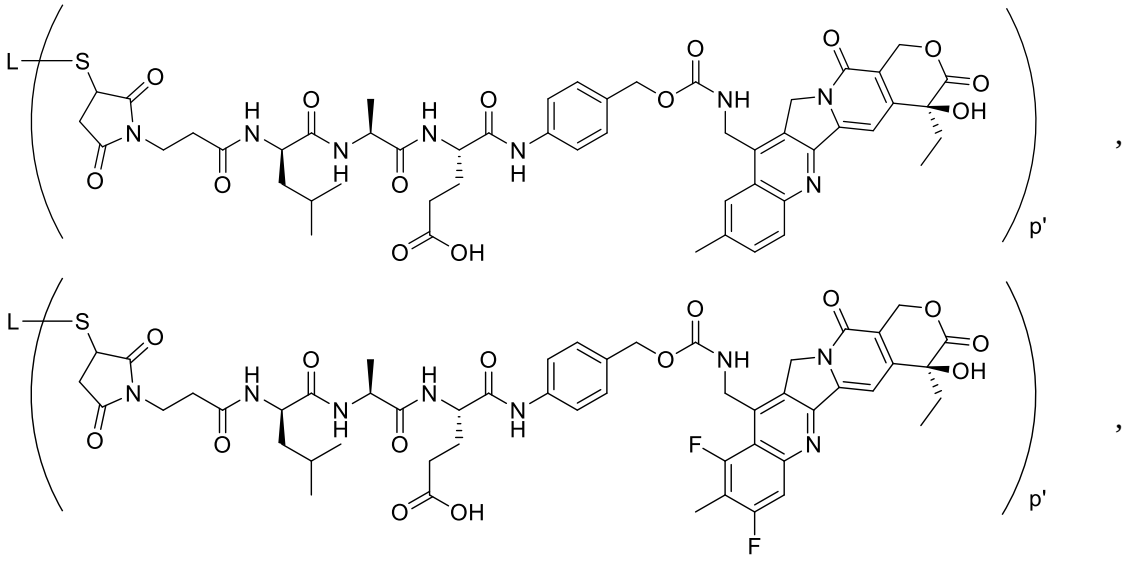
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or a pharmaceutical acceptable salt thereof, and optionally having a minority of Ligand Drug Conjugate compounds in which one or more of the drug linker moieties in each of such compounds has the succinimide ring in hydrolyzed form, and wherein: subscript a' is 0, and A' is absent; and the wavy line indicates the site of covalent attachment to a sulfur atom of the Ligand Unit.

[0052] In some examples, 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.

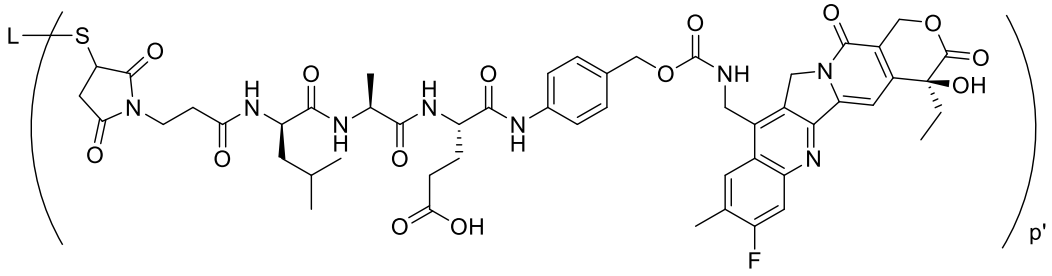
[0053] In some examples, the P3 amino acid is D-Leu or D-Ala. In some examples, the P2 or P1 amino acid has an aliphatic side chain with hydrophobicity no greater than that of valine, and the other of the P2 or P1 amino acid is negatively charged at plasma physiological pH. In some examples, the P2 amino 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. In some examples, -P2-P1- is -Ala-Glu- or -Ala-Asp-. In some examples, -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-. In some examples, the P3 amino acid is D-Leu or D-Ala, the P2 amino acid is Ala, Glu, or Asp, and the P1 amino acid is Ala, Glu, or Asp.

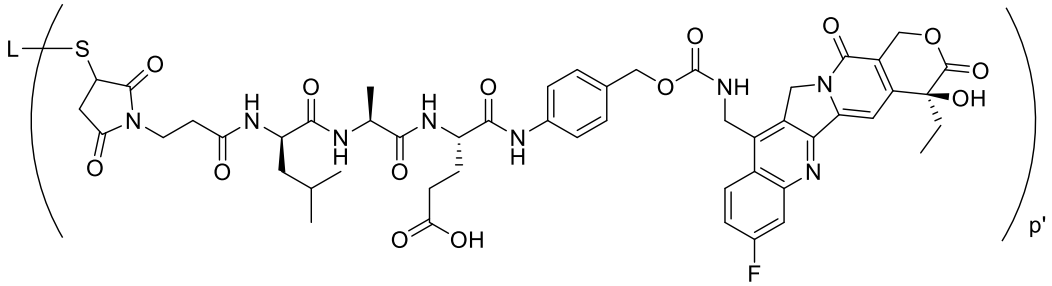
[0054] In some examples, the composition comprises Ligand Drug Conjugate compounds having the structure of:

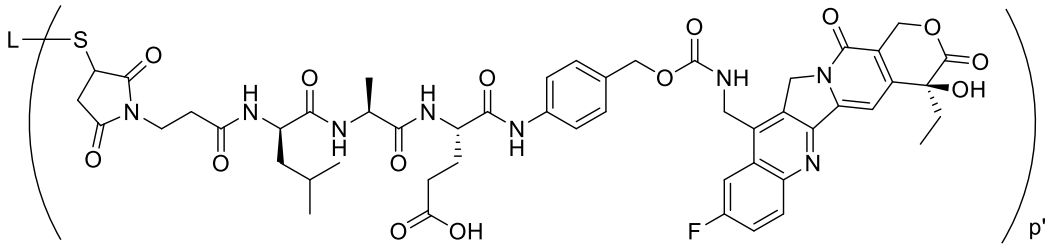


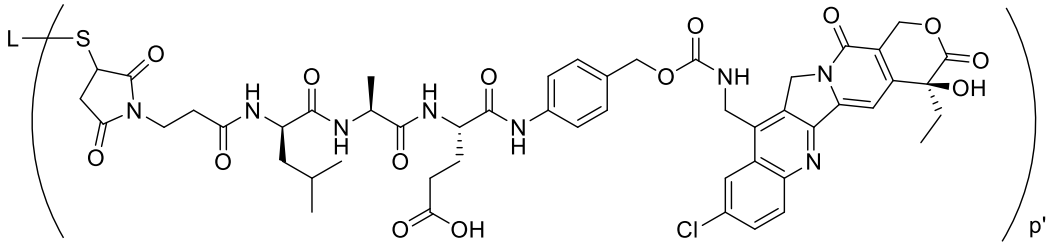
,

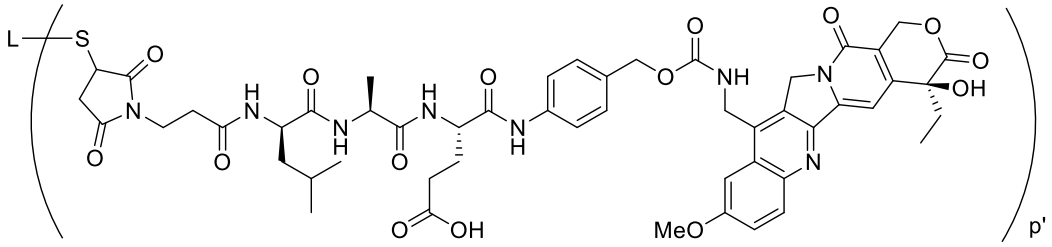
,


,


,


,


, or


,

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

[0055] In some examples, L is an antibody Ligand Unit of an intact antibody or an antigen-binding fragment thereof. In some examples, the intact antibody is an intact chimeric, humanized or human antibody. In some examples, the intact antibody or fragment thereof is capable of selectively binding to a cancer cell antigen. In some examples, the intact antibody or fragment thereof is capable of selectively binding to an immune cell antigen. In some examples, the intact antibody or fragment thereof is capable of selectively binding CD30. In some examples, the intact antibody or fragment

thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively. In some examples, the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8. In some examples, the intact antibody is cAC10. In some examples, the intact antibody or fragment thereof is capable of selectively binding LIV1. In some examples, the intact antibody or fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 518, 519, 520, 521, 522, and 523, respectively. In some examples, the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 524 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 525. In some examples, the intact antibody is ladiratuzumab. In some examples, the intact antibody or fragment thereof is capable of selectively binding TROP2. In some examples, the intact antibody is sacituzumab or datopotamab. In some examples, the intact antibody or fragment thereof is capable of selectively binding ALPP. In some examples, the intact antibody or fragment thereof is capable of selectively binding IL1RAP. In some examples, the intact antibody or fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 96, 97, 98, 99, 100, and 101, respectively. In some examples, the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 102 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 103. In some examples, the intact antibody is nidanilimab. In some examples, the intact antibody or fragment thereof is capable of selectively binding ASCT2. In some examples, the intact antibody or fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 794, 795, 796, 797, 798, and 799, respectively. In some examples, the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 801 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 802. In some examples, the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 790 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 791. In some examples, the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid

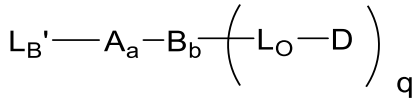
sequence of SEQ ID NO: 792 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 793.

[0056] In some examples, subscript p ranges from about 2 to about 12, or from about 2 to about 10, or from about 2 to about 8, or subscript p is about 2, about 4 or about 8.

[0057] In another example, provided herein is a pharmaceutically acceptable formulation, wherein the formulation comprises an effective amount of a Ligand Drug Conjugate composition described herein and at least one pharmaceutically acceptable excipient. In some examples, 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. In some examples, the formulation is a lyophilized solid or a liquid formulation, wherein the at least one excipient of the solid formulation is a lyoprotectant.

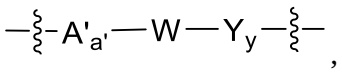
[0058] In another example, provided herein is a method of treating cancer comprising administering to a subject in need thereof a therapeutically effective amount of a Ligand Drug Conjugate composition described herein or a pharmaceutically acceptable formulation of any Ligand Drug Conjugate composition described herein.

[0059] In another example, provided herein is a Drug Linker compound of Formula **IA**:



(**IA**)

or a salt thereof, wherein D is a Drug Unit, wherein the Drug Unit is a camptothecin; 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;

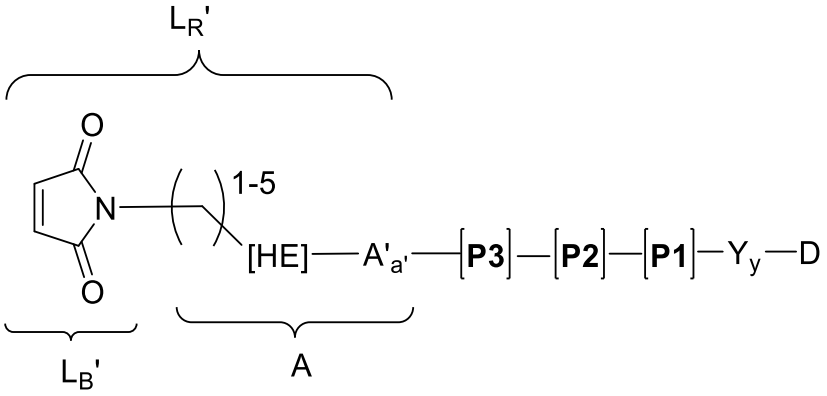


wherein the wavy line adjacent to Y indicates the site of covalent attachment of L_O to the Drug Unit and the wavy line adjacent to A' indicates the site of covalent attachment of L_O to the remainder of the Drug Linker compound; A' is a second optional Stretcher Unit, which when present and in the absence 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 comprises 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 or is serine; a second one of the amino acids P1, P2, or P3 has

an aliphatic side chain with hydrophobicity no greater than that of leucine, or is glycine or serine or proline; and a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine, or is proline, 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, 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, and provided that subscript q is 1 when subscript b is 0 and subscript q is 2, 3 or 4 when subscript b is 1.

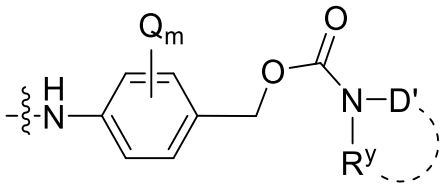
[0060] In some examples, a first one of the amino acids P1, P2, or P3 is negatively charged; a second one of the amino acids P1, P2, or P3 has an aliphatic side chain with hydrophobicity no greater than that of leucine; and a third one of the amino acids P1, P2, or P3 has hydrophobicity lower than that of leucine.

[0061] In some examples, the Drug Linker compound has the structure of Formula IH:



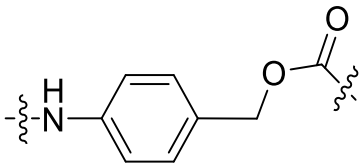
(Formula IH)

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', respectively. In some examples, HE is –C(=O). In some examples, -Y_y-D has the structure of:

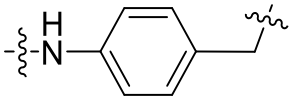


wherein -N(R^y)D' represents D, wherein D' is the remainder of D; the wavy line indicates the site of covalent attachment to P1; the dotted line indicates optional cyclization of R^y to

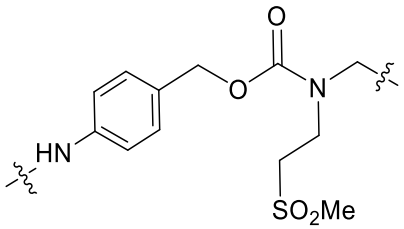
D'; R^y is optionally substituted C_1-C_6 alkyl in absence of cyclization to D' or optionally substituted C_1-C_6 alkylene when cyclized to D'; each Q is independently selected from the group consisting of -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), halogen, nitro and cyano; and subscript m is 0, 1 or 2. In some examples, Y_y- has the structure of:



wherein the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to an oxygen, nitrogen, or sulfur atom of D to form a carbonate, carbamate, or thiocarbamate functional group that is shared between D and Y, or to a secondary nitrogen atom to form a carbamate that is shared between D and Y, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1. In some examples, Y_y- has the structure of:

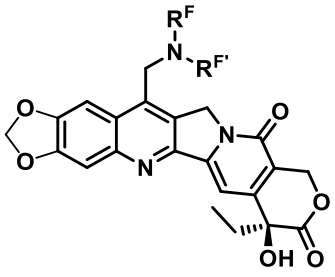


wherein the wavy line adjacent to the methylene carbon atom indicates the site of covalent attachment to a tertiary amine of D, such that -Y_y- is attached to D by way of a quaternized nitrogen atom that is part D, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1. In some examples, Y_y- has the structure of:



wherein the wavy line adjacent to the carbon atom of the methylene carbamate moiety indicates the site of covalent attachment to an oxygen atom of D to form a methylene alkoxy carbamate moiety that is shared between D and Y and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid residue of P1.

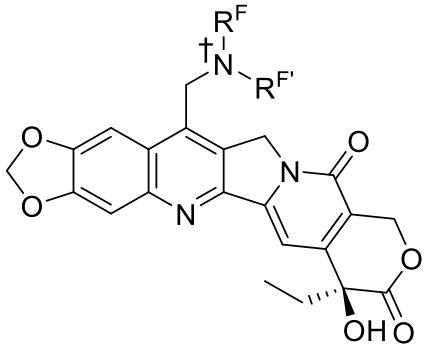
[0062] In some examples, D incorporates the structure of a camptothecin having a structure of



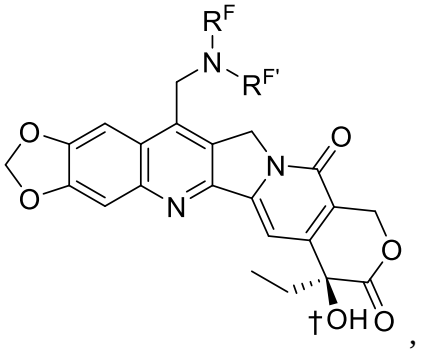
CPT6,

or a salt thereof, wherein each R^F and $R^{F'}$ is independently selected from the group consisting of -H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl, or and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; wherein the cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^F and $R^{F'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$.

[0063] In some examples, D has a formula of



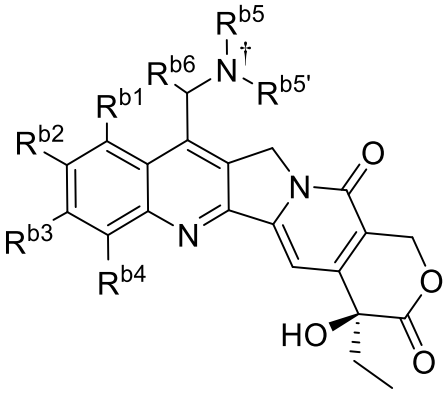
or



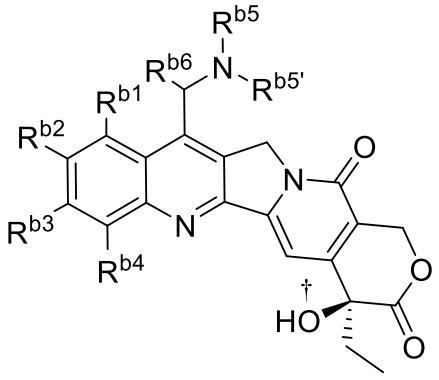
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wherein the dagger represents the point of attachment of D to the remainder of the Drug Linker compound. In some examples, R^F is selected from the group consisting of C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl. In some examples, $R^{F'}$ is -H. In some examples, $R^{F'}$ is methyl. In some examples, R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl.

[0064] In some examples, D has a formula selected from the group consisting of



D_{1a}, and



$D1_b$,

or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to the secondary linker of the drug linker moiety;

R^{b1} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, (C_6-C_{12} aryl)-C_2-C_8 alkenyl-, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminoalkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_6-C_{12} aryl-C(O)-, C_6-C_{12} aryl-O-C(O)-NR^a-, C_6-C_{12} aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

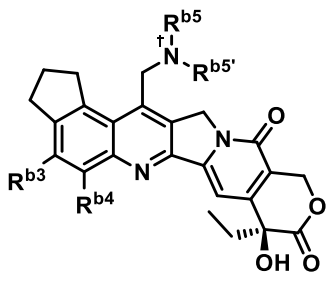
R^{b2} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, C_1-C_8 haloalkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-$S(O)_2$-, C_1-C_8 aminoalkyl, C_1-C_8 alkyl-

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkyl-$S(O)_2$-, C_1-C_6 alkyl-C(O)-, C_1-C_6 aminoalkyl-C(O)-, and C_1-C_6 hydroxyalkyl-C(O)-.

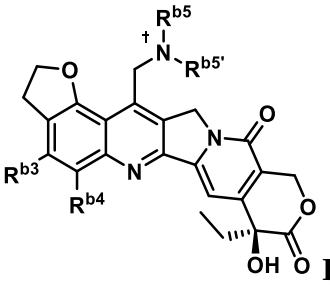
[0065] In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is halogen. In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is C_1-C_6 alkyl. In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is -OR^a, and R^a is H or C_1-C_6 alkyl. In some examples, R^{b5} and $R^{b5'}$ are each H.

[0066] In some examples, the site of covalent attachment of D to the secondary linker of the drug linker moiety is indicated by the dagger in formula D1a or D1b or any variation thereof (e.g., D1a-I through D1a-X, D1b-I through D1b-X, etc.). It is also contemplated that D may be covalently attached to the secondary linker of the drug linker moiety at any site in D that is compatible with attachment to the secondary linker (e.g., at any OH, NH_2, NHR, NR_2, SH, etc.), whether or not said site is marked by a dagger in any of the formulae herein.

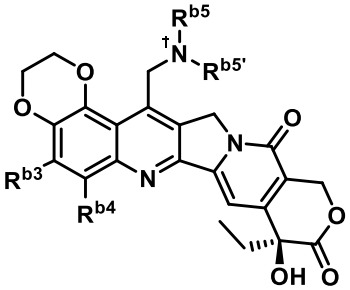
[0067] In some examples, D has a formula selected from the group consisting of



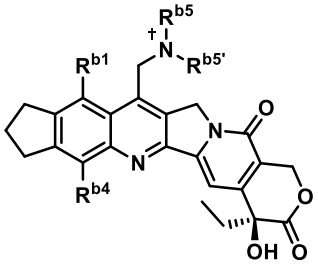
D_{1a}-I,



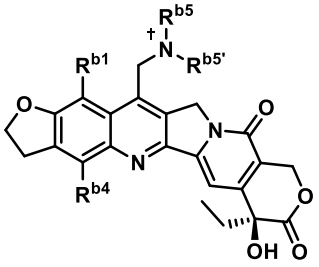
D_{1a}-II,



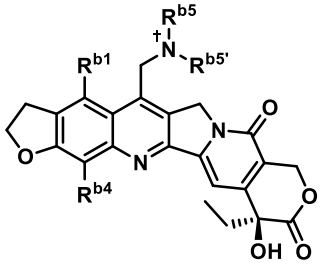
D_{1a}-III,



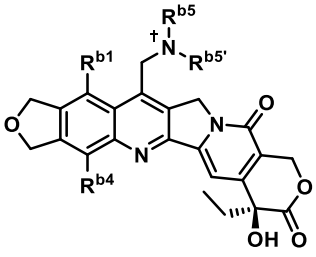
D_{1a}-IV,

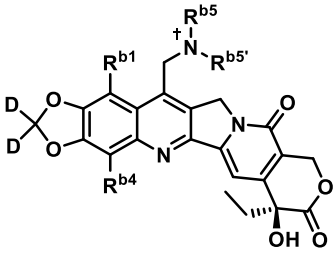


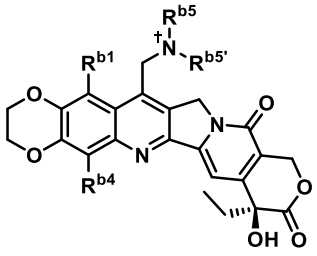
D_{1a}-V,

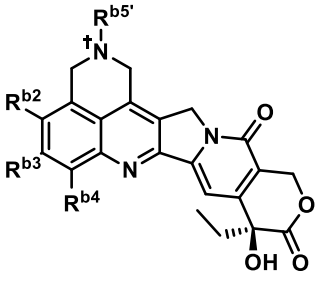


D_{1a}-VI,

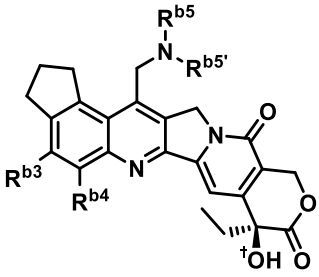

D_{1a}-VII,

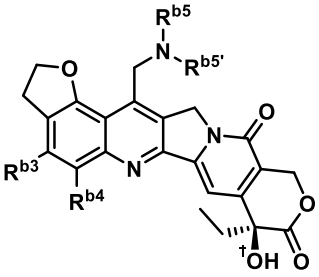

D_{1a}-VIII,

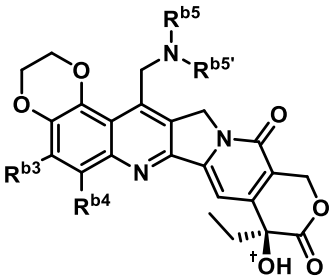

D_{1a}-IX , and

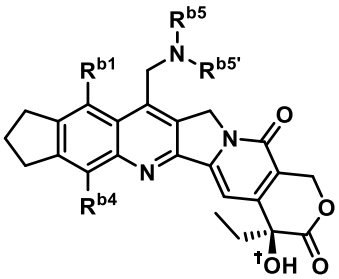

D_{1a}-X.

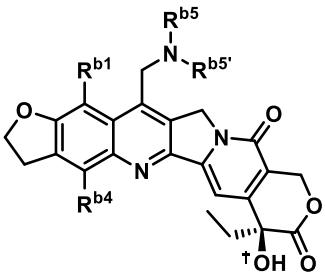
[0068] In some examples, D has a formula selected from the group consisting of

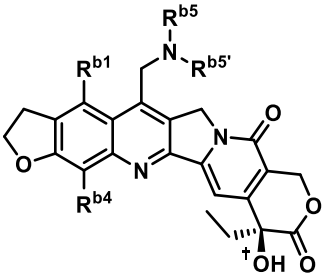

D_{1b}-I,

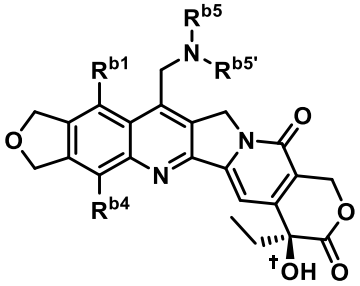

D_{1b}-II,

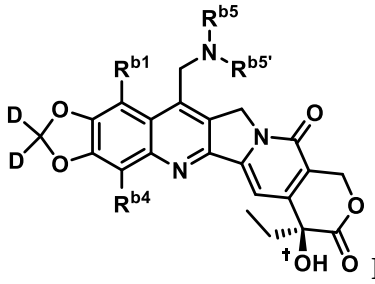

D_{1b}-III,

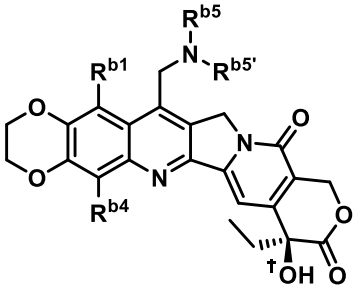

D_{1b}-IV,

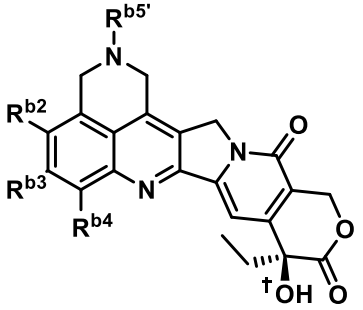

D_{1b}-V,


D_{1b}-VI,

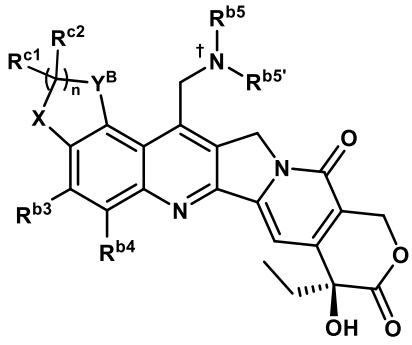

D_{1b}-VII,

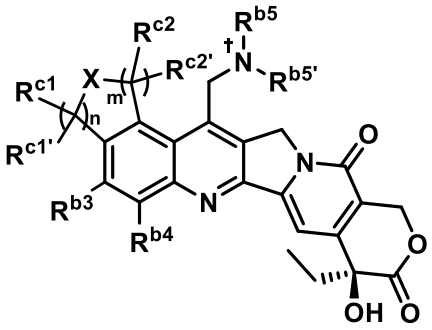

D_{1b}-VIII,

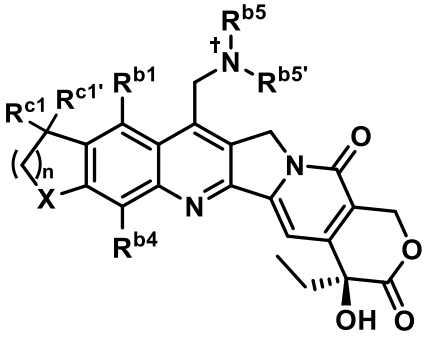

D_{1b}-IX , and

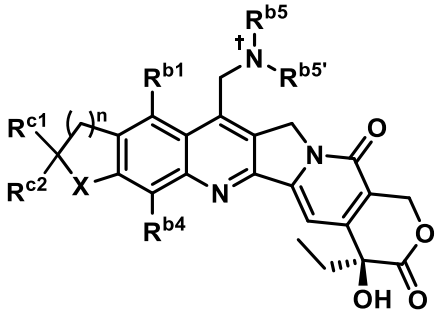

D_{1b}-X.

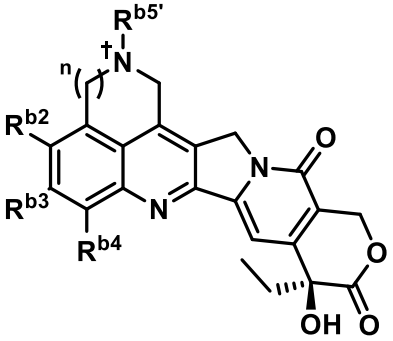
[0069] In some examples, D has a formula selected from the group consisting of


D1a-IIa,


D1a-IIb,


D1a-IVa,


D1a-IVb,


and **D1a-Xa**,

wherein

X and Y^B are each independently O, S, $S(O)_2$, $CR^xR^{x'}$, or NR^x;

R^x and $R^{x'}$ are each independently selected from the group consisting of H, OH, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 aminoalkyl-C(O)-, C_1-C_6 alkyl-C(O)-, C_1-C_6 hydroxyalkyl-C(O)-, C_1-C_6 alkyl-NH-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; and

m and n are each 1 or 2;

each R^{c1}, $R^{c1'}$, R^{c2}, and $R^{c2'}$ is independently

(i) selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; or

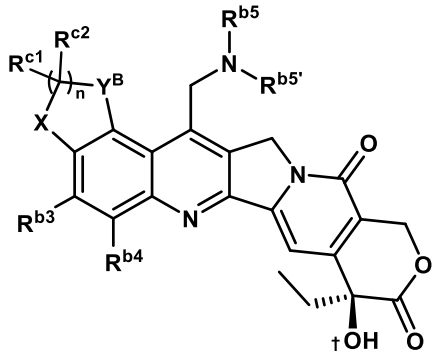
(ii) taken together with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo;

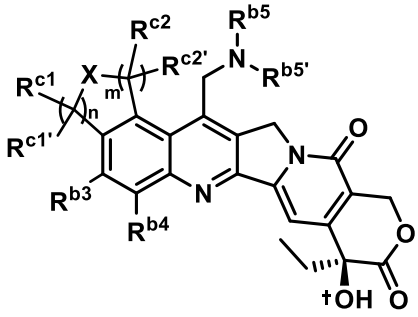
when m and n are both present, the sum of m + n is 2 or 3; and

the remaining variables are as defined for D_{1a} and D_{1b}.

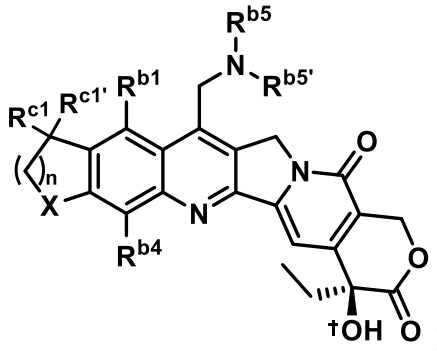
[0070] In some examples, D has a formula selected from the group consisting of



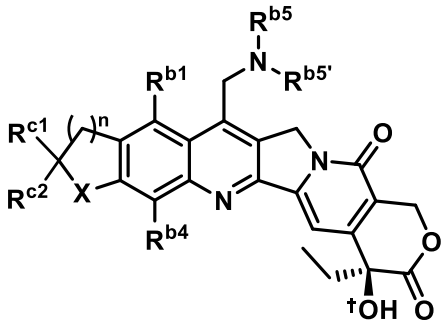
D1b-IIa,



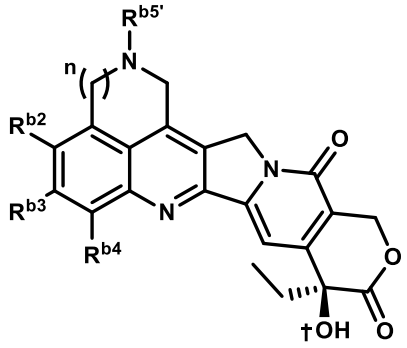
D1b-IIb,



D1b-IVa,



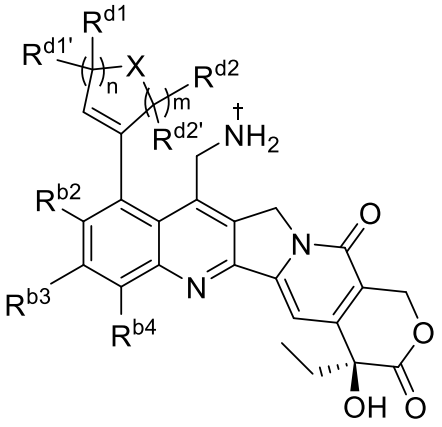
D1b-IVb,



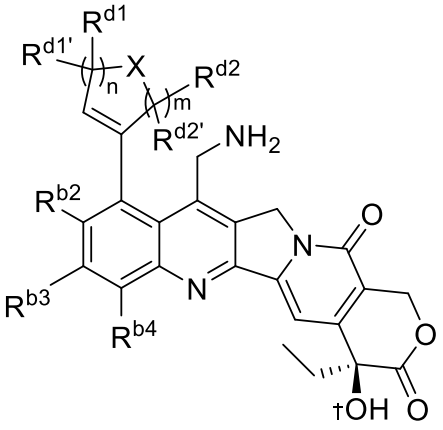
and **D1b-Xa**,

wherein the variables are as defined for **D_{1a}**, **D_{1b}**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**.

[0071] In some examples, D has a formula selected from the group consisting of



D1a-XI and



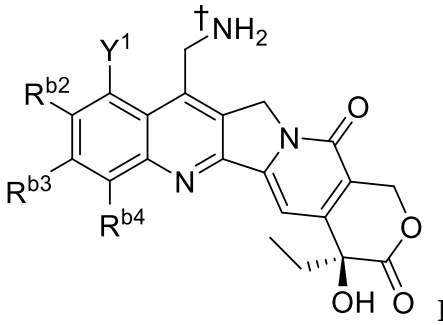
D1b-XI,

wherein

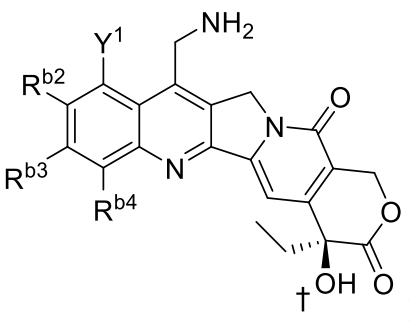
R^{d1}, $R^{d1'}$, R^{d2}, and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; and

the remaining variables are as defined for **D_{1a}**, **D_{1b}**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**.

[0072] In some examples, D has a formula selected from the group consisting of



D1a-XII and



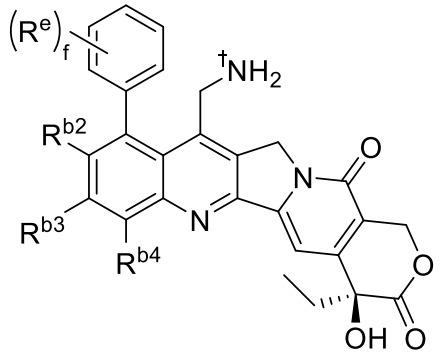
D1b-XII,

wherein

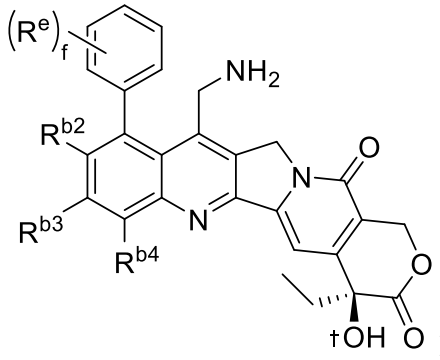
Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, or C_1-C_6 alkyl-$S(O)_2$-; and

the remaining variables are as defined for **D_{1a}**, **D_{1b}**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**.

[0073] In some examples, D has a formula selected from the group consisting of



D1a-XIII and



D1b-XIII,

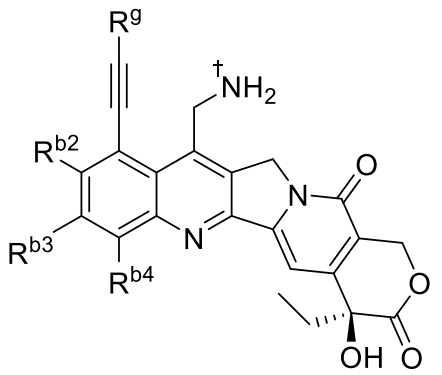
wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkyl-$S(O)_2$-, and C_1-C_6 alkyl-NR^a-C(O)-;

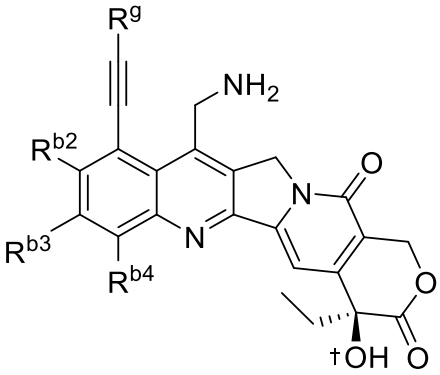
f is 0, 1, 2, 3, 4, or 5; and

the remaining variables are as defined for **D_{1a}**, **D_{1b}**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**.

[0074] In some examples, D has a formula selected from the group consisting of



D1a-XIV and



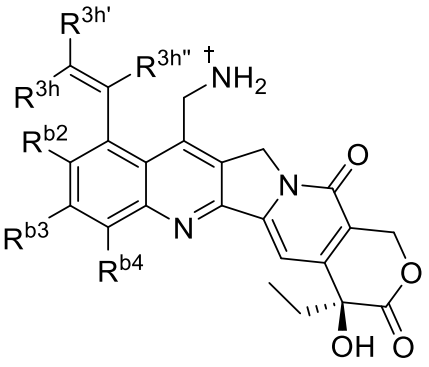
D1b-XIV,

wherein

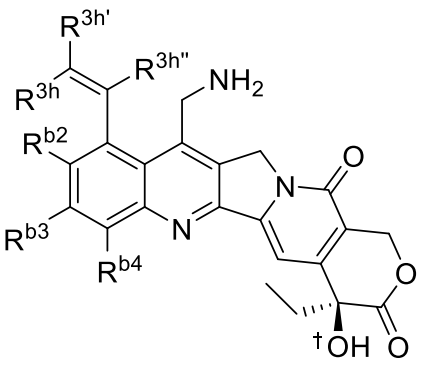
R^g is H, C_1-C_6 alkyl, or 3 to 8-membered heterocyclyl; and

the remaining variables are as defined for **D_{1a}**, **D_{1b}**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**.

[0075] In some examples, D has a formula selected from the group consisting of



D1a-XV and

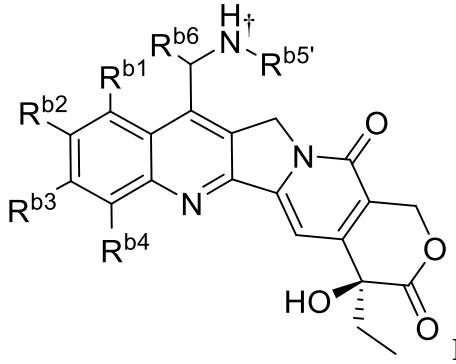


D1b-XV,

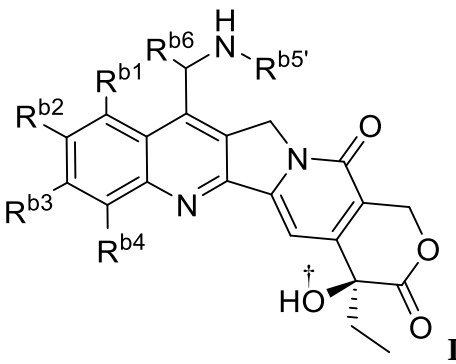
wherein

R^{3h}, $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -C(O)-C_1-C_6 alkyl, -C(O)O-C_1-C_6 alkyl, -C(O)NH-C_1-C_6 alkyl, C_6-C_{10} aryl, -C_6-C_{10} aryl-C_1-C_6 alkyl, and -C_6-C_{10} aryl-C_1-C_6 alkoxy; each optionally substituted with, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a; and the remaining variables are as defined for **D_{1a}**, **D_{1b}**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**.

[0076] In some examples, D has a formula selected from the group consisting of



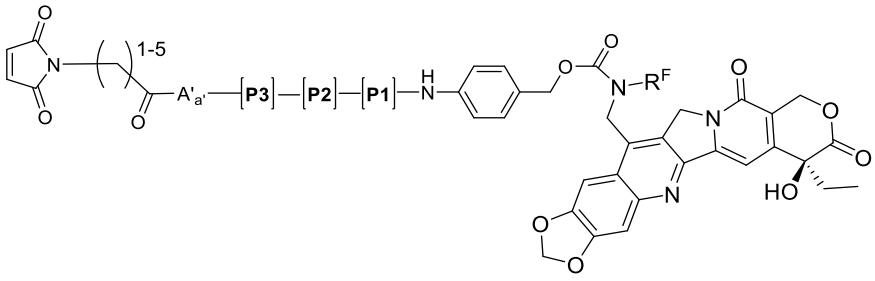
D1a-XVI and



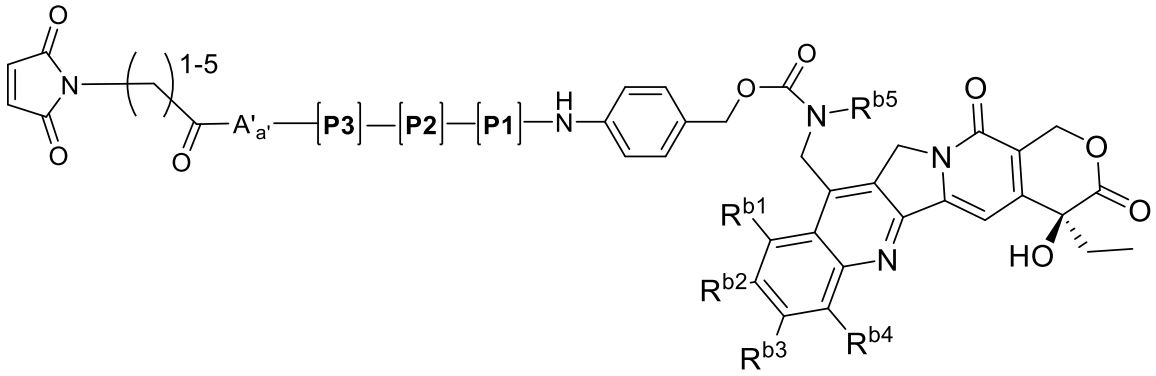
DIb-XVI,

wherein the variables are as defined for **D_{1a}**, **D_{1b}**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**.

[0077] In some examples, the Drug Linker compound has the structure:

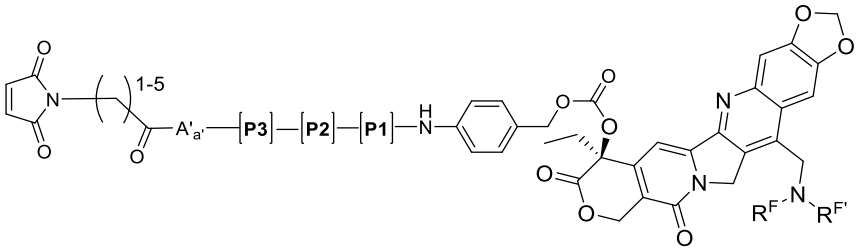


or

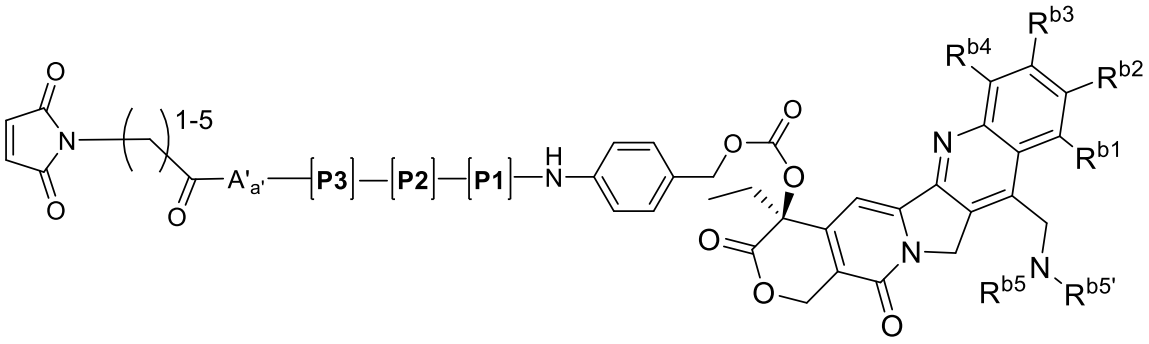


,

or a salt thereof, wherein subscript a' is 0, and A' is absent. In some examples, the Drug Linker compound has the structure:



or



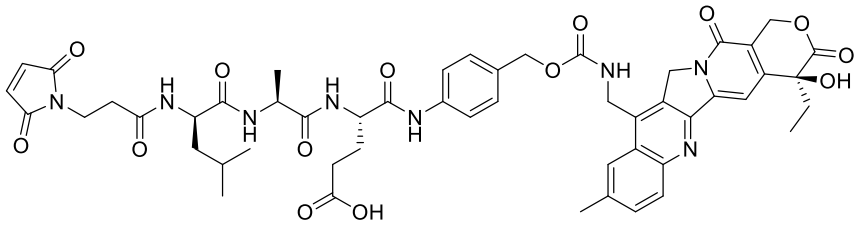
,

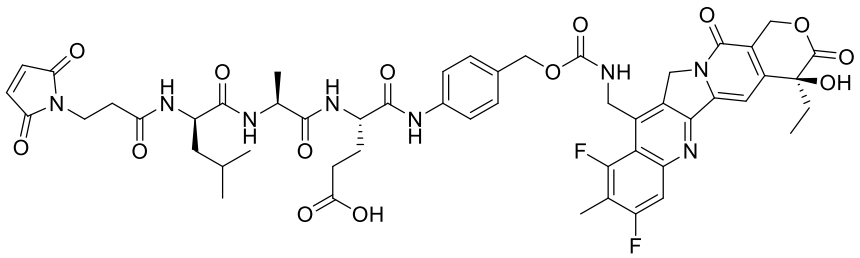
or a salt thereof, wherein subscript a' is 0, and A' is absent.

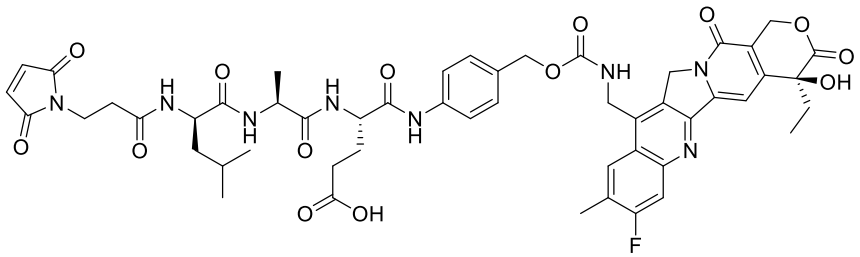
[0078] In some examples, Peptide Cleavable Unit is a tripeptide having the sequence -P3-P2-P1-, wherein P1, P2, and P3 are each an amino acid, wherein: the P3 amino acid of the tripeptide is in the D-amino acid configuration; one of the P2 and P1 amino acids has an aliphatic side chain with hydrophobicity lower than that of leucine; and the other of the P2 and P1 amino acids is negatively charged. In some examples, the P3 amino acid is D-Leu or D-Ala. In some examples, one of the P2 or P1 amino acid has an aliphatic side chain

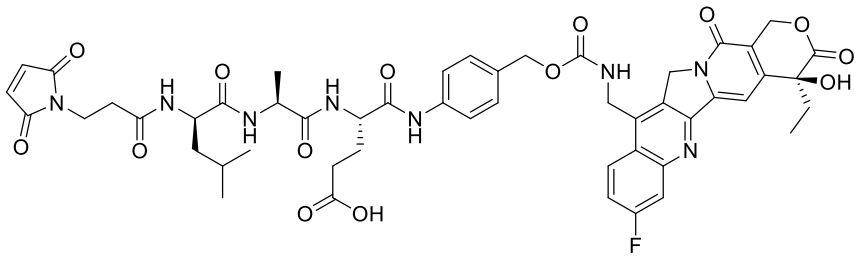
with hydrophobicity no greater than that of valine, and the other of the P2 or P1 amino acid is negatively charged at plasma physiological pH. In some examples, the P2 amino acid has an aliphatic side chain with hydrophobicity no greater than that of valine, and the P1 amino acid is negatively charged at plasma physiological pH. In some examples, -P2-P1- is -Ala-Glu- or -Ala-Asp-. In some examples, -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-. In some examples, the P3 amino acid is D-Leu or D-Ala, the P2 amino acid is Ala, Glu, or Asp, and the P1 amino acid is Ala, Glu, or Asp.

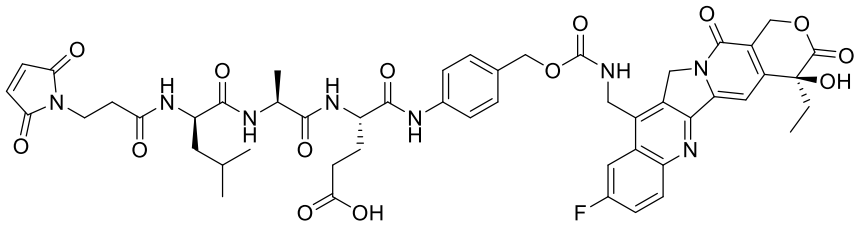
[0079] In some examples, the Drug Linker compound has the structure of:

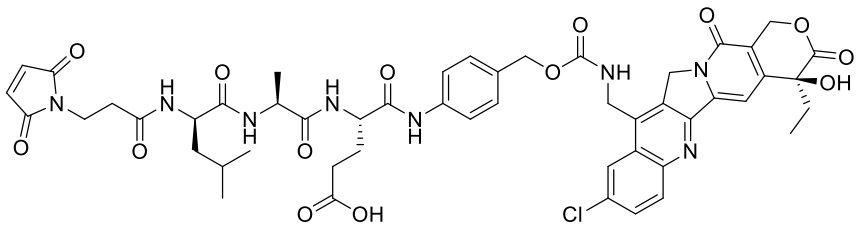

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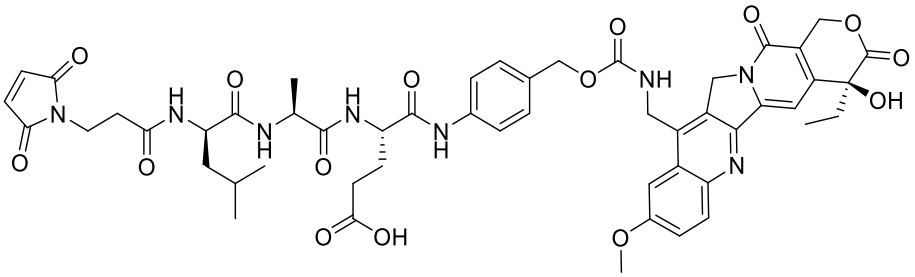

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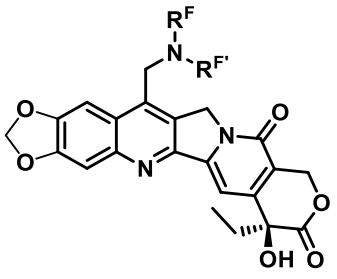
, or



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or a salt thereof.

[0080] In another example, provided is a compound of Formula **CPT6**:

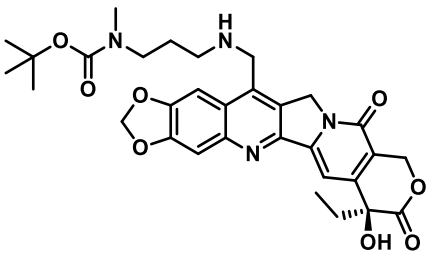
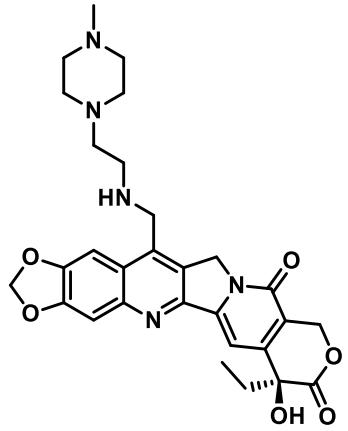
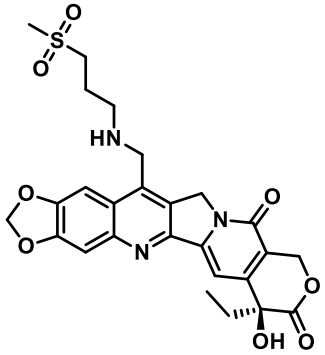
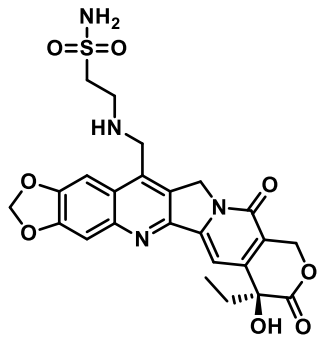


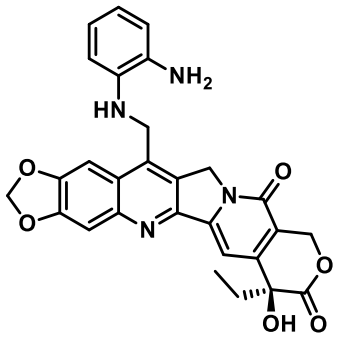
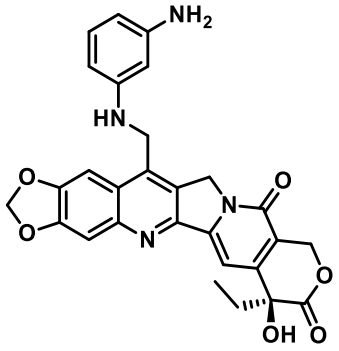
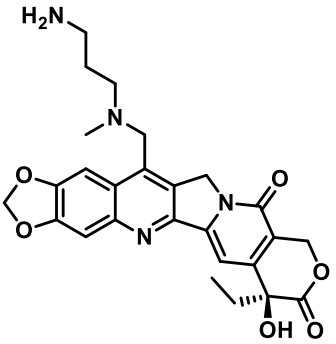
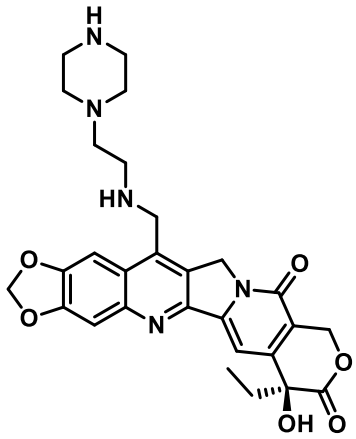
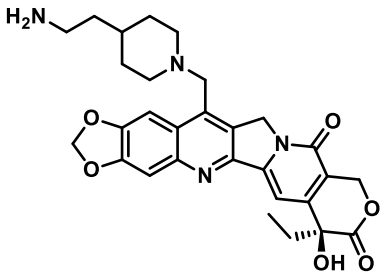
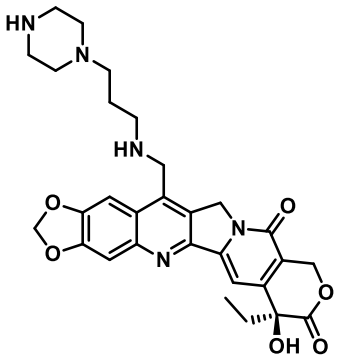
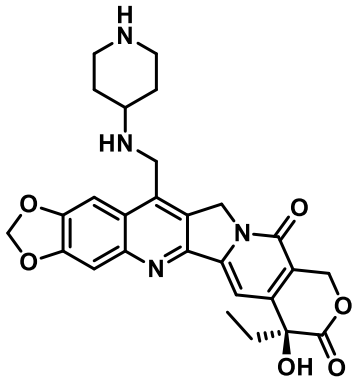
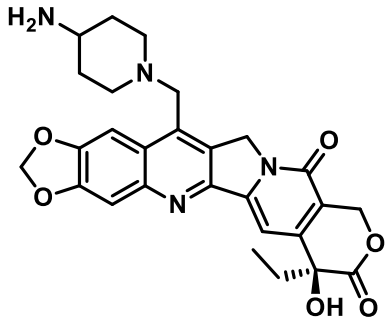
CPT6,

or a salt thereof, wherein each R^F and $R^{F'}$ is independently selected from the group consisting of -H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl, or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; wherein the cycloalkyl, heterocycloalkyl, phenyl

and heteroaryl portions of R^F and $R^{F'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$.

[0081] In some examples, R^F is selected from the group consisting of C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl. In some examples, $R^{F'}$ is -H. In some examples, $R^{F'}$ is methyl. In some examples, R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl. In some examples, the compound is selected from the group consisting of:

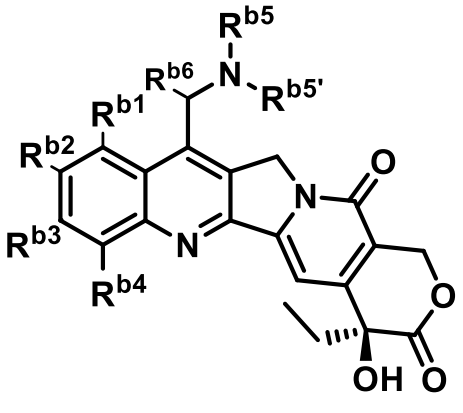

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[0082] In another example, provided is a compound of Formula $\mathbf{D_A}$:

wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$; and each R^a is independently selected from the group consisting of H, C_1-C_6 alkyl, and C_1-C_6 haloalkyl.

[0083] In some examples, D is a Drug Unit having a formula of



D1,

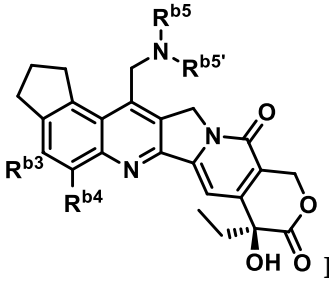
or a salt thereof; wherein

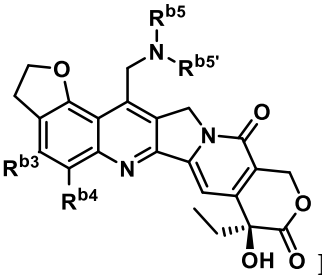
R^{b1} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, (C_6-C_{12} aryl)-C_2-C_8 alkenyl-, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminoalkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_6-C_{12} aryl-C(O)-, C_6-C_{12} aryl-O-C(O)-NR^a-, C_6-C_{12} aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

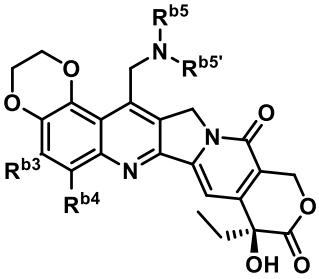
R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

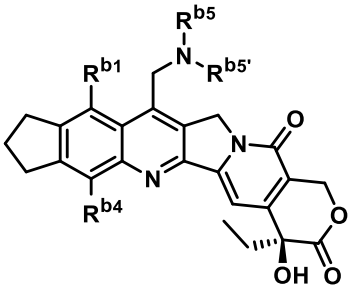
R^{b2} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, C_1-C_8 haloalkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-S(O)$_2$-, C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminolkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-NR^a-, C_1-C_8 alkyl-NR^a-C(O)O-, C_1-C_8 alkyl-OC(O)-NR^a-, C_6-C_{12} aryl-C(O)-, C_6-C_{12} aryl-O-C(O)-NR^a-, C_6-C_{12} aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

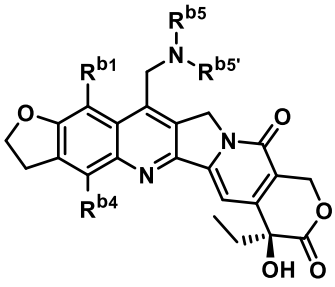
[0084] In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is halogen. In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is C_1-C_6 alkyl. In some examples, at least one of R^{b1}, R^{b2}, R^{b3}, and R^{b4} is -OR^a, and R^a is H or C_1-C_6 alkyl. In some examples, R^{b5} and $R^{b5'}$ are each H. In some examples, the compound has a formula selected from the group consisting of

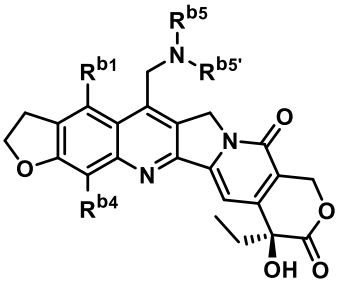

D1-I,

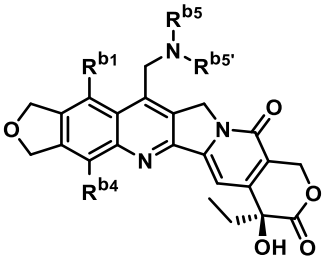

D1-II,

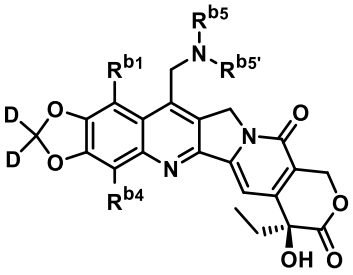

D1-III,

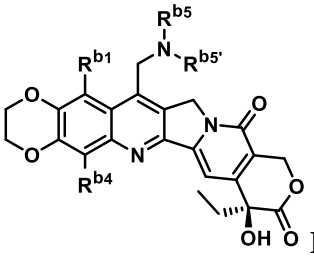

D1-IV,

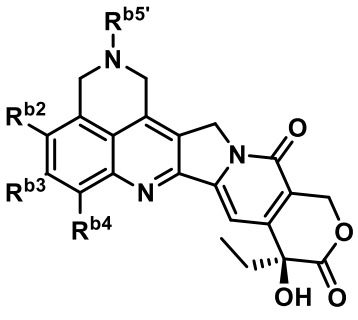

D1-V,


D1-VI,

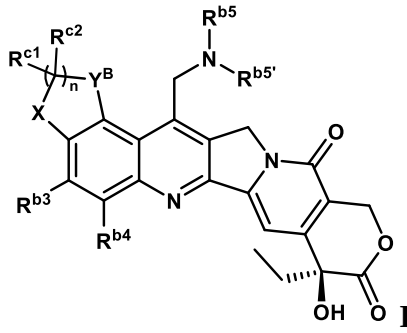

D1-VII,


D1-VIII,

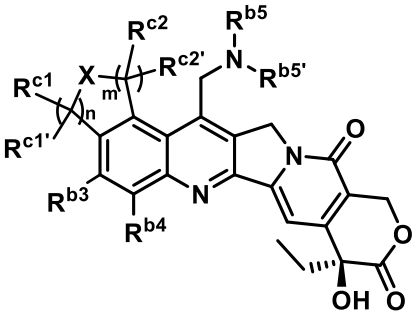

D1-IX, and


D1-X.

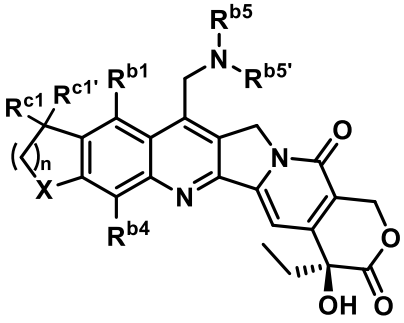
[0085] In some examples, D has a formula selected from the group consisting of



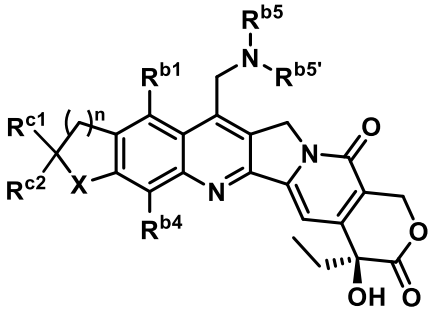
D1-IIa,



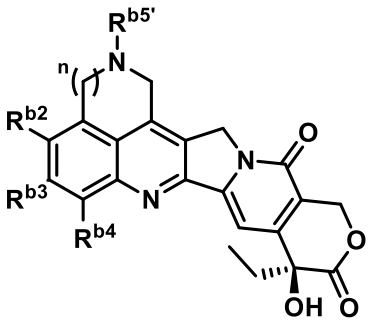
D1-IIb,



D1-IVa,



D1-IVb,



and **D1-Xa**,

wherein

X and Y^B are each independently O, S, $S(O)_2$, $CR^xR^{x'}$, or NR^x;

R^x and $R^{x'}$ are each independently selected from the group consisting of H, OH, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 aminoalkyl-C(O)-, C_1-C_6 alkyl-C(O)-, C_1-C_6 hydroxyalkyl-C(O)-, C_1-C_6 alkyl-NH-C(O)-, or C_1-C_6 alkyl-$S(O)_2$-; and

m and n are each 1 or 2;

each R^{c1}, $R^{c1'}$, R^{c2}, and $R^{c2'}$ is independently

(i) selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; or

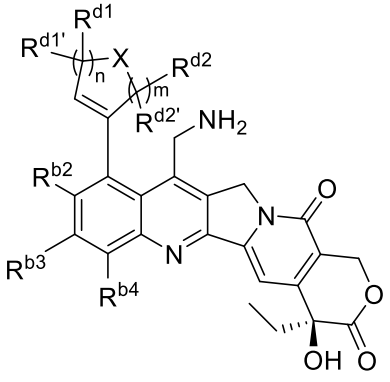
(ii) taken together with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo;

when m and n are both present, the sum of m + n is 2 or 3; and

the remaining variables are as defined for D_1.

[0086] In some examples, D has a formula selected from the group consisting of



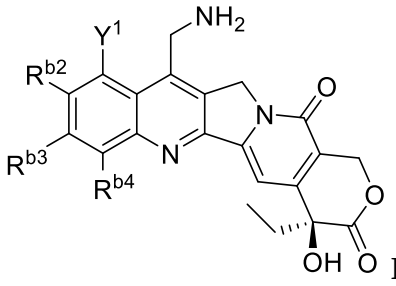
D1-XI,

wherein

R^{d1}, $R^{d1'}$, R^{d2}, and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; and

the remaining variables are as defined for **D_1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0087] In some examples, D has a formula selected from the group consisting of



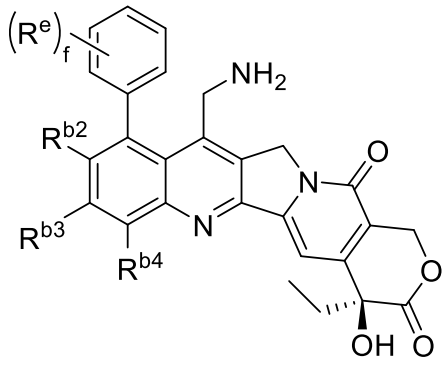
D1-XII,

wherein

Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, or C_1-C_6 alkyl-$S(O)_2$-; and

the remaining variables are as defined for **D_1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0088] In some examples, D has a formula selected from the group consisting of



D1-XIII,

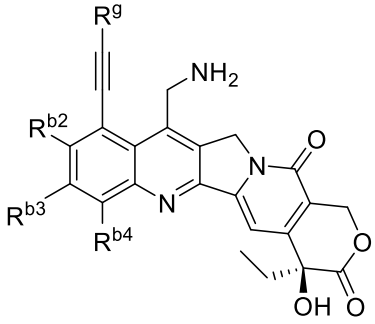
wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkyl-$S(O)_2$-, and C_1-C_6 alkyl-NR^a-C(O)-;

f is 0, 1, 2, 3, 4, or 5; and

the remaining variables are as defined for **D_1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0089] In some examples, D has a formula selected from the group consisting of



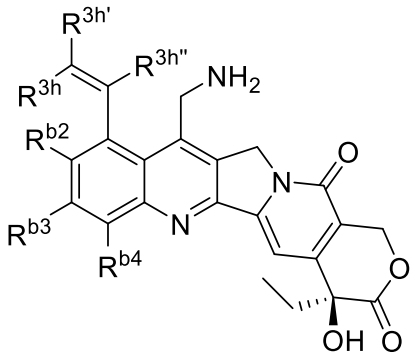
D1-XIV,

wherein

R^g is H, C_1-C_6 alkyl, or 3 to 8-membered heterocyclyl; and

the remaining variables are as defined for **D_1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0090] In some examples, D has a formula selected from the group consisting of



D1-XV,

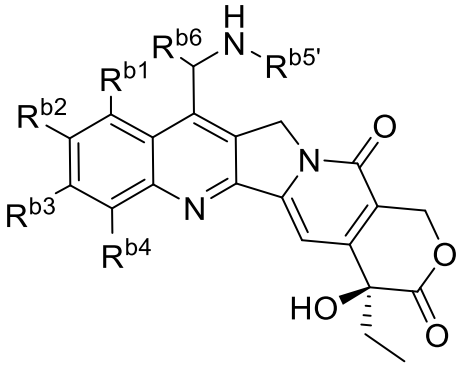
wherein

R^{3h}, $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H,

C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -C(O)-C_1-C_6 alkyl, -C(O)O-C_1-C_6 alkyl, -

C(O)NH-C_1-C_6 alkyl, C_6-C_{10} aryl, -C_6-C_{10} aryl-C_1-C_6 alkyl, and -C_6-C_{10} aryl-C_1-C_6 alkoxy; each optionally substituted with, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a; and the remaining variables are as defined for **D_1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0091] In some examples, D has a formula selected from the group consisting of



D1-XVI,

[0092] wherein the variables are as defined for **D_1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0093] Those and other examples of the present disclosure are described in more detail in the following "Detailed Description of the Invention" and "Claims".

BRIEF DESCRIPTION OF THE DRAWINGS

[0094] Figures 1A, 1B, 1C, and 1D. Tumor volume vs days post implant in a xenograft model treated with a series of 4-loaded ADCs having varying tripeptide sequences as the Peptide Cleavable Unit with drug-linker moieties represented by the formula of mp-P_3-P_2-P_1-PABC-MMAE at sub-curative doses compared to a subcurative dose of a 4-loaded ADC targeting the same cancer cell antigen and having drug-linker moieties represented by the formula of mc-val-cit-PABC-MMAE. Compounds in Figure 1A were tested at at 4 mg/kg. Compounds in Figure 1B and Figure 1D were tested at 3 mg/kg. Compounds in Figure 1C were tested at 6 mg/kg.

[0095] Figures 2A-2C. Neutrophil counts after day 4 of 10 mg/Kg administration (Figures 2A and 2B) or after days 8 and 22 of a highest tolerated dose (Figure 2C) of a series of 4-loaded non-binding control conjugates having varying tripeptide sequences as the Peptide Cleavable Unit with drug-linker moieties represented by the formula of mp-P_3-P_2-P_1-PABC-MMAE in comparison to 4-loaded non-binding conjugates having drug-linker moieties represented by the formula of mc-val-cit-PABC-MMAE or mp-val-cit-PABC-MMAE.

WHAT IS CLAIMED IS:

1. 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;

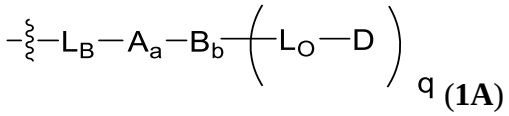
LU is a Linker Unit;

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 about 4 or about 8,

wherein the Ligand Unit is from an antibody or an antigen-binding fragment of an antibody, wherein the antibody or the antigen-binding fragment 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, wherein the Drug Unit is a camptothecin;

L_B is a ligand covalent binding moiety;

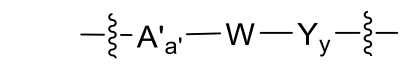
A is a first optional Stretcher Unit;

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 of L_O to the remainder of the drug linker moiety;

A' is a second optional Stretcher Unit, which when present and 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 comprises 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 or is serine;

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

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

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,

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

each Y when present 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.

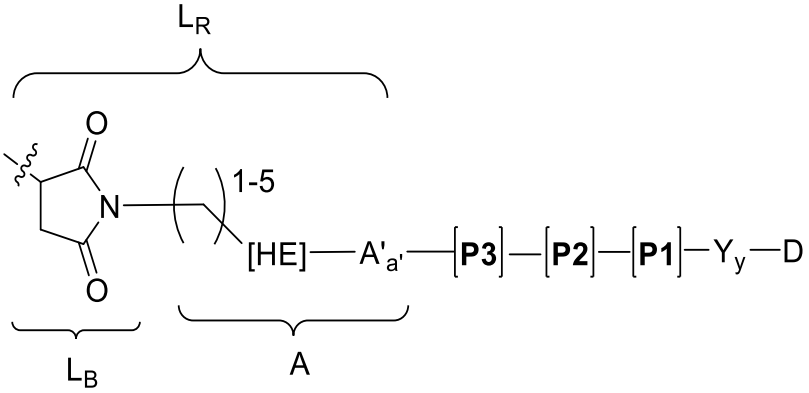
2. The Ligand Drug Conjugate composition of claim 1, wherein

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

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

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

(b) the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition predominately 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

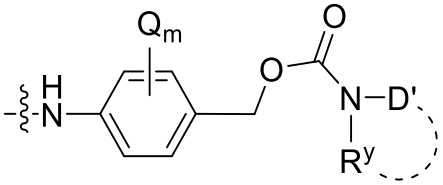
HE is a Hydrolysis Enhancing Unit, optionally, wherein HE is –C(=O);

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', respectively; and

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

3. The Ligand Drug Conjugate composition of claim 1 or 2, wherein:

(a) -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;

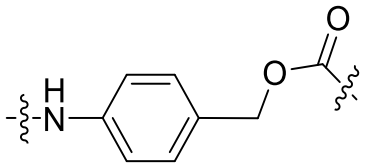
the dotted line indicates optional cyclization of R^y to D';

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

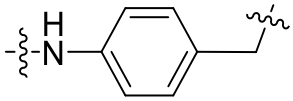
subscript m is 0, 1 or 2;

(b) Y_y- has the structure of:



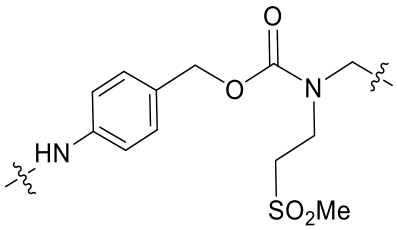
wherein the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to an oxygen, nitrogen, or sulfur atom of D to form a carbonate, carbamate, or thiocarbamate functional group that is shared between D and Y, or to a secondary nitrogen atom to form a carbamate that is shared between D and Y, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1;

(c) Y_y- has the structure of:



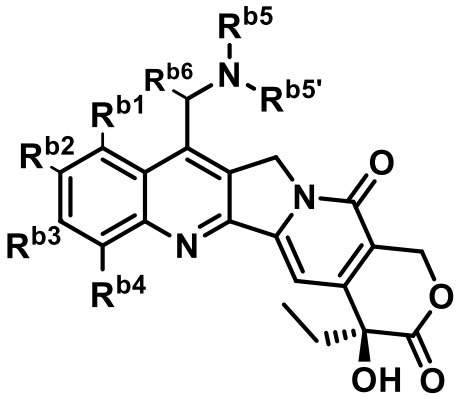
wherein the wavy line adjacent to the methylene carbon atom indicates the site of covalent attachment to a tertiary amine of D, such that -Y_y- is attached to D by way of a quaternized nitrogen atom that is part D, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1; or

(d)Y_y- has the structure of:



wherein the wavy line adjacent to the carbon atom of the methylene cabamate moiety indicates the site of covalent attachment to an oxygen atom of D to form a methylene alkoxy

carbamate moiety that is shared between D and Y and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1.

4. The Ligand Drug Conjugate composition of any one of claims 1-3, wherein D has a formula of  **D_1**,

or a salt thereof; wherein

R^{b1} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, C_3-C_{10} heterocycloalkyl, (C_6-C_{12} aryl)-C_2-C_8 alkenyl-, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminoalkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_1-C_6 aryl-C(O)-, C_1-C_6 aryl-O-C(O)-NR^a-, C_1-C_6 aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-$S(O)_2$-, C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminolkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-NR^a-, C_1-C_8 alkyl-NR^a-C(O)O-, C_1-C_8 alkyl-OC(O)-NR^a-, C_1-C_6 aryl-C(O)-, C_1-C_6 aryl-O-C(O)-NR^a-, C_1-C_6 aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and $R^{b5'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl-, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl-, NH_2-SO_2-C_1-C_8 alkyl-, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; or

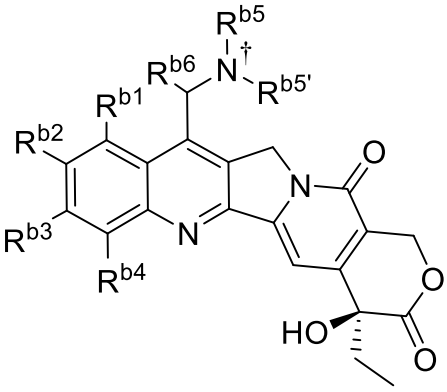
$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$;

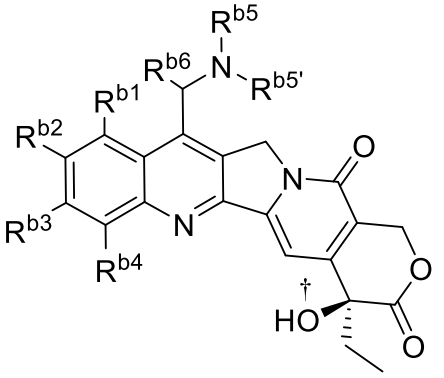
R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^{a} and $R^{a'}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkyl-S(O)$_2$-, C_1-C_6 alkyl-C(O)-, C_1-C_6 aminoalkyl-C(O)-, and C_1-C_6 hydroxyalkyl-C(O)-,

wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

5. The Ligand Drug Conjugate composition of claim 4, wherein D has a formula selected from the group consisting of



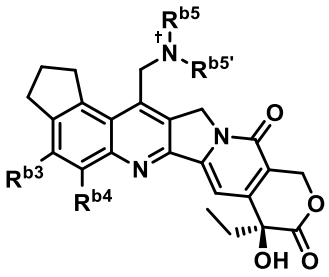
D_{1a}, and 

$D1_b$,

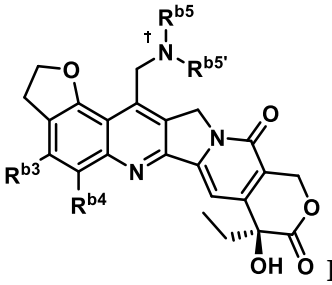
or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to the secondary linker of the drug linker moiety.

6. The Ligand Drug Conjugate composition of claim 5, wherein D has a formula selected from selected from the group consisting of

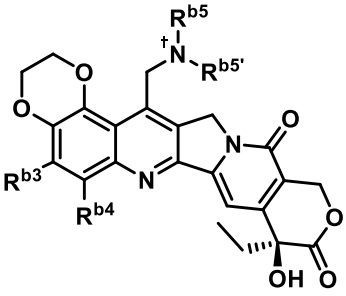
(i)



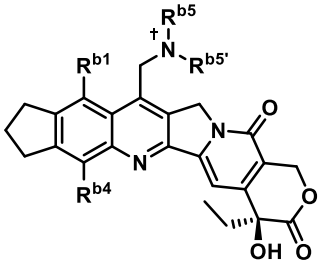
D_{1a}-I,



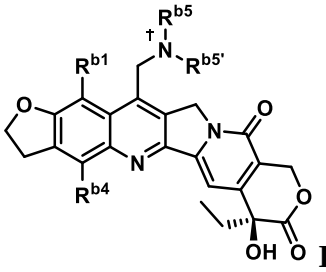
D_{1a}-II,



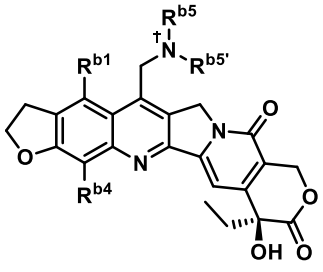
D_{1a}-III,



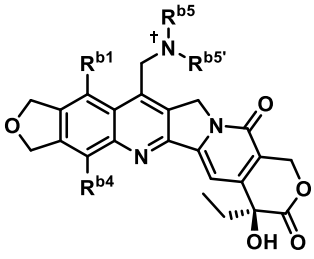
D_{1a}-IV,



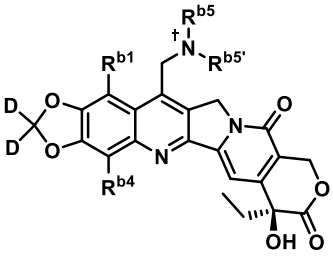
D_{1a}-V,



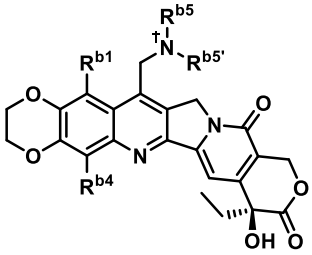
D_{1a}-VI,



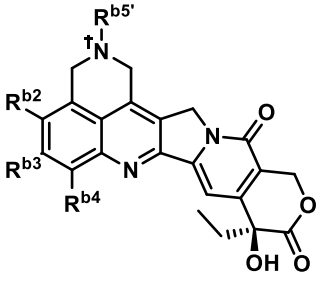
D_{1a}-VII,



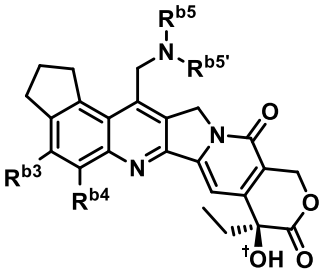
D_{1a}-VIII,



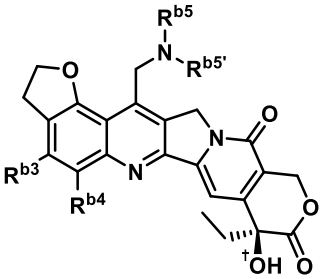
D_{1a}-IX ,



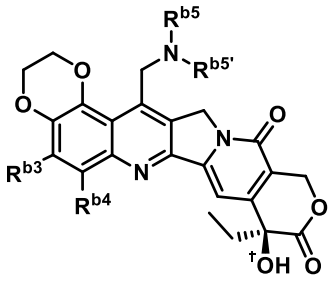
D_{1a}-X,



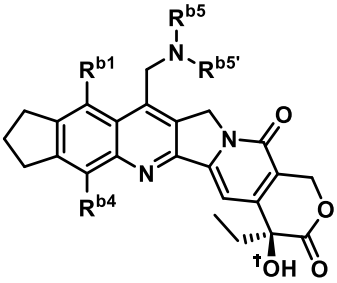
D_{1b}-I,



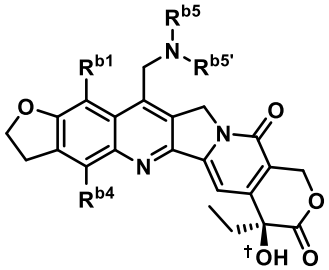
D_{1b}-II,



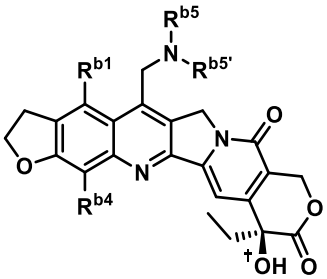
D_{1b}-III,



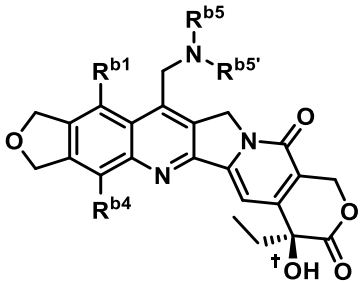
D_{1b}-IV,



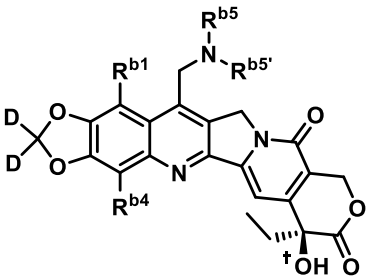
D_{1b}-V,



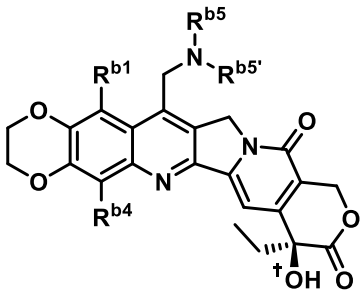
D_{1b}-VI,



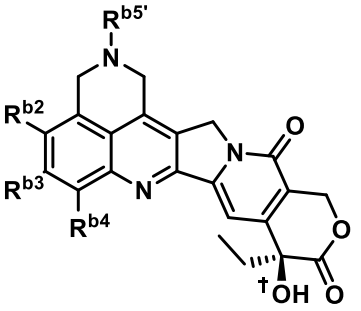
D_{1b}-VII,



D_{1b}-VIII,

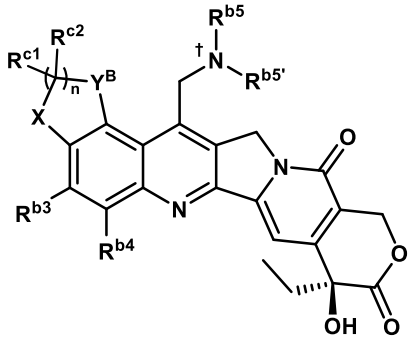


D1b-IX, and

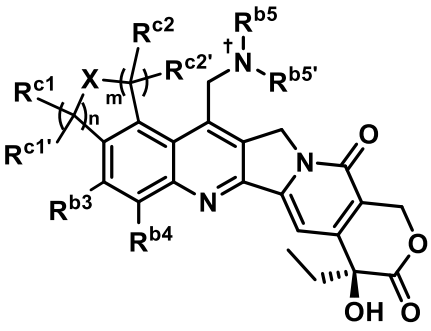


D1b-X;

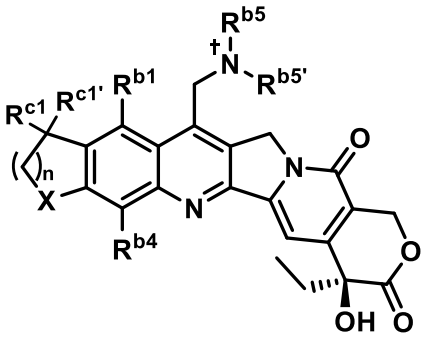
(ii)



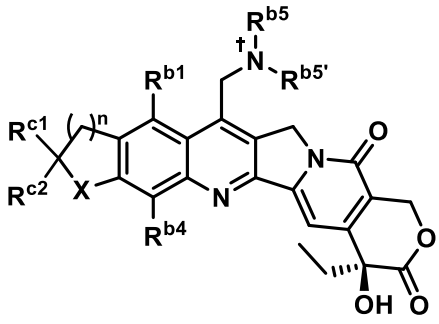
D1a-IIa,



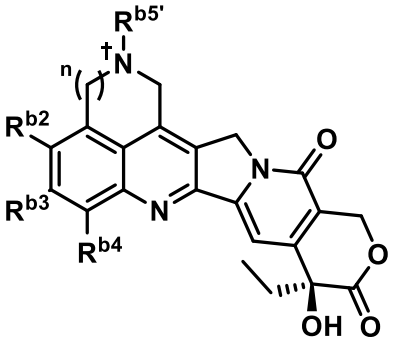
D1a-IIb,



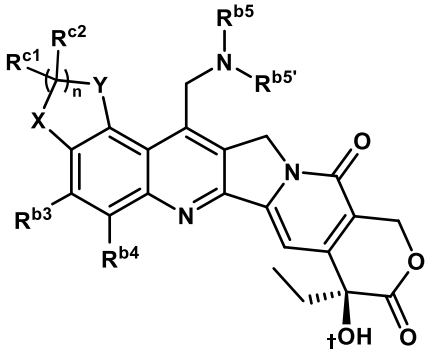
D1a-IVa,



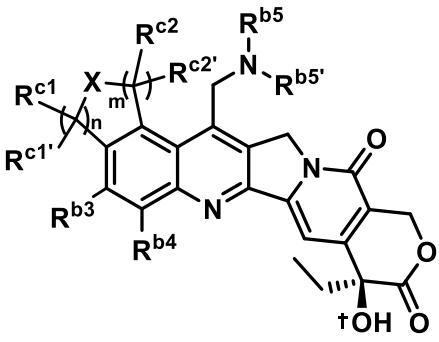
D1a-IVb,



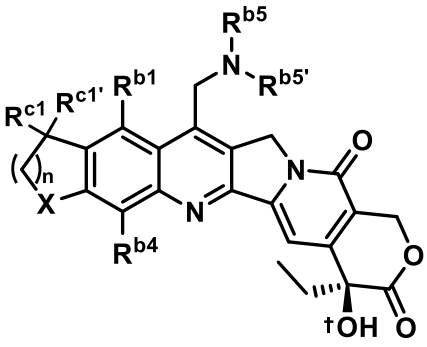
D1a-Xa,



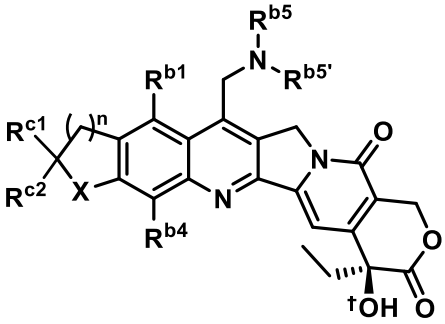
D1b-IIa,



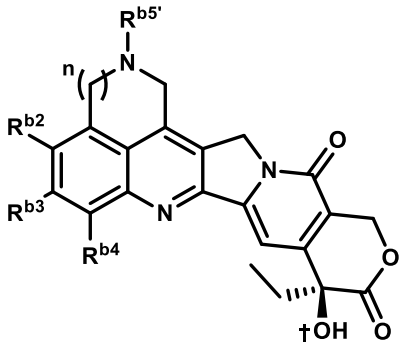
D1b-IIb,



D1b-IVa,



D1b-IVb, and



D1b-Xa,

wherein

X and Y^B are each independently O, S, $S(O)_2$, $CR^xR^{x'}$, or NR^x;

R^x and $R^{x'}$ are each independently selected from the group consisting of H, OH, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 aminoalkyl-C(O)-, C_1-C_6 alkyl-C(O)-, C_1-C_6 hydroxyalkyl-C(O)-, C_1-C_6 alkyl-NH-C(O)-, or C_1-C_6 alkyl-$S(O)_2$-; and

m and n are each 1 or 2;

each R^{c1}, $R^{c1'}$, R^{c2}, and $R^{c2'}$ is independently

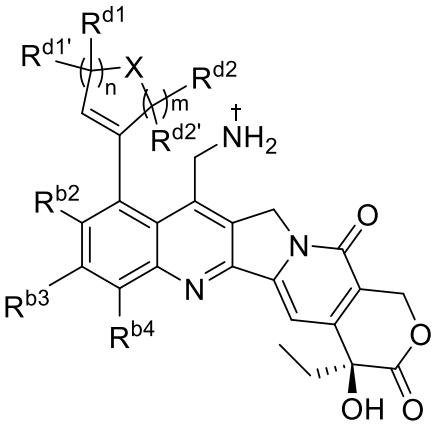
(i) selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; or

(ii) taken together with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

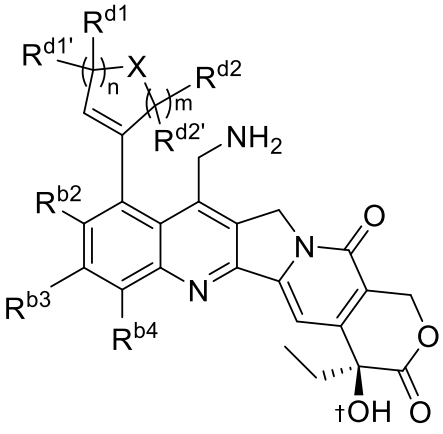
(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo; and

when m and n are both present, the sum of m + n is 2 or 3;

(iii)



D1a-XI and

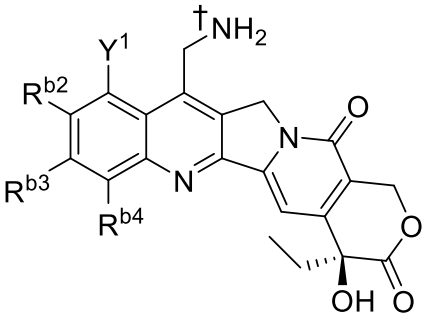


D1b-XI,

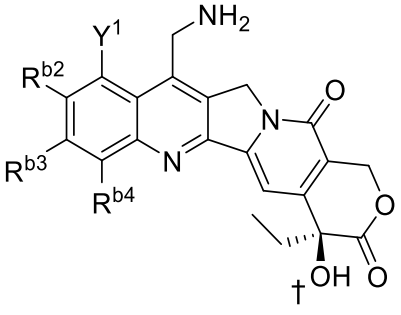
wherein

R^{d1}, $R^{d1'}$, R^{d2}, and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-;

(iv)



D1a-XII and

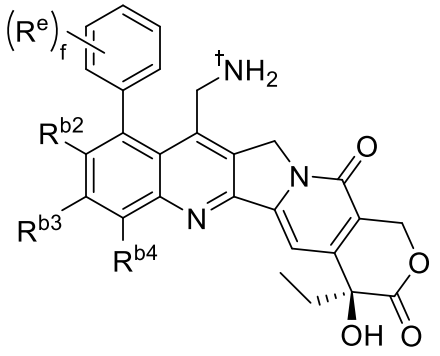


D1b-XII

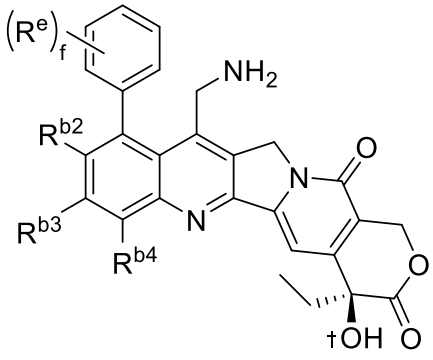
wherein

Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, or C_1-C_6 alkyl-$S(O)_2$-;

(v)



D1a-XIII and

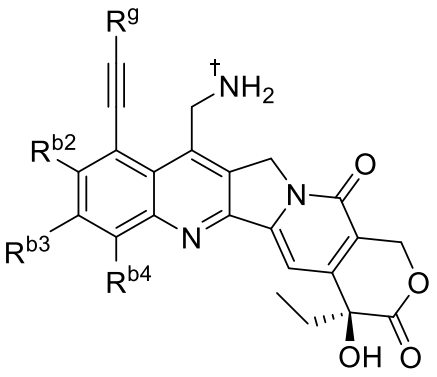


D1b-XIII,

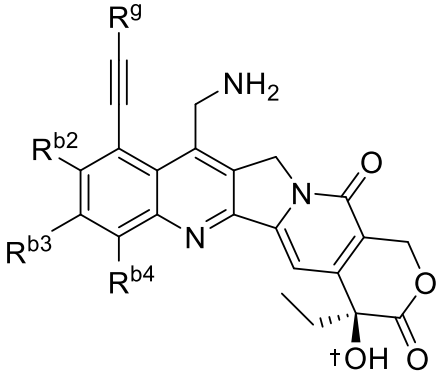
wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkyl-$S(O)_2$-, and C_1-C_6 alkyl-NR^a-C(O)-; and f is 0, 1, 2, 3, 4, or 5;

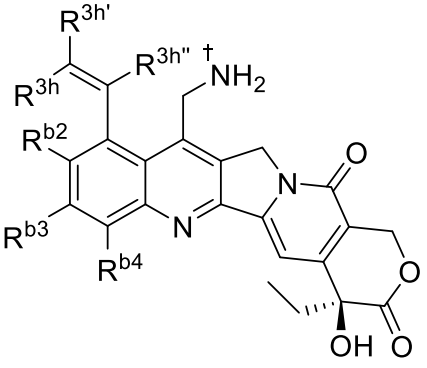
(vi)



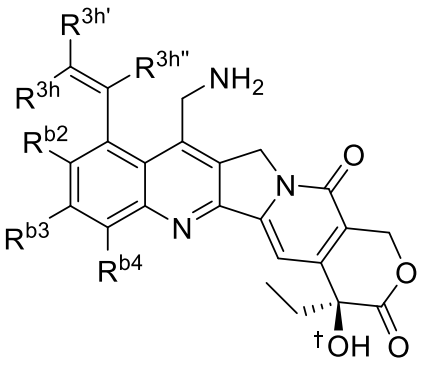
D1a-XIV,



D1b-XIV,



D1a-XV, and



D1b-XV,

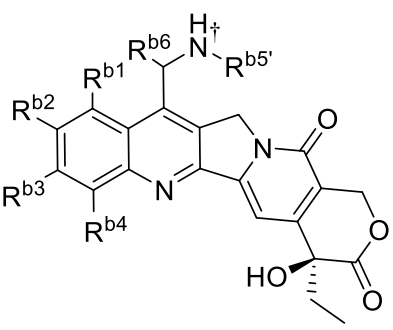
wherein

R^g is H, C_1-C_6 alkyl, or 3 to 8-membered heterocyclyl, and

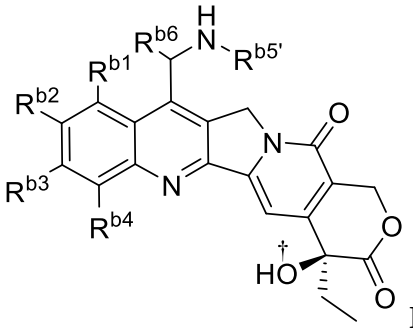
R^{3h}, $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -C(O)-C_1-C_6 alkyl, -C(O)O-C_1-C_6 alkyl, -

C(O)NH-C_1-C_6 alkyl, C_6-C_{10} aryl, -C_6-C_{10} aryl-C_1-C_6 alkyl, and -C_6-C_{10} aryl-C_1-C_6 alkoxy; each optionally substituted with, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a; or

(vii)

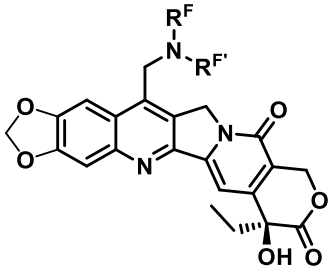


D1a-XVI and



DIb-XVI.

7. The Ligand Drug Conjugate composition of any one of claims 1-6, wherein D incorporates the structure of a camptothecin having a structure of



CPT6,

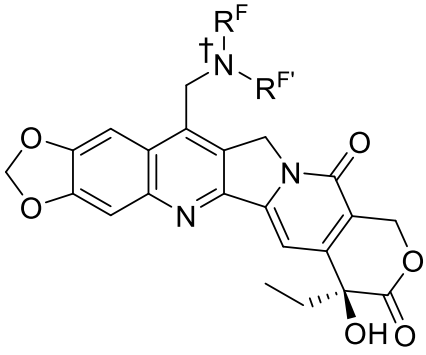
or a pharmaceutically acceptable salt thereof,

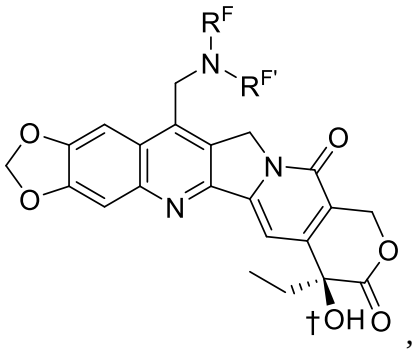
wherein each R^F and $R^{F'}$ is independently selected from the group consisting of -H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl, or

R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl;

wherein the cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^F and $R^{F'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$.

8. The Ligand Drug Conjugate composition of claim 7, wherein D has a formula of



or


,

wherein the dagger represents the point of covalent attachment of D to the secondary linker of the drug linker moiety.

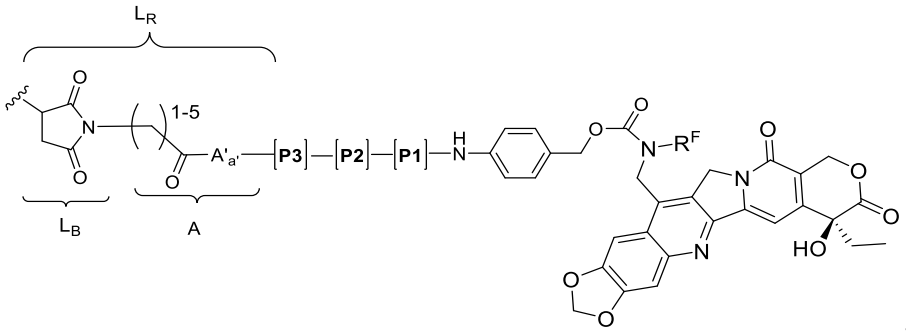
9. The Ligand Drug Conjugate composition of claim 7 or 8, wherein:

(i) R^F is selected from the group consisting of C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl; or

(ii) R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl.

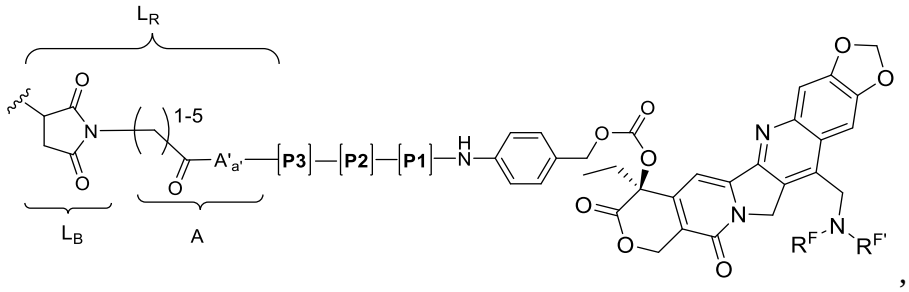
10. The Ligand Drug Conjugate composition of claim 1, wherein subscript q is 1 and the Ligand Drug Conjugate compounds in the Ligand Drug Conjugate composition predominately have drug linker moieties of:

(a)



, or

(b)



,

or a pharmaceutical 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 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 attachment to a sulfur atom of the Ligand Unit.

11. The Ligand Drug Conjugate composition of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein:

(a) 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; and/or

(b) the P3 amino acid is D-Leu or D-Ala; and/or

(c) 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; and/or

(d) 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; and/or

(e) -P2-P1- is -Ala-Glu- or -Ala-Asp-; and/or

(f) -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-; and/or

(g) the P3 amino acid is D-Leu or D-Ala, the P2 amino acid is Ala, Glu, or Asp, and the P1 amino acid is Ala, Glu, or Asp.

12. The Ligand Drug Conjugate composition of any one of claims 1-11, wherein L is an antibody Ligand Unit of an intact antibody or an antigen-binding fragment thereof,

optionally wherein the intact antibody is an intact chimeric, humanized or human antibody,

optionally wherein the intact antibody or fragment thereof is capable of selectively binding to a cancer cell antigen,

optionally wherein the intact antibody or fragment thereof is capable of selectively binding to an immune cell antigen.

13. The Ligand Drug Conjugate composition of claim 12, wherein:

(a) the intact antibody or fragment thereof is capable of selectively binding CD30,

optionally wherein the intact antibody or fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively,

optionally wherein the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8,

optionally wherein the intact antibody is cAC10;

(b) the intact antibody or fragment thereof is capable of selectively binding LIV1,

optionally wherein the intact antibody or fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 518, 519, 520, 521, 522, and 523, respectively,

optionally wherein the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 524 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 525,

optionally wherein the intact antibody is ladiratuzumab;

(c) the intact antibody or fragment thereof is capable of selectively binding TROP2,

optionally wherein the intact antibody is sacituzumab or datopotamab;

(d) the intact antibody or fragment thereof is capable of selectively binding ALPP;

(e) the intact antibody or fragment thereof is capable of selectively binding IL1RAP,

optionally wherein the intact antibody or fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 96, 97, 98, 99, 100, and 101, respectively,

optionally wherein the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 102 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 103,

optionally wherein the intact antibody is nidanilimab; or

(f) the intact antibody or fragment thereof is capable of selectively binding ASCT2,

optionally wherein the intact antibody or fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 794, 795, 796, 797, 798, and 799, respectively,

optionally wherein the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 801 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 802,

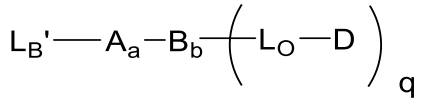
optionally wherein the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 790 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 791,

optionally wherein the intact antibody or fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 792 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 793.

14. A pharmaceutically acceptable formulation, wherein the formulation comprises an effective amount of a Ligand Drug Conjugate composition of any one of claims 1-13 and at least one pharmaceutically acceptable excipient.

15. Use of the Ligand Drug Conjugate composition of any one of claims 1-13 or the pharmaceutically acceptable formulation of claim 14, in the manufacture of a medicament for the treatment of cancer.

16. A Drug Linker compound of Formula **IA**:



(**IA**)

or a salt thereof, wherein

D is a Drug Unit, wherein the Drug Unit is a camptothecin;

L_B' is a ligand covalent binding precursor moiety;

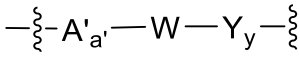
A is a first optional Stretcher Unit;

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 of L_O to the remainder of the Drug Linker compound;

A' is a second optional Stretcher Unit, which when present and 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 comprises 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 or is serine;

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

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

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,

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

each Y when present 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, and

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

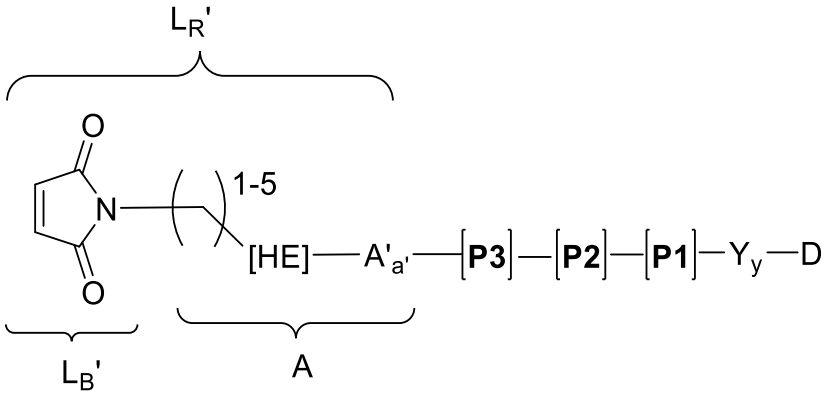
17. The Drug Linker compound of claim 16, wherein:

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

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

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

(b) the Drug Linker compound has the structure of Formula IH:



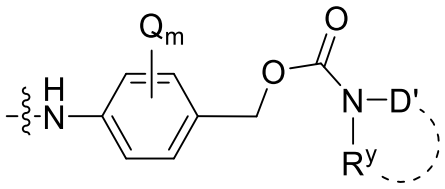
(Formula IH)

or salt thereof, wherein:

HE is a Hydrolysis Enhancing Unit, preferably, wherein HE is –C(=O); 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', respectively.

18. The Drug Linker compound of claim 16 or 17, 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';

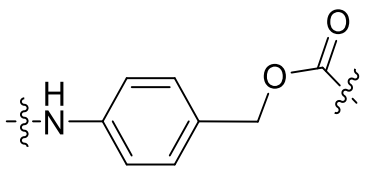
R^y is optionally substituted C_1-C_6 alkyl in absence of cyclization to D' or optionally substituted C_1-C_6 alkylene when cyclized to D';

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.

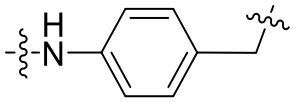
19. The Drug Linker compound of claim 16 or 17, wherein Y_y- has the structure of:

(a)



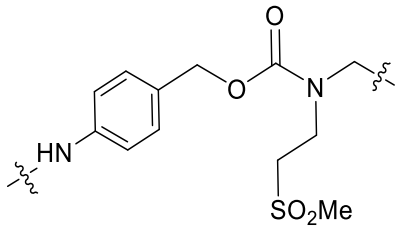
wherein the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to an oxygen, nitrogen, or sulfur atom of D to form a carbonate, carbamate, or thiocarbamate functional group that is shared between D and Y, or to a secondary nitrogen atom to form a carbamate that is shared between D and Y, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1;

(b)



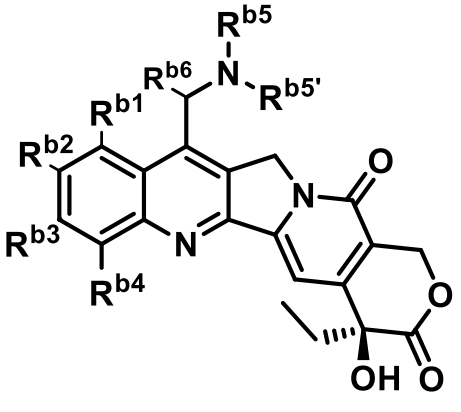
wherein the wavy line adjacent to the methylene carbon atom indicates the site of covalent attachment to a tertiary amine of D, such that -Y_y- is attached to D by way of a quaternized nitrogen atom that is part D, and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid of P1; or

(c)



wherein the wavy line adjacent to the carbon atom of the methylene carbamate moiety indicates the site of covalent attachment to an oxygen atom of D to form a methylene alkoxy carbamate moiety that is shared between D and Y and the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment as an amide bond to the carboxylic acid residue of P1.

20. The Drug Linker compound of any one of claims 16-19, wherein D has a formula of



D_1,

or a salt thereof; wherein

R^{b1} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, C_3-C_{10} heterocycloalkyl, (C_6-C_{12} aryl)-C_2-C_8 alkenyl-, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminoalkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_1-C_6 aryl-C(O)-, C_1-C_6 aryl-O-C(O)-NR^a-, C_1-C_6 aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-$S(O)_2$-, C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminolkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-NR^a-, C_1-C_8 alkyl-NR^a-C(O)O-, C_1-C_8 alkyl-OC(O)-NR^a-, C_1-C_6 aryl-C(O)-, C_1-C_6 aryl-O-C(O)-NR^a-, C_1-C_6 aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and $R^{b5'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl-, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl-, NH_2-SO_2-C_1-C_8 alkyl-, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl-, or R^{b5} and $R^{b5'}$ are combined

with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; or

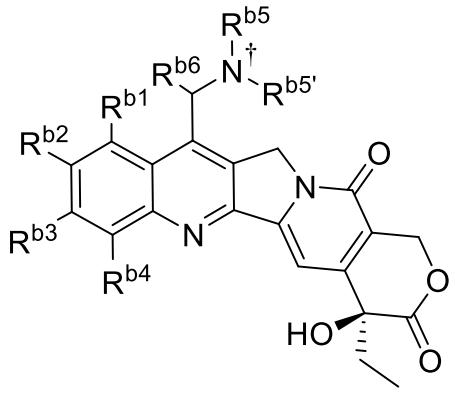
$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

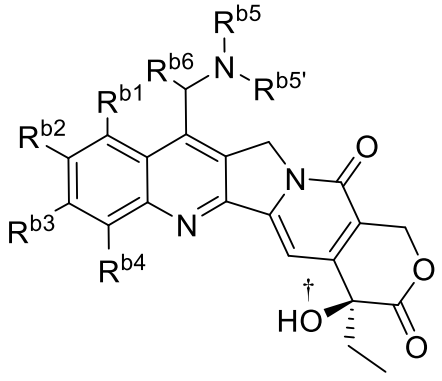
R^a and $R^{a'}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkyl-S(O)$_2$-, C_1-C_6 alkyl-C(O)-, C_1-C_6 aminoalkyl-C(O)-, and C_1-C_6 hydroxyalkyl-C(O)-,

wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

21. The Drug Linker compound of claim 20, wherein D has a formula selected from the group consisting of



D_{1a}, and

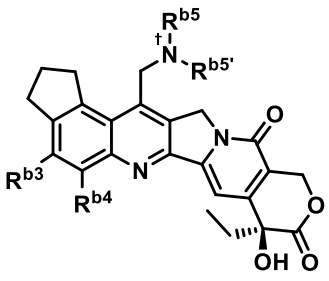


$D1_b$,

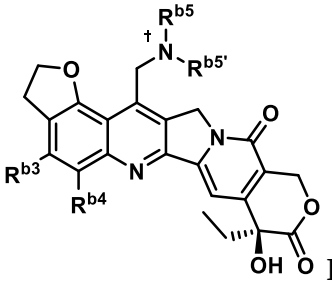
or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to the secondary linker of the drug linker moiety.

22. The Drug Linker compound of claim 21, wherein D has a formula selected from selected from the group consisting of:

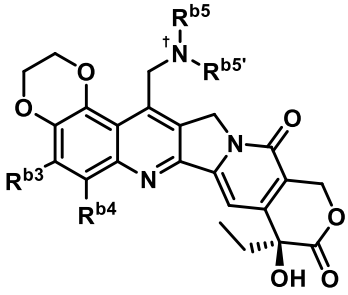
(a)



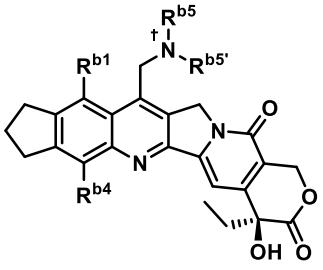
D_{1a}-I,



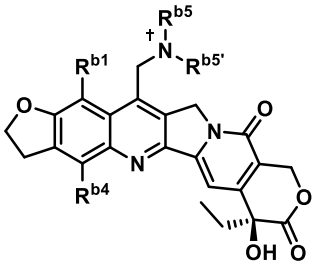
D_{1a}-II,



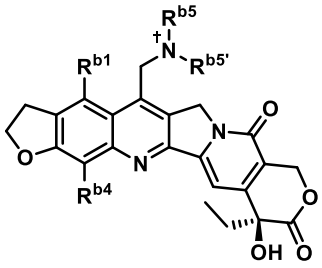
D_{1a}-III,



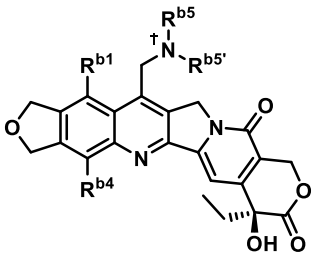
D_{1a}-IV,



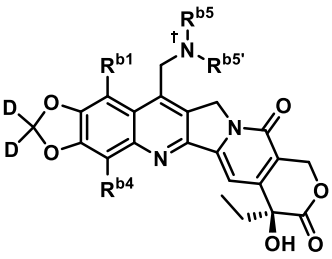
D_{1a}-V,



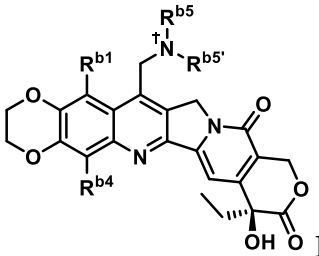
D_{1a}-VI,



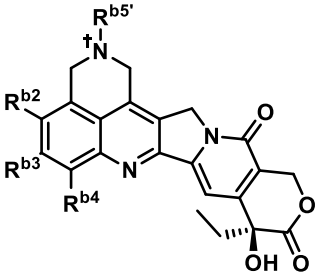
D_{1a}-VII,



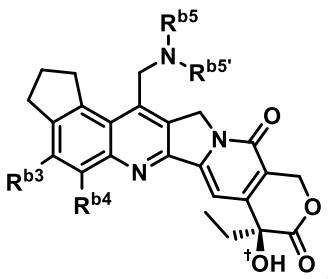
D_{1a}-VIII,



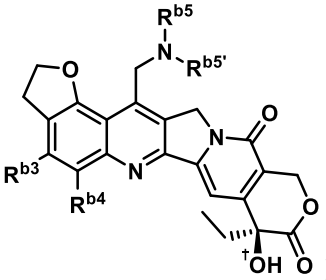
D_{1a}-IX ,



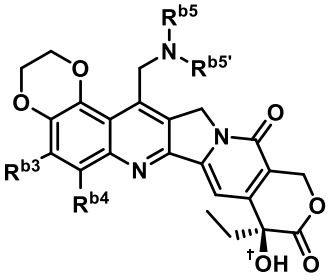
D_{1a}-X,



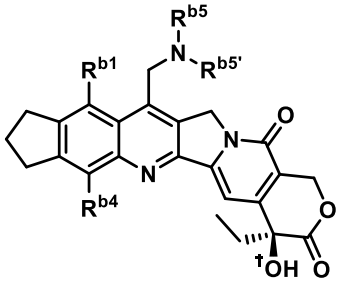
D1b-I,



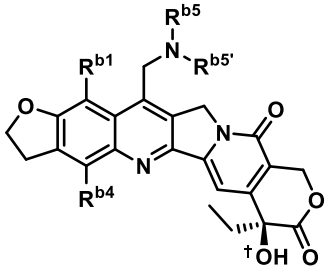
D1b-II,



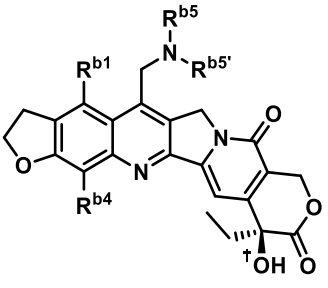
D1b-III,



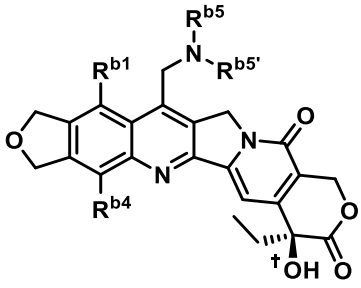
D1b-IV,



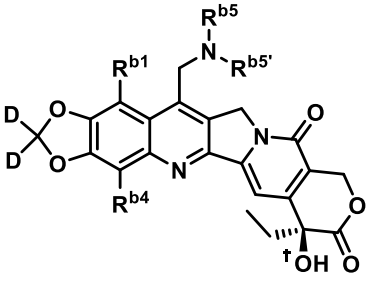
D1b-V,



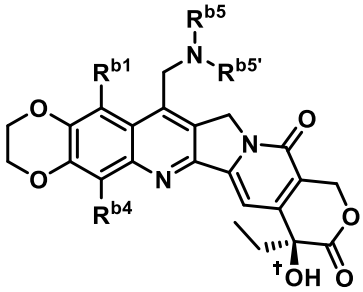
D1b-VI,



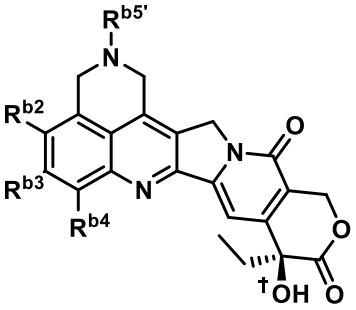
D1b-VII,



D1b-VIII,

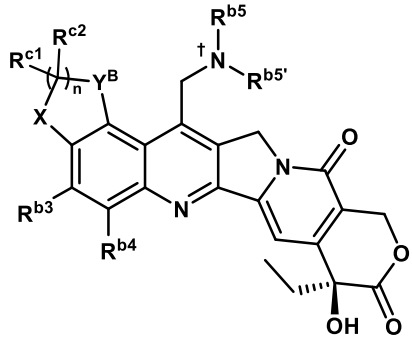


D1b-IX, and

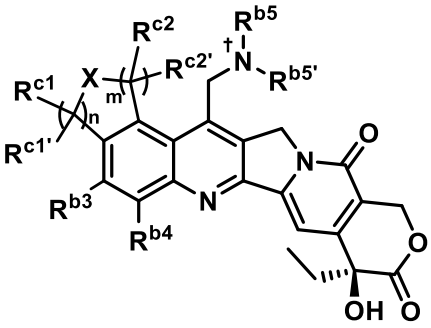


D1b-X;

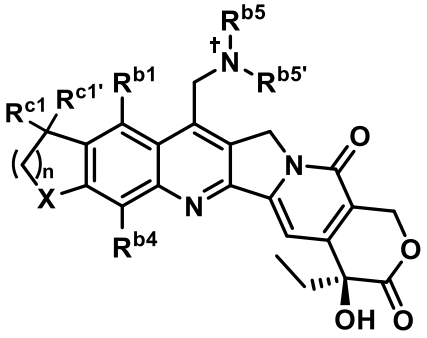
(b)



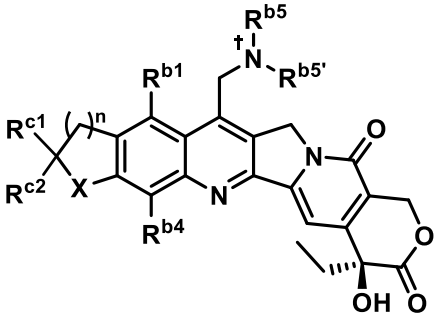
D1a-IIa,



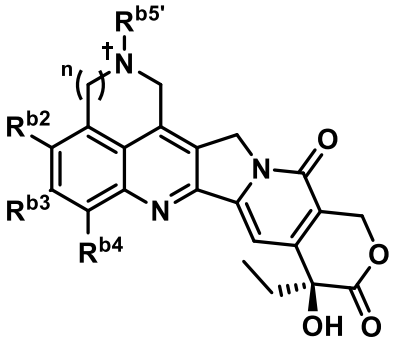
D1a-IIb,



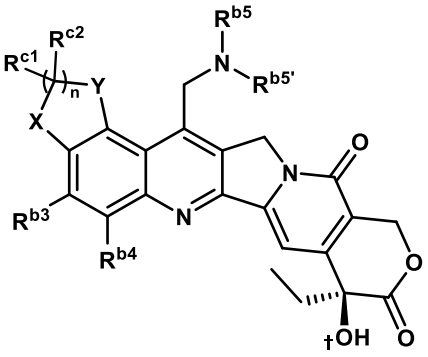
D1a-IVa,



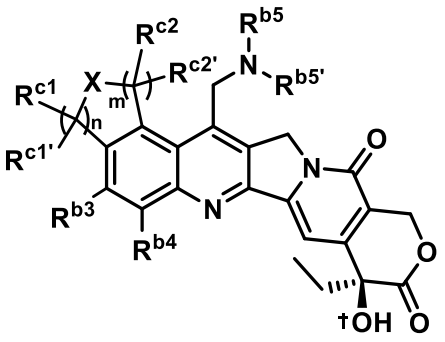
D1a-IVb,



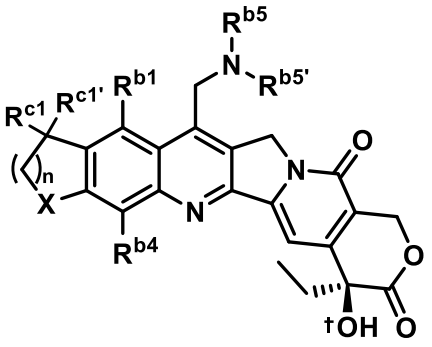
D1a-Xa,



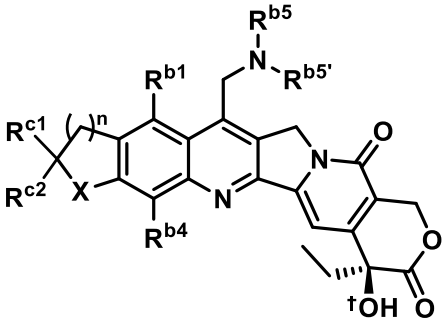
D1b-IIa,



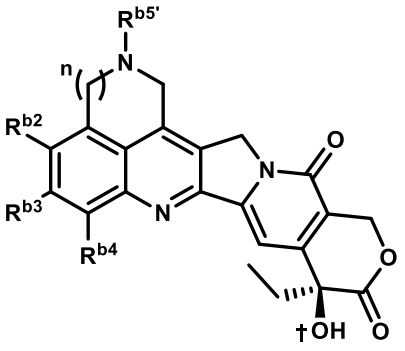
D1b-IIb,



D1b-IVa,



D1b-IVb, and



D1b-Xa,

wherein

X and Y^B are each independently O, S, $S(O)_2$, $CR^xR^{x'}$, or NR^x;

R^x and $R^{x'}$ are each independently selected from the group consisting of H, OH, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 aminoalkyl-C(O)-, C_1-C_6 alkyl-C(O)-, C_1-C_6 hydroxyalkyl-C(O)-, C_1-C_6 alkyl-NH-C(O)-, or C_1-C_6 alkyl-$S(O)_2$-; and

m and n are each 1 or 2;

each R^{c1}, $R^{c1'}$, R^{c2}, and $R^{c2'}$ is independently

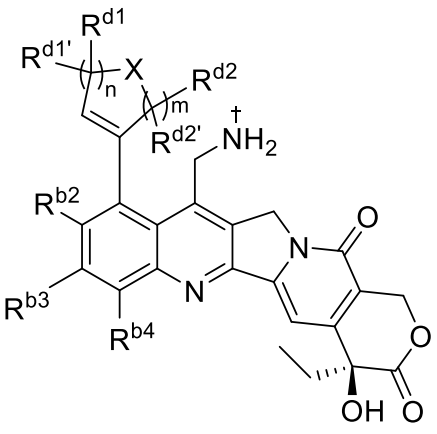
(i) selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; or

(ii) taken together with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

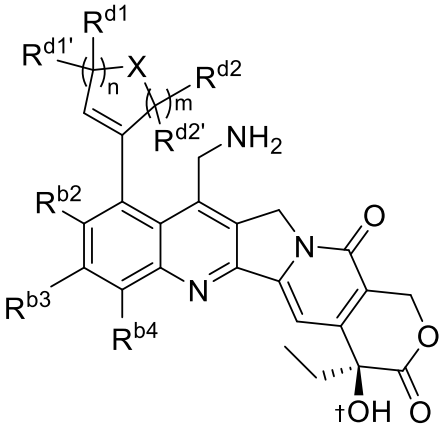
(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo; and

when m and n are both present, the sum of m + n is 2 or 3;

(c)



D1a-XI and

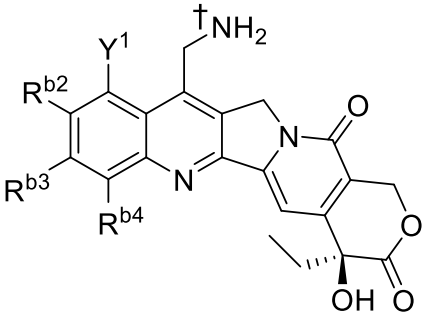


D1b-XI

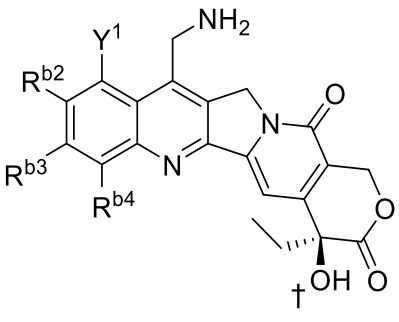
wherein

R^{d1}, $R^{d1'}$, R^{d2}, and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-;

(d)



D1a-XII and

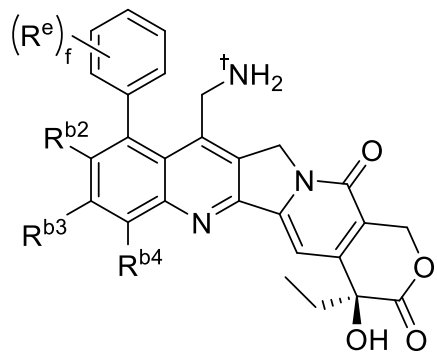


D1b-XII

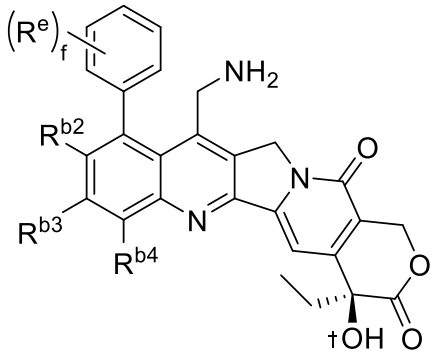
wherein

Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, or C_1-C_6 alkyl-$S(O)_2$-;

(e)



D1a-XIII and

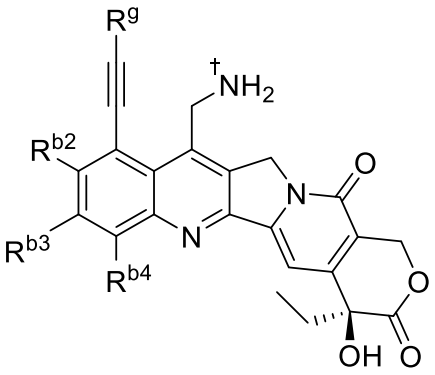


D1b-XIII,

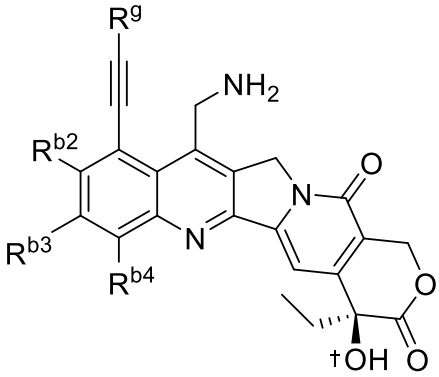
wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkyl-$S(O)_2$-, and C_1-C_6 alkyl-NR^a-C(O)-; and f is 0, 1, 2, 3, 4, or 5;

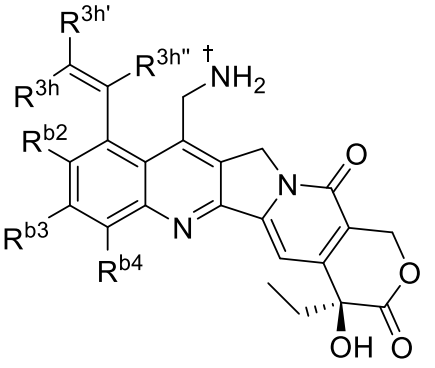
(f)



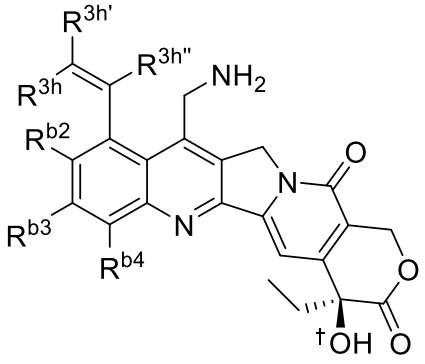
D1a-XIV,



D1b-XIV,



D1a-XV, and



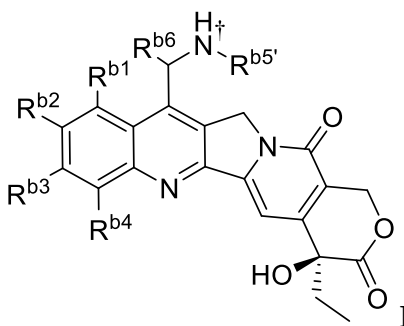
D1b-XV,

wherein

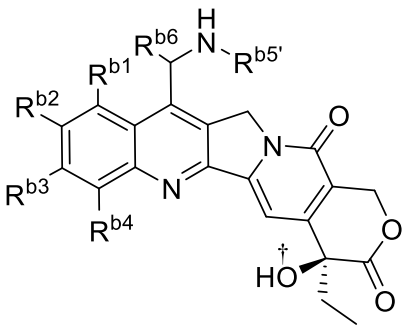
R^g is H, C_1-C_6 alkyl, or 3 to 8-membered heterocyclyl, and.

R^{3h}, $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -C(O)-C_1-C_6 alkyl, -C(O)O-C_1-C_6 alkyl, -C(O)NH-C_1-C_6 alkyl, C_6-C_{10} aryl, -C_6-C_{10} aryl-C_1-C_6 alkyl, and -C_6-C_{10} aryl-C_1-C_6 alkoxy; each optionally substituted with, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a; or

(g)

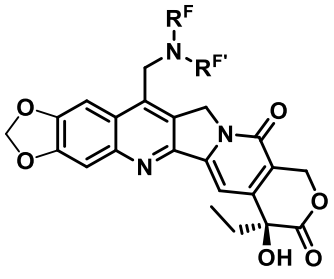


D1a-XVI and



DIb-XVI.

23. The Drug Linker compound of any one of claims 16-19, wherein D incorporates the structure of a camptothecin having a structure of



CPT6,

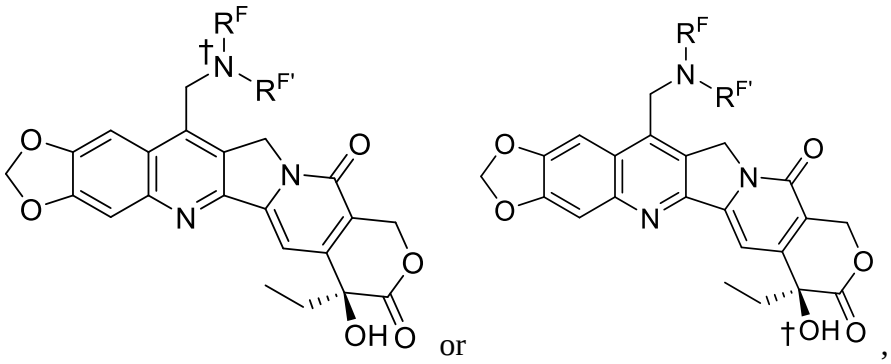
or a salt thereof,

wherein each R^F and $R^{F'}$ is independently selected from the group consisting of -H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl, or

R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl;

wherein the cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^F and $R^{F'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$.

24. The Drug Linker compound of claim 23, wherein D has a formula of



wherein the dagger represents the point of attachment of D to the remainder of the Drug Linker compound.

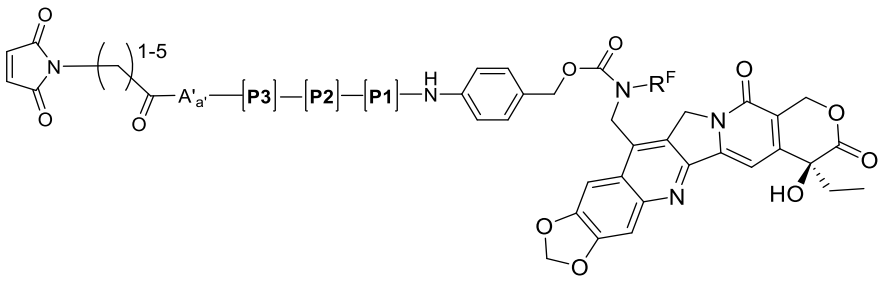
25. The Drug Linker compound of claim 23 or 24, wherein:

(i) R^F is selected from the group consisting of C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl, NH_2-SO_2-C_1-C_8 alkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl, or

(ii) R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl.

26. The Drug Linker compound of claim 16, wherein the Drug Linker compound has the structure of:

(a)

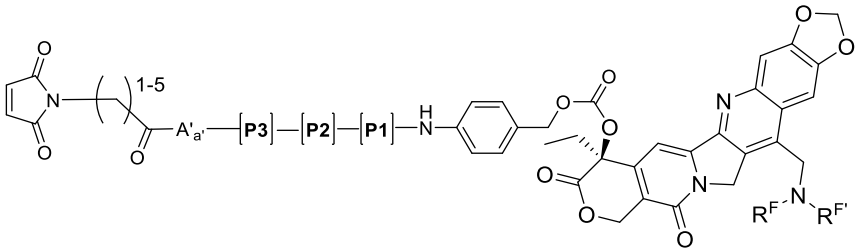


(a)

or a salt thereof, wherein

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

(b)



or a salt thereof, wherein

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

27. The Drug Linker compound of any one of claims 16-26, or a pharmaceutically acceptable salt thereof, wherein:

(a) 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; and/or

(b) the P3 amino acid is D-Leu or D-Ala; and/or

(c) 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; and/or

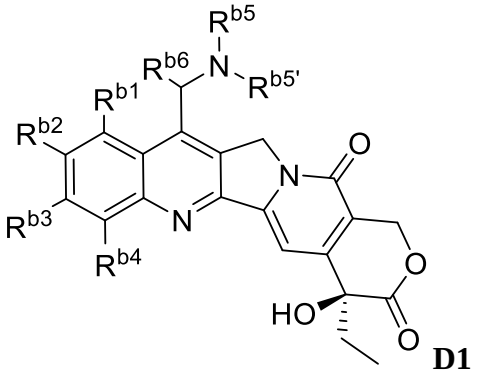
(d) the P2 amino acid has an aliphatic side chain with hydrophobicity no greater than that of valine, and the P1 amino acid is negatively charged at plasma physiological pH; and/or

(e) -P2-P1- is -Ala-Glu- or -Ala-Asp-; and/or

(f) -P3-P2-P1- is -D-Leu-Ala-Asp-, -D-Leu-Ala-Glu-, -D-Ala-Ala-Asp-, or -D-Ala-Ala-Glu-; and/or

(g) the P3 amino acid is D-Leu or D-Ala, the P2 amino acid is Ala, Glu, or Asp, and the P1 amino acid is Ala, Glu, or Asp.

28. A compound of formula D1



D1

or a salt thereof, wherein

R^{b1} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, (C_6-C_{12} aryl)-C_2-C_8 alkenyl-, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminoalkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_6-C_{12} aryl-C(O)-, C_6-C_{12} aryl-O-C(O)-NR^a-, C_6-C_{12} aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_6-C_{12} aryl, 5- to 12-membered heteroaryl, C_3-C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, C_1-C_8 haloalkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 alkyl-$S(O)_2$-, C_1-C_8 aminoalkyl, C_1-C_8 alkyl-C(O)-C_1-C_8 aminoalkyl-, C_1-C_8 aminolkyl-C(O)-C_1-C_8 alkyl-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-, C_1-C_8 alkyl-OC(O)-, C_1-C_8 alkyl-NR^a-C(O)-, C_1-C_8 alkyl-C(O)-NR^a-, C_1-C_8 alkyl-NR^a-C(O)O-, C_1-C_8 alkyl-OC(O)-NR^a-, C_6-C_{12} aryl-C(O)-, C_6-C_{12} aryl-O-C(O)-NR^a-, C_6-C_{12} aryl-NR^a-C(O)-O-, -$COOR^a$, -OR^a, -$NR^aR^{a'}$, and -SR^a; each optionally substituted with -OR^a, -$NR^aR^{a'}$, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and $R^{b5'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, (C_1-C_4 alkylamino)-C_1-C_8 alkyl-, *N*,*N*-(C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*,*N*-di(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, *N*-(C_1-C_4 hydroxyalkyl)-C_1-C_8 aminoalkyl-, C_1-C_8 alkyl-C(O)-, C_1-C_8 hydoxyalkyl-C(O)-, C_1-C_8 aminoalkyl-C(O)-, C_3-C_{10} cycloalkyl, (C_3-C_{10} cycloalkyl)-C_1-C_4 alkyl-, C_3-C_{10} heterocycloalkyl, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 alkyl-, phenyl, phenyl-C_1-C_4 alkyl-, diphenyl-C_1-C_4 alkyl-, heteroaryl, and heteroaryl-C_1-C_4 alkyl-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, C_1-C_6 alkoxy-C(O)-*N*-(C_1-C_4 alkyl)amino-C_1-C_8 alkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, C_1-C_4 alkyl-SO_2-C_1-C_8 alkyl-, NH_2-SO_2-C_1-C_8 alkyl-, (C_3-C_{10} heterocycloalkyl)-C_1-C_4 hydroxyalkyl-, C_1-C_6 alkoxy-C(O)-(C_3-C_{10} heterocycloalkyl)-C_1-C_8 alkyl-, phenyl-C(O)-, phenyl-SO_2-, and C_1-C_8 hydroxyalkyl-C_3-C_{10} hetercycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NH-C_1-C_4 alkyl, -N(C_1-C_4 alkyl)$_2$, C_1-C_6 alkoxy-C(O)-NH-, C_1-C_6 alkoxy-C(O)-C_1-C_8 aminoalkyl-, and C_1-C_8 aminoalkyl; or

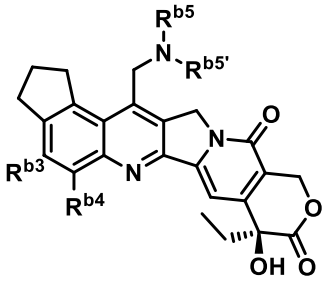
$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1-C_4 alkyl, -OH, -OC_1-C_4 alkyl, -NH_2, -NHC_1-C_4 alkyl, and -N(C_1-C_4 alkyl)$_2$;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

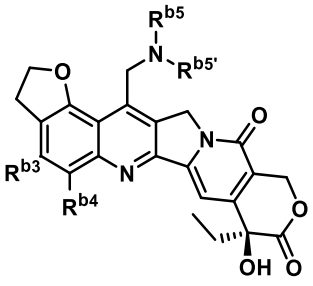
R^a and $R^{a'}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkyl-S(O)$_2$-, C_1-C_6 alkyl-C(O)-, C_1-C_6 aminoalkyl-C(O)-, and C_1-C_6 hydroxyalkyl-C(O)-.

29. The compound of claim 28, or a salt thereof, wherein the compound has a formula selected from selected from the group consisting of:

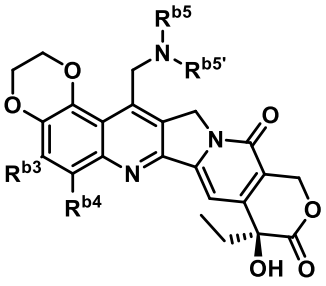
(a)



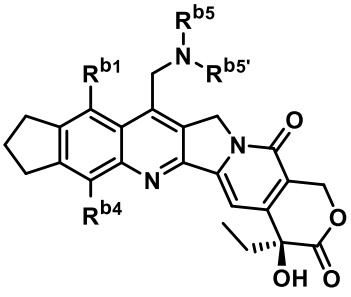
D1-I,



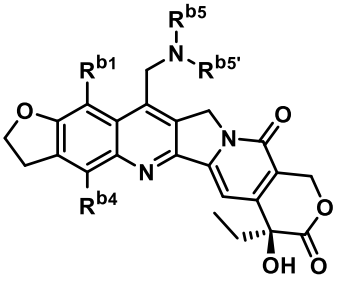
D1-II,



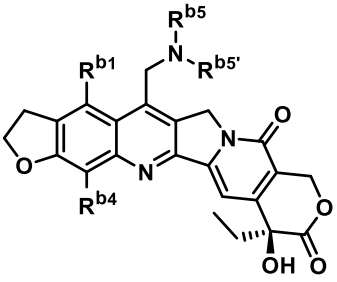
D1-III,



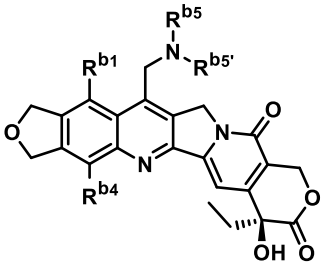
D1-IV,



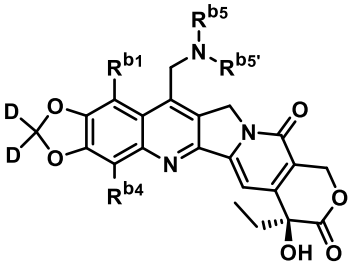
D1-V,



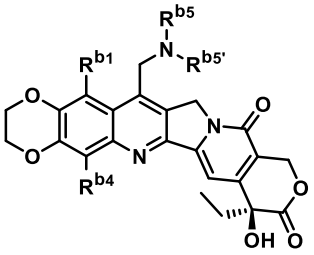
D1-VI,



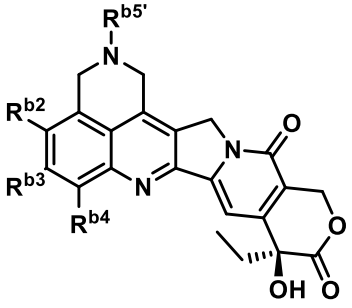
D1-VII,



D1-VIII,

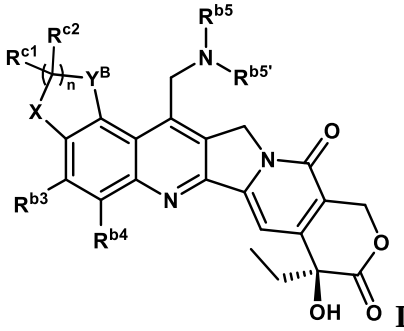


D1-IX, and

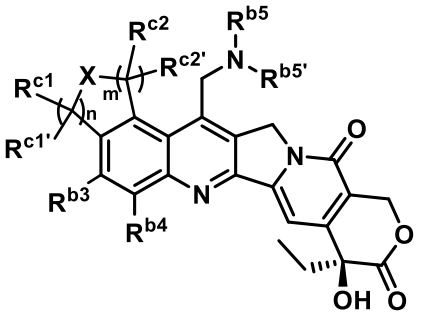


D1-X;

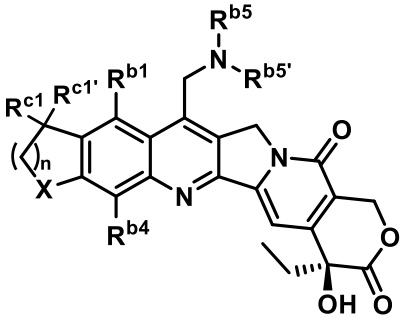
(b)



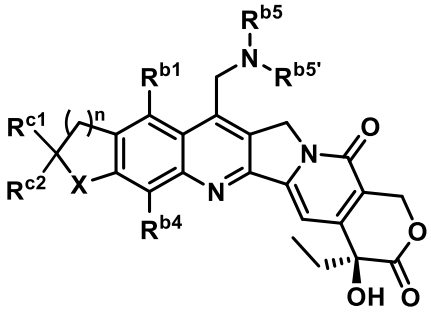
D1-IIa,



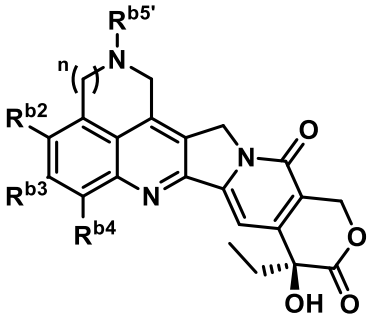
D1-IIb,



D1-IVa,



D1-IVb,



and **D1-Xa**,

wherein

X and Y^B are each independently O, S, $S(O)_2$, $CR^xR^{x'}$, or NR^x;

R^x and $R^{x'}$ are each independently selected from the group consisting of H, OH, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 aminoalkyl-C(O)-, C_1-C_6 alkyl-C(O)-, C_1-C_6 hydroxyalkyl-C(O)-, C_1-C_6 alkyl-NH-C(O)-, or C_1-C_6 alkyl-$S(O)_2$-; and

m and n are each 1 or 2;

each R^{c1}, $R^{c1'}$, R^{c2}, and $R^{c2'}$ is independently

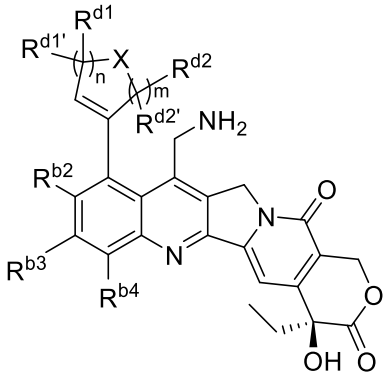
(i) selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-; or

(ii) taken together with R^{b1} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo; and

when m and n are both present, the sum of m + n is 2 or 3;

(c)

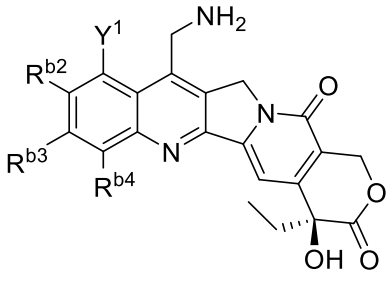


D1-XI,

or a salt thereof, wherein

R^{d1}, $R^{d1'}$, R^{d2}, and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a, C_1-C_6 alkyl-C(O)-, C_1-C_6 alkyl-NR^a-C(O)-, and C_1-C_6 alkyl-$S(O)_2$-;

(d)

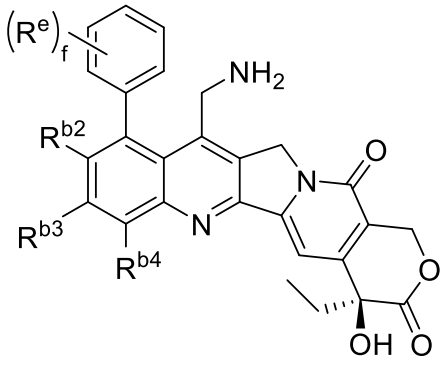


D1-XII,

or a salt thereof, wherein

Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, or C_1-C_6 alkyl-$S(O)_2$-;

(e)

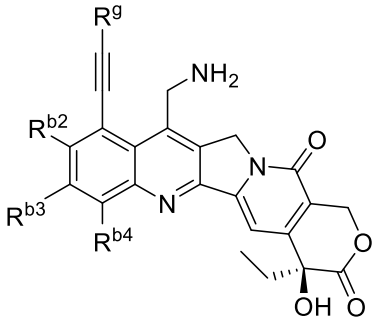


D1-XIII,

or a salt thereof, wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkyl-$S(O)_2$-, and C_1-C_6 alkyl-NR^a-C(O)-; and f is 0, 1, 2, 3, 4, or 5;

(f)

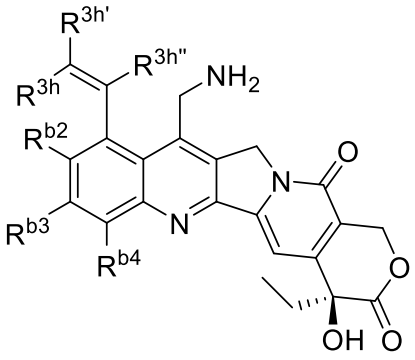


D1-XIV,

or a salt thereof, wherein

R^g is H, C_1-C_6 alkyl, or 3 to 8-membered heterocyclyl;

(g)

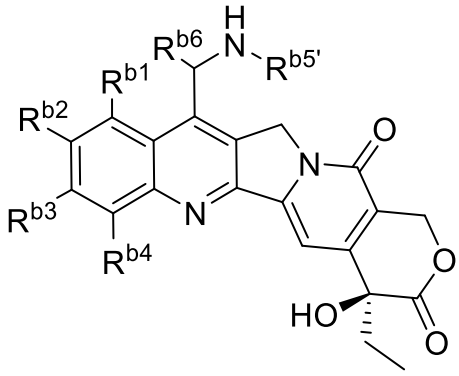


D1-XV,

or a salt thereof, wherein

R^{3h}, $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 aminoalkyl, -C(O)-C_1-C_6 alkyl, -C(O)O-C_1-C_6 alkyl, -C(O)NH-C_1-C_6 alkyl, C_6-C_{10} aryl, -C_6-C_{10} aryl-C_1-C_6 alkyl, and -C_6-C_{10} aryl-C_1-C_6 alkoxy; each optionally substituted with, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^a, -$NR^aR^{a'}$, and -SR^a; or

(h)



D1-XVI,

or a salt thereof.

30. A Ligand Drug Conjugate composition of any one of claims 1-13 or the pharmaceutically acceptable formulation of claim 14, for use in therapy.