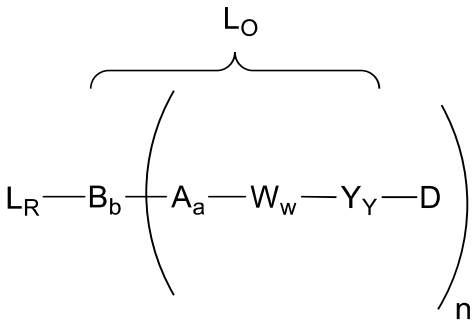
thereof within abnormal cells, or is released in the vicinity of the abnormal cells targeted by the Ligand Drug Conjugate, to exert a therapeutic effect due intracellular inhibition of NAMPT in the abnormal cells.

[0023] Those and other examples of Ligand Drug Conjugates and NAMPT Drug Units therein are further described by the examples of the disclosure.

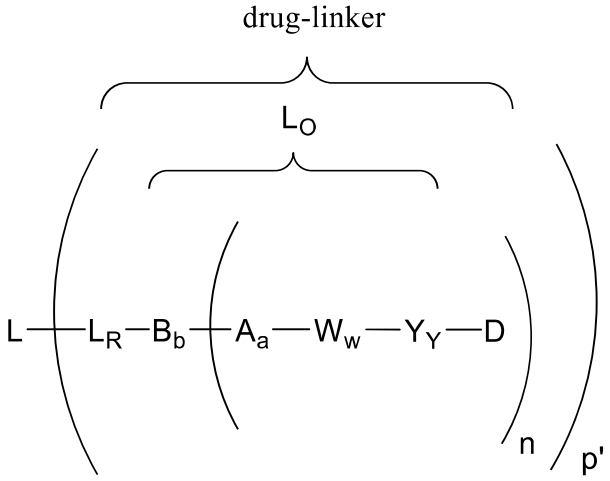
[0024] Other principle examples of the disclosure provide for compounds having the structure of Formula I:



(Formula I),

[0025] or a salt thereof, wherein L_R is a primary linker having a functional group capable of forming a covalent bond to a targeting moeity that becomes the Ligand Unit of a Ligand Drug Conjugate of Formula 1 wherein the other variable groups of Formula I are as defined for Formula 1.

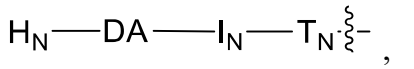
[0025a] In one aspect, there is provided a Ligand Drug Conjugate (LDC) compound, wherein the compound is represented by the structure of:



or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

D is a NAMPT Drug Unit represented by the general structure of:

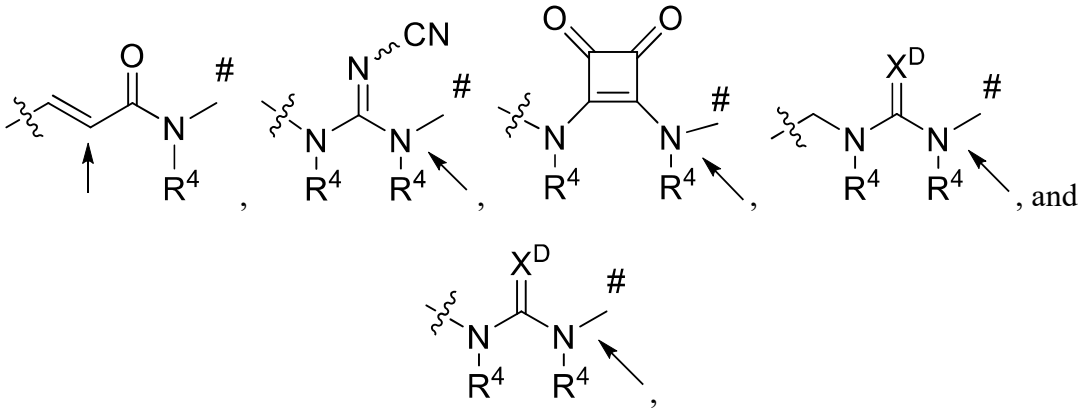


, wherein

the wavy line indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O;

H_N is a NAMPT Head Unit, wherein the NAMPT Head Unit is pyridin-3-yl or pyridin-4-yl, each of which is optionally substituted ;

DA is a Donor-Acceptor Unit selected from the group consisting of:



, and

wherein

X^D is O, S or NR^D, wherein the nitrogen atom is optionally protonated and R^D is hydrogen or optionally substituted C_1-C_4 alkyl;

each R^4 is independently selected from the group consisting of hydrogen and optionally substituted C_1-C_4 alkyl, or both R^4 together with the nitrogen atoms to which they are attached and the intervening carbon atom(s) define an optionally substituted C5-C6 heterocyclo;

the pound sign (#) indicates the site of covalent attachment to I_N; and the wavy line indicates the site of covalent attachment to H_N;

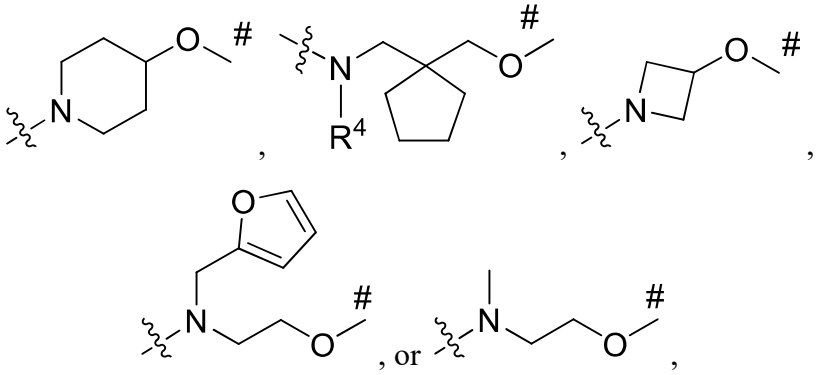
wherein DA is optionally cyclized back to an adjacent aromatic carbon atom of H_N, wherein said cyclization is from the nitrogen atom (indicated by an arrow), or DA is optionally cyclized to H_N, wherein said cyclization is to the sp^2 carbon atom proximal to the carbonyl carbon (as indicated by an arrow);

I_N is an Interconnecting Unit, wherein the Interconnecting Unit is or comprises $-X^1-[C(=O)]_{0,1}$

X^1 is optionally substituted C_5-C_7 alkylene;

T_N is a NAMPT Tail Unit, wherein the NAMPT Tail Unit is or comprises an optionally substituted amino-alcohol residue, the –O- of which is the site of covalent attachment to L_O, or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein

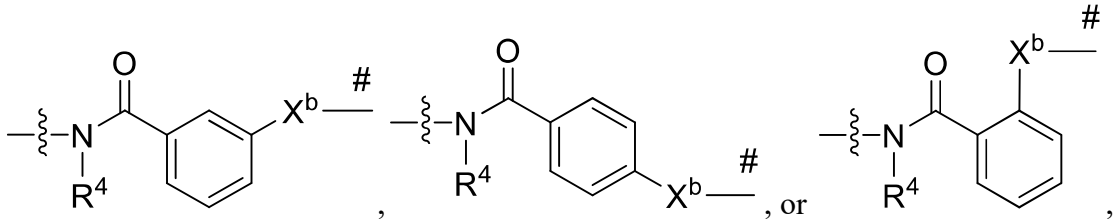
R^4 is hydrogen or optionally substituted C_1-C_4 alkyl;

the wavy line indicates the site of covalent attachment to I_N; and

the pound sign (#) indicates the site of covalent to L_O or L_R, depending on the presence or absence of L_O, respectively, or

T_N is or comprises an optionally substituted benzamide moiety, the amide nitrogen atom of which is bonded to I_N with optional cyclization of that atom back to I_N or to the remainder of T_N, and the aromatic ring of which is at least substituted with a hydroxyl or amino residue, the –O-, or nitrogen atom of which is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein X^b is –O- or -NH-, optionally substituted; and

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl, wherein

the benzamide moeity is optionally cyclized to I_N, wherein the amide nitrogen atom of the benzamide moiety is the site of said cyclization so that R^4 is replaced by a covalent bond to I_N;

L_R is a primary linker, which interconnects the Ligand Unit and Drug Unit optionally through L_O, as indicated, which is an optional secondary linker;

subscripts a and b independently are 0 or 1, indicating the absence or presence, respectively, of A or B;

subscript n is 1, 2, 3 or 4;

A is a first optional Stretcher; and

B is a Branching Unit, when subscript b is 1 and subscript n is 2, 3 or 4, or B is absent, so that subscript b is 0, when subscript n is 1,

wherein each of A and B is an independently selected single unit or is optionally comprised or consists of at least two, three or four independently selected subunits;

Y is a Spacer Unit; and subscript y is 0, 1 or 2, indicating the absence or presence of one or two of Y, respectively,

provided that when subscript y is 1, Y is a Spacer Unit covalently attached to a heteroatom or moiety thereof of T_N selected from the group consisting of –O-, -S- and optionally substituted nitrogen,

provided that when subscript y is 2 so that Y_y is –Y-Y', Y is a first Spacer Unit and Y' is a second Spacer Unit or a functional group comprising the optionally substituted heteroatom from T_N; and

provided that subscript y is 1 or 2 when W is a Glucuronide Unit of formula Y(W'), in which instance subscript y is inclusive of a first Spacer Unit Y, wherein that Spacer Unit is a required self-immolative Spacer Unit; and

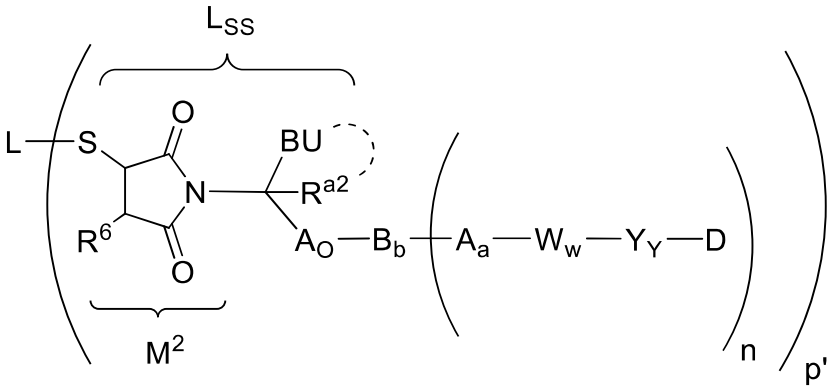
subscript w is 0 or 1, indicating the absence or presence, respectively, of W; wherein

when subscript w is 1, W is a Peptide Cleavable Unit or said Glucuronide Unit in which W' represents a carbohydrate moiety with glycosidic bonding to the required self-immolative Spacer Unit through an optionally substituted heteroatom, wherein enzymatic or non-enzymatic cleavage of either Unit initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from a drug linker moiety of Ligand Drug Conjugate compound; and

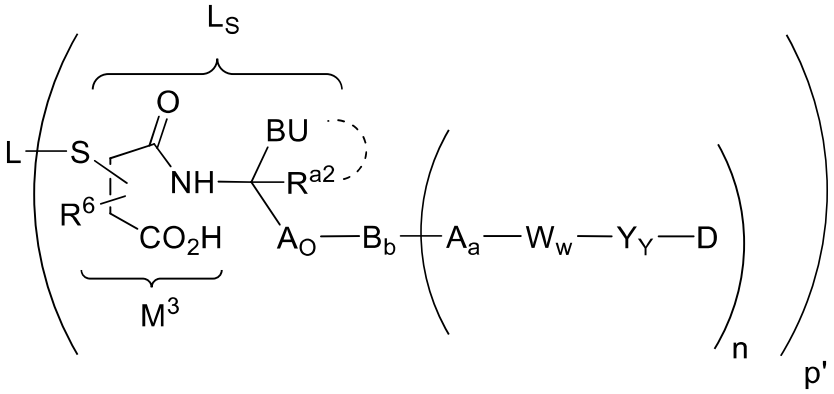
when subscript w is 0, which indicates the absence of a Cleavable Unit, enzymatic or non-enzymatic cleavage of the bond between L_R and L_O, when L_O is present, or the bond between L_R and D, when L_O is absent, initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof;

wherein when a derivative of a NAMPTi compound is released, the derivitized NAMPTi compound inhibits NAMPT and/or undergoes further enzymatic or non-enzymatic action(s) to release the parent NAMPTi compound;

wherein the Ligand Drug Conjugate compound corresponds in structure to that of Formula 1 or Formula 2 wherein p' is an integer ranging from 1 to 24:



(Formula 1)



(Formula 2)

, wherein

S is a sulfur atom of the Ligand Unit, which in Formula 2 is bonded to the carbon atom α or β to the carboxylic acid functional group of the indicated succinic acid amide (M^3) moiety;

R^6 is hydrogen or an optionally substituted C_1-C_6 alkyl, which in Formula 2 is bonded to the saturated carbon atom adjacent to the carbon substituted by L-S-;

A_O is a second optional Stretcher Unit;

BU is a Basic Unit and R^{a2} is an optionally substituted C_1-C_{12} alkyl group; and

the dotted curved line indicates optional cyclization so that in the absence of said cyclization BU is an acyclic Basic Unit or in the presence of said cyclization BU is a cyclized Basic Unit in which R^{a2} and BU together with the carbon atom to which both are attached, define an optionally substituted spiro C_3-C_{20} heterocyclo containing a skeletal basic nitrogen atom of a secondary or tertiary amine functional group as the basic function group of the cyclic Basic Unit,

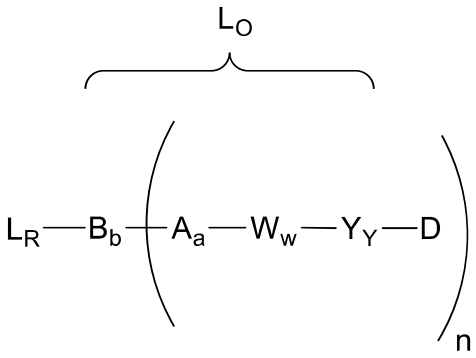
wherein the basic nitrogen atom of the acyclic Basic Unit or cyclic Basic Unit is optionally suitably protected by a nitrogen protecting group, dependent on the degree of substitution of the basic nitrogen atom, or is optionally protonated.

[0025b] In another aspect, there is provided a formulation comprising a Ligand Drug Conjugate compound disclosed herein and at least one, two, three or more excipients, in particular, wherein the formulation is a pharmaceutically acceptable formulation or a precursor thereof, particularly wherein the pharmaceutically acceptable formulation precursor is a solid suitable for reconstitution as a solution for intravenous injection to a subject in need thereof, or the pharmaceutically acceptable formulation is a liquid suitable for intravenous injection to a subject in need thereof, more particularly in which the Ligand Drug Conjugate compound is present in an effective amount for treatment of a hyperproliferative disease or condition in said solid or liquid formulation.

[0025c] In another aspect, there is provided use of an effective amount of a Ligand Drug Conjugate compound disclosed herein in the manufacture of a medicament for treating a hyperproliferative disease or condition in a subject in need thereof having said disease or condition, in particular having a cancer, more particularly a leukemia or lymphoma.

[0025d] In another aspect, there is provided a method of inhibiting the multiplication of a tumor cell or cancer cell *in vitro*, or causing apoptosis in a tumor or cancer cell *in vitro* by exposing said cell to an effective amount of a Ligand Drug Conjugate compound or a compound thereof disclosed herein.

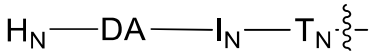
[0025e] In another aspect, there is provided a Drug Linker compound, wherein the compound is represented by the structure of:



or a salt thereof, wherein

L_R is a primary linker having a functional group capable interacting with a targeting agent to form a covalent bond to a Ligand Unit corresponding to or incorporating the targeting agent in a Ligand Drug Conjugate compound;

D is a NAMPT Drug Unit represented by the general structure of:

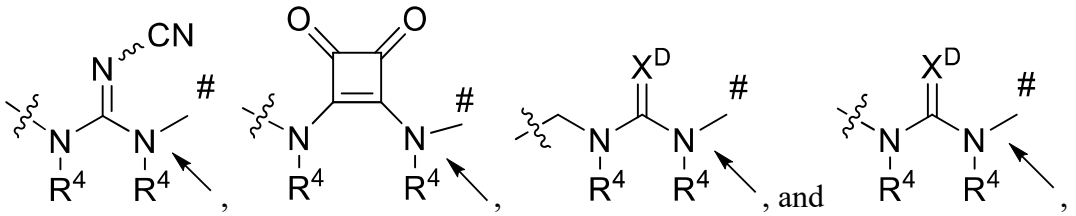


, wherein

the wavy line indicates the site of covalent attachment to L_O, as indicated, which is an optional secondary linker, or L_R, depending on the presence or absence of L_O, respectively;

H_N is a NAMPT Head Unit, wherein the NAMPT Head Unit is pyridin-3-yl or pyridin-4-yl, each of which is optionally substituted ;

DA is a Donor-Acceptor Unit selected from the group consisting of:



wherein

X^D is O, S or NR^D, wherein the nitrogen atom is optionally protonated and R^D is hydrogen or optionally substituted C_1-C_4 alkyl;

each R^4 is independently selected from the group consisting of hydrogen and optionally substituted C_1-C_4 alkyl, or both R^4 together with the nitrogen atoms to which they are attached and the intervening carbon atom(s) define an optionally substituted C5-C6 heterocyclo;

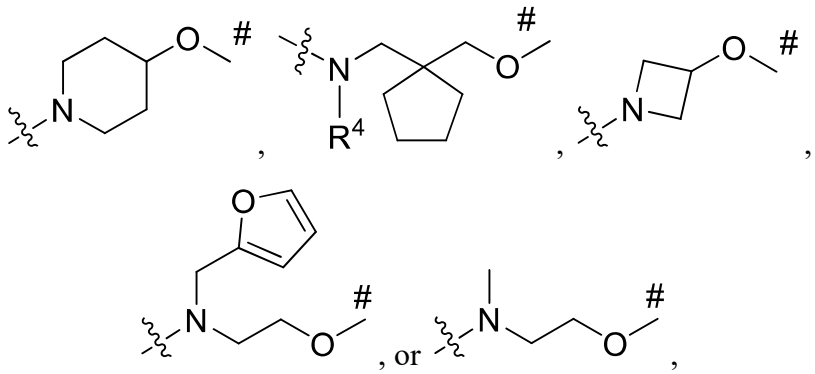
the pound sign (#) indicates the site of covalent attachment to I_N; and the wavy line indicates the site of covalent attachment to H_N;

I_N is an Interconnecting Unit, wherein the Interconnecting Unit is or comprises $-X^1-[C(=O)]_{0,1}$;

X^1 is optionally substituted C_5-C_7 alkylene;

T_N is a NAMPT Tail Unit, wherein the NAMPT Tail Unit is or comprises an optionally substituted amino-alcohol residue, the –O- of which is the site of covalent attachment to L_O, or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein

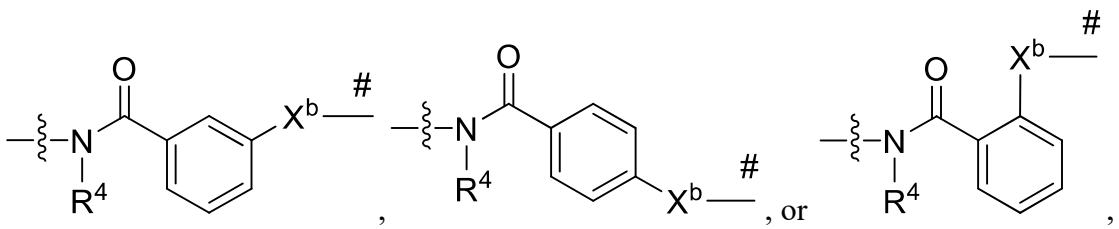
R^4 is hydrogen or optionally substituted C_1-C_4 alkyl;

the wavy line indicates the site of covalent attachment to I_N; and

the pound sign (#) indicates the site of covalent to L_O or L_R, depending on the presence or absence of L_O, respectively, or

T_N is or comprises an optionally substituted benzamide moiety, the amide nitrogen atom of which is bonded to I_N with optional cyclization of that atom back to I_N or to the remainder of T_N, and the aromatic ring of which is at least substituted with a hydroxylor amino residue, the –O-, -S- or optionally substituted nitrogen atom of which is attached is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein X^b is –O- or -NH-, optionally substituted; and

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl, wherein

the benzamide moeity is optionally cyclized to I_N, wherein the amide nitrogen atom of the benzamide moiety is the site of said cyclization so that R^4 is replaced by a covalent bond to I_N;

subscripts a and b independently are 0 or 1, indicating the absence or presence, respectively, of A or B;

subscript n is 1, 2, 3 or 4;

A is an first optional Stretcher; and

B is a Branching Unit, when subscript b is 1 and subscript n is 2, 3 or 4, or B is absent, so that subscript b is 0, when subscript n is 1,

wherein each of A and B is an independently selected single unit or is optionally comprised or consists of at least two, three or four independently selected subunits;

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

Y is a Spacer Unit; and subscript y is 0, 1 or 2, indicating the absence or presence of one or two of Y, respectively,

provided that when subscript y is 1, Y is a Spacer Unit covalently attached to a heteroatom or moiety thereof of T_N selected from the group consisting of –O-, -S- and optionally substituted nitrogen,

provided that when subscript y is 2 so that Y_y is –Y-Y', Y is a first Spacer Unit and Y' is a second Spacer Unit or a functional group comprising the optionally substituted heteroatom from T_N; and

provided that subscript y is 1 or 2 when W is a Glucuronide Unit of formula Y(W'), in which instance subscript y is inclusive of a first Spacer Unit Y, wherein that Spacer Unit is a required self-immolative Spacer Unit; and

subscript w is 0 or 1, indicating the absence or presence, respectively, of W; wherein

when subscript w is 1, W is a Peptide Cleavable Unit or said Glucuronide Unit in which W' represents a carbohydrate moiety with glycosidic bonding to the required self-immolative Spacer Unit through an optionally substituted heteroatom, enzymatic or non-enzymatic cleavage of that Unit in the Drug Linker Compound, or in a drug linker moiety of a Ligand Drug Conjugate compound or a N-acetyl-cysteine (NAC)conjugate prepared

from the Drug Linker compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative therefrom, and

when subscript w is 0, which indicates the absence of a Cleavable Unit, enzymatic or non-enzymatic cleavage of the bond between the indicated L_R and L_O moieties, when L_O is present, or the bond between L_R and D, when L_O is absent, initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from the Drug Linker compound or said drug linker moiety or NAC conjugate, wherein when a derivative of a NAMPTi compound is released, the derivitized NAMPTi compound inhibits NAMPT and/or undergoes further enzymatic or non-enzymatic action(s) to release the parent NAMPTi compound.

[0025f] In another aspect, there is provided a method of preparing a Ligand Drug Conjugate compound or compound disclosed herein, the method comprising the step of: contacting a Drug Linker compound disclosed herein with a targeting agent having a reactive function group capable of interacting with the reactive functional group of the primary linker of the Drug Linker compound so as to form a covalent bond to between the Ligand Unit corresponding to the targeting agent and the primary linker of the Ligand Drug Conjugate compound corresponding in structure to the the primary linker of the Drug Linker compound.

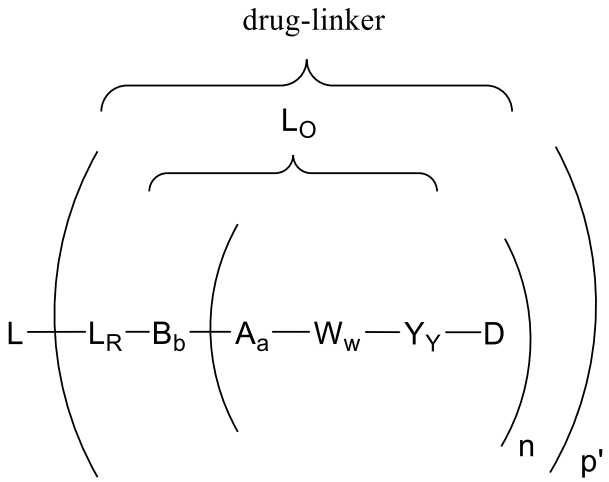
BRIEF DESCRIPTION OF THE DRAWINGS

[0026] Figure 1 shows variation over time (days) in tumor volume (mm^3) in a L450cy xenograft model post tumor implant in untreated SCID mice in comparison to those treated with 1, 3 or 10 mg/Kg (i.p.) of an Antibody Drug Conjugate (8 NAMPT Drug Units/Ab) prepared from chimeric antibody cAC10, which targets Ag2 (CD30) expressed by the implanted L450cy tumor cells, and Drug Linker compound **21**.

[0027] Figure 2 shows variation over time (days) in tumor volume (mm^3) in a L450cy xenograft model post tumor implant in untreated SCID mice in comparison to those treated with 10 mg/Kg (i.p.) Antibody Drug Conjugates (8 NAMPT Drug Units/Ab) prepared from chimeric antibody cAC10, which targets Ag2 (CD30) expressed by the implanted L450cy tumor cells, and Drug Linker compound **21** or Drug Linker compound **51**.

CLAIMS

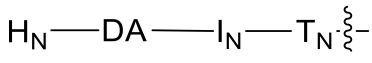
1. A Ligand Drug Conjugatea (LDC) compound, wherein the compound is represented by the structure of:



or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

D is a NAMPT Drug Unit represented by the general structure of:

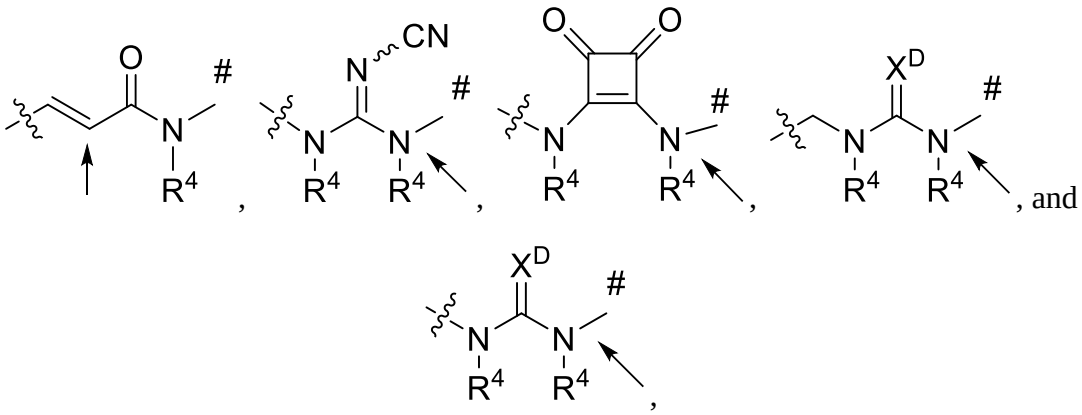


wherein

the wavy line indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O;

H_N is a NAMPT Head Unit, wherein the NAMPT Head Unit is pyridin-3-yl or pyridin-4-yl, each of which is optionally substituted;

DA is a Donor-Acceptor Unit selected from the group consisting of:



, and

wherein

X^D is O, S or NR^D, wherein the nitrogen atom is optionally protonated and R^D is hydrogen or optionally substituted C_1-C_4 alkyl;

each R^4 is independently selected from the group consisting of hydrogen and optionally substituted C_1-C_4 alkyl, or both R^4 together with the nitrogen atoms to which they are attached and the intervening carbon atom(s) define an optionally substituted C5-C6 heterocyclo;

the pound sign (#) indicates the site of covalent attachment to I_N; and the wavy line indicates the site of covalent attachment to H_N;

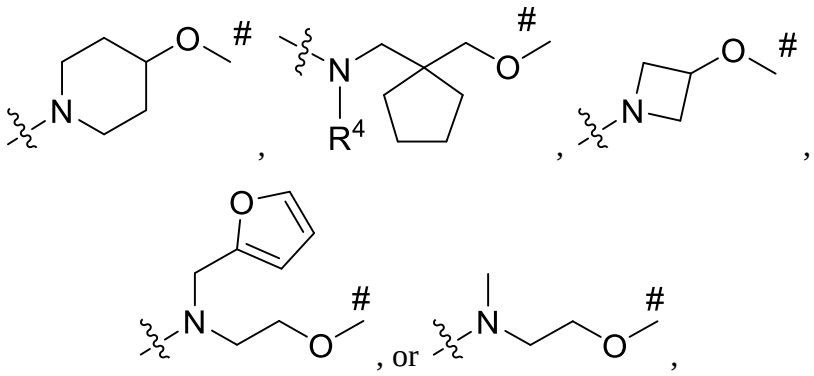
wherein DA is optionally cyclized back to an adjacent aromatic carbon atom of H_N, wherein said cyclization is from the nitrogen atom (indicated by an arrow), or DA is optionally cyclized to H_N, wherein said cyclization is to the sp^2 carbon atom proximal to the carbonyl carbon (as indicated by an arrow);

I_N is an Interconnecting Unit, wherein the Interconnecting Unit is or comprises $-X^1-[C(=O)]_{0,1}-$;

X^1 is optionally substituted C_5-C_7 alkylene;

T_N is a NAMPT Tail Unit, wherein the NAMPT Tail Unit is or comprises an optionally substituted amino-alcohol residue, the –O- of which is the site of covalent attachment to L_O, or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl;

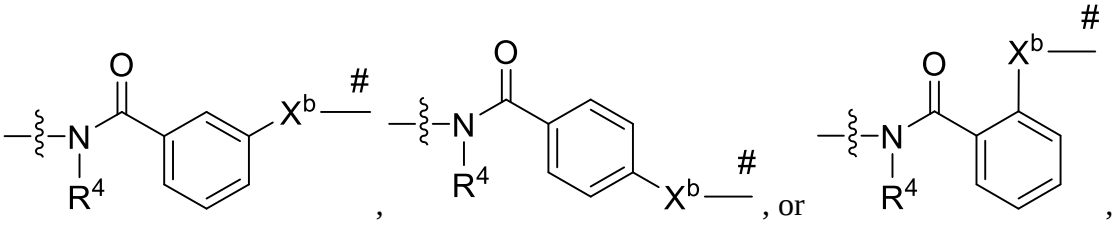
the wavy line indicates the site of covalent attachment to I_N; and

the pound sign (#) indicates the site of covalent to L_O or L_R, depending on the presence or absence of L_O, respectively, or

T_N is or comprises an optionally substituted benzamide moiety, the amide nitrogen atom of which is bonded to I_N with optional cyclization of that atom back to I_N or to the remainder

of T_N, and the aromatic ring of which is at least substituted with a hydroxyl or amino residue, the –O-, or nitrogen atom of which is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein X^b is –O- or -NH-, optionally substituted; and

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl, wherein

the benzamide moeity is optionally cyclized to I_N, wherein the amide nitrogen atom of the benzamide moiety is the site of said cyclization so that R^4 is replaced by a covalent bond to I_N;

L_R is a primary linker, which interconnects the Ligand Unit and Drug Unit optionally through L_O, as indicated, which is an optional secondary linker;

subscripts a and b independently are 0 or 1, indicating the absence or presence, respectively, of A or B;

subscript n is 1, 2, 3 or 4;

A is a first optional Stretcher; and

B is a Branching Unit, when subscript b is 1 and subscript n is 2, 3 or 4, or B is absent, so that subscript b is 0, when subscript n is 1,

wherein each of A and B is an independently selected single unit or is optionally comprised or consists of at least two, three or four independently selected subunits;

Y is a Spacer Unit; and subscript y is 0, 1 or 2, indicating the absence or presence of one or two of Y, respectively,

provided that when subscript y is 1, Y is a Spacer Unit covalently attached to a heteroatom or moiety thereof of T_N selected from the group consisting of –O-, -S- and optionally substituted nitrogen,

provided that when subscript y is 2 so that Y_y is –Y-Y', Y is a first Spacer Unit and Y' is a second Spacer Unit or a functional group comprising the optionally substituted heteroatom from T_N; and

provided that subscript y is 1 or 2 when W is a Glucuronide Unit of formula Y(W'), in which instance subscript y is inclusive of a first Spacer Unit Y, wherein that Spacer Unit is a required self-immolative Spacer Unit; and

subscript w is 0 or 1, indicating the absence or presence, respectively, of W;

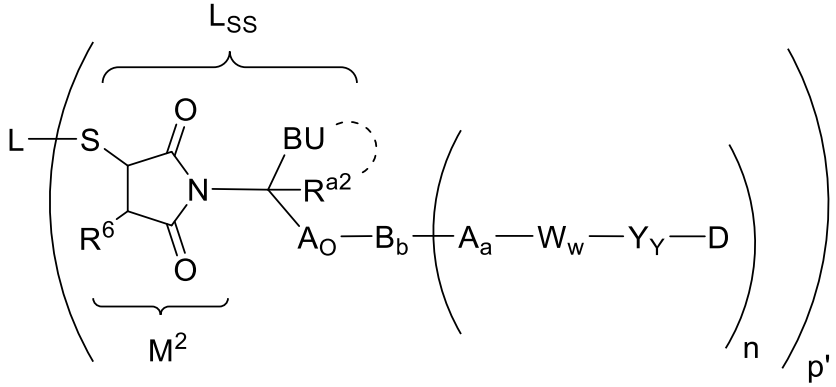
wherein

when subscript w is 1, W is a Peptide Cleavable Unit or said Glucuronide Unit in which W' represents a carbohydrate moiety with glycosidic bonding to the required self-immolative Spacer Unit through an optionally substituted heteroatom, wherein enzymatic or non-enzymatic cleavage of either Unit initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from a drug linker moiety of a Ligand Drug Conjugate compound; and

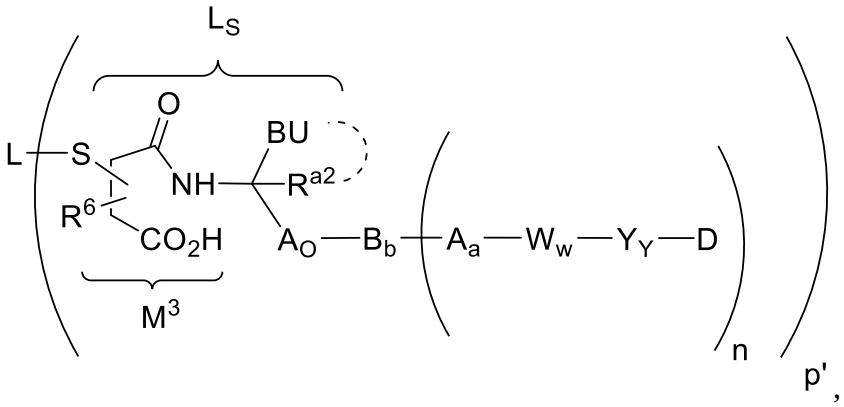
when subscript w is 0, which indicates the absence of a Cleavable Unit, enzymatic or non-enzymatic cleavage of the bond between L_R and L_O, when L_O is present, or the bond between L_R and D, when L_O is absent, initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof;

wherein when a derivative of a NAMPTi compound is released, the derivitized NAMPTi compound inhibits NAMPT and/or undergoes further enzymatic or non-enzymatic action(s) to release the parent NAMPTi compound;

wherein the Ligand Drug Conjugate compound corresponds in structure to that of Formula 1 or Formula 2 wherein p' is an integer ranging from 1 to 24:



(Formula 1)



(Formula 2)

wherein

S is a sulfur atom of the Ligand Unit, which in Formula 2 is bonded to the carbon atom α or β to the carboxylic acid functional group of the indicated succinic acid amide (M^3) moiety;

R^6 is hydrogen or an optionally substituted C_1-C_6 alkyl, which in Formula 2 is bonded to the saturated carbon atom adjacent to the carbon substituted by L-S-;

A_O is a second optional Stretcher Unit;

BU is a Basic Unit and R^{a2} is an optionally substituted C_1-C_{12} alkyl group; and

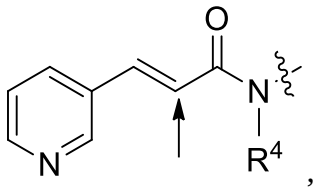
the dotted curved line indicates optional cyclization so that in the absence of said cyclization BU is an acyclic Basic Unit or in the presence of said cyclization BU is a cyclized Basic Unit in which R^{a2} and BU together with the carbon atom to which both are attached, define an optionally substituted spiro C_3-C_{20} heterocyclo containing a skeletal basic nitrogen atom of a secondary or tertiary amine functional group as the basic function group of the cyclic Basic Unit,

wherein the basic nitrogen atom of the acyclic Basic Unit or cyclic Basic Unit is optionally suitably protected by a nitrogen protecting group, dependent on the degree of substitution of the basic nitrogen atom, or is optionally protonated.

2. The Ligand Drug Conjugate compound of claim 1, wherein the Donor Acceptor (DA) Unit comprises an optionally substituted amide functional group or bioisostere thereof.

3. The Ligand Drug Conjugate compound of claim 1, wherein each of the NAMPT homodimers of the enzymatically competent NAMPT homodimer has the amino acid sequence of SEQID 1.

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



,

or a pharmaceutically acceptable salt thereof, wherein

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl; and

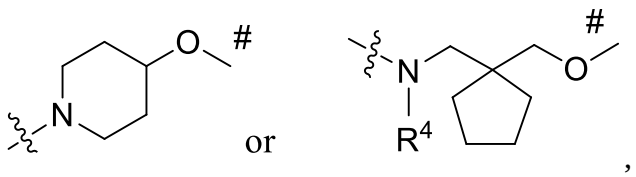
the wavy line indicates the site of covalent attachment to I_N, and

wherein the sp^2 carbon atom proximal to the carbonyl carbon atom is the site (as indicated by an arrow) of optional cyclization to H_N through an introduced optionally substituted non-aromatic carbon atom or an optionally substituted aromatic heteroatom.

5. The Ligand Drug Conjugate compound of any one of claims 1 to 4, wherein the NAMPT Tail Unit is or comprises an optionally substituted amino alcohol moeity,

wherein the oxygen atom of the alcohol is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively,

in particular having the structure of.



or a pharmaceutically acceptable salt thereof, wherein

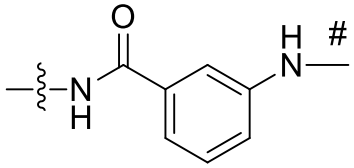
R^4 is hydrogen or optionally substituted C_1-C_4 alkyl;

the wavy line indicates the site of covalent attachment to I_N; and

the pound sign (#) indicates the site of covalent to L_O or L_R, depending on the presence or absence of L_O, respectively, or

wherein the Tail Unit is or comprises an optionally substituted benzamide moiety having a functional group providing a heteroatom that is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively,

or more particularly, having the structure of:



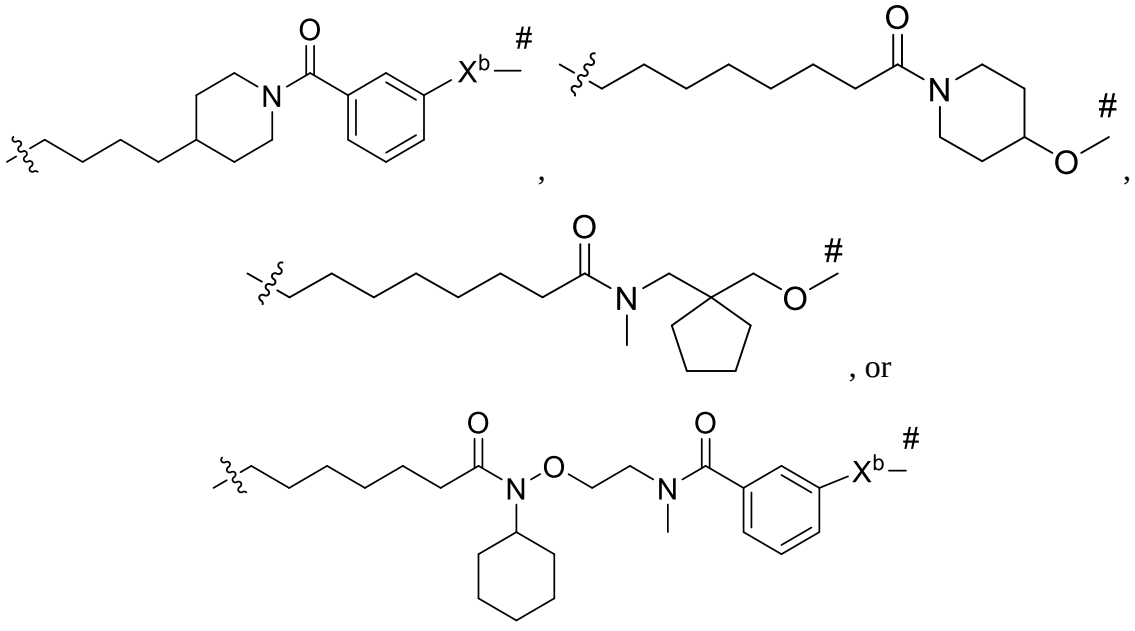
;

wherein the wavy line indicates the site of covalent attachment to I_N;

the pound sign (#) indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively.

6. The Ligand Drug Conjugate compound of claim 5, wherein I_N is $-CH_2-(CH_2)_{3-7}-CH_2-$, $-CH_2-(CH_2)_{3-7}-CH_2-O-$, or $-CH_2-(CH_2)_{3-7}-C(=O)-$.

7. The Ligand Drug Conjugate compound of claim 6, wherein $–I_N-T_N-$ has the structure of:



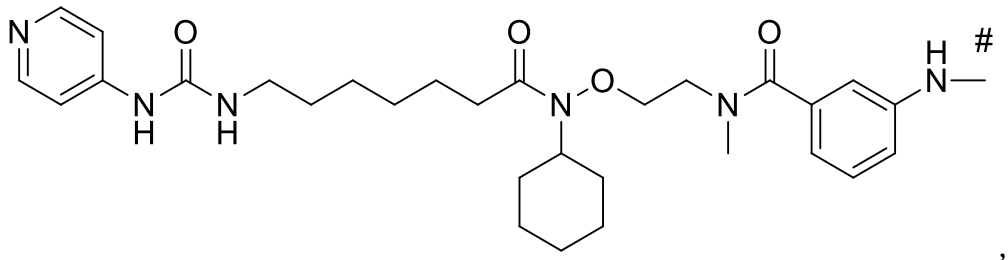
, or

wherein X^b is -NH-, –O- or –S-;

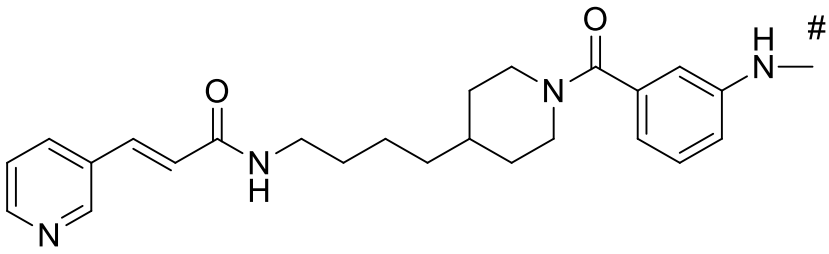
the wavy line indicates the site of covalent attachment to DA; and

the pound sign (#) indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively.

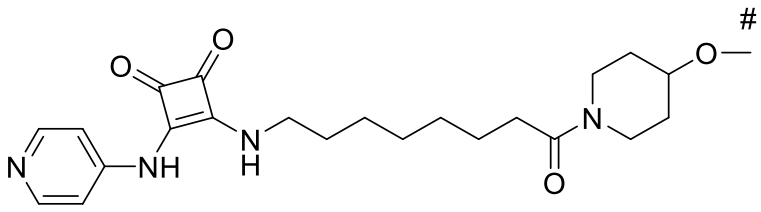
8. The Ligand Drug Conjugate compound of claim 1, wherein the NAMPT Drug Unit has the structure of:



,



, or

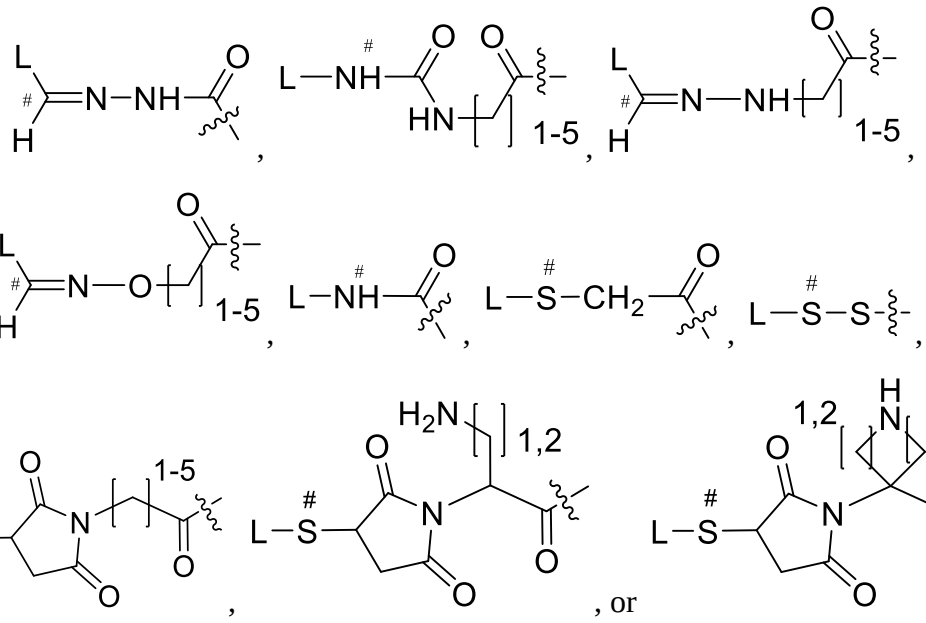


,

or a pharmaceutically acceptable salt thereof, wherein

the pound sign (#) indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively.

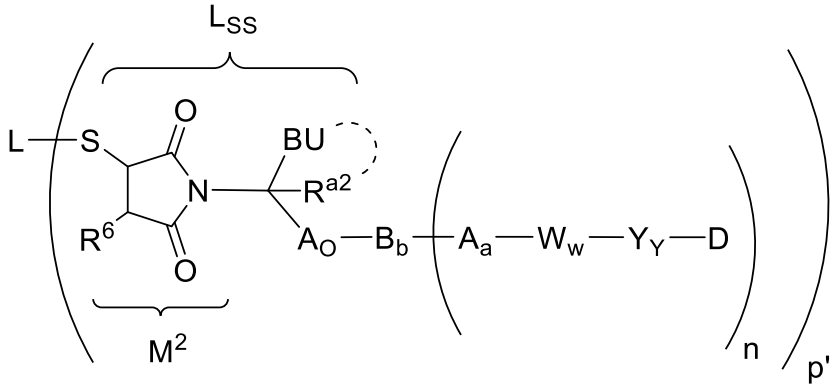
9. The Ligand Drug Conjugate compound of claim 1 or 8, wherein L-L_R- has the structure of:



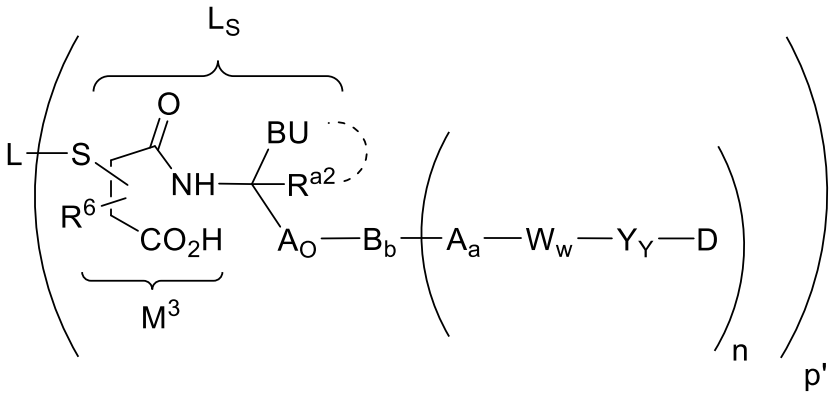
or a pharmaceutically acceptable salt thereof, wherein

the indicated (#) nitrogen, carbon or sulfur atom is from the Ligand Unit; and wherein the wavy line indicates the site of covalent attachment to the remainder of the Conjugate structure.

10. The Ligand Drug Conjugate compound of claim 1, wherein the compound is represented by the structure of Formula 1 or Formula 2:

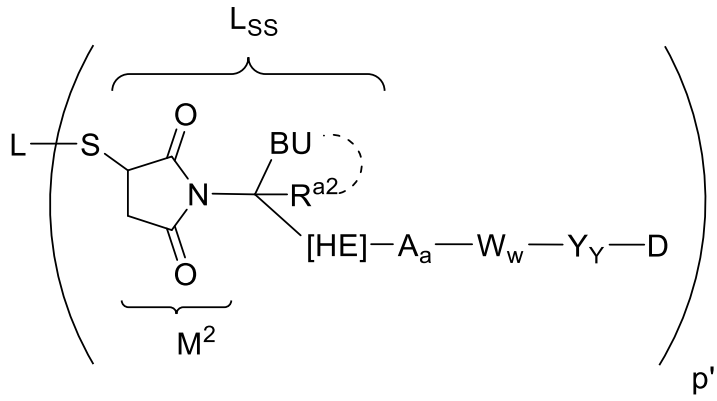


(Formula 1)

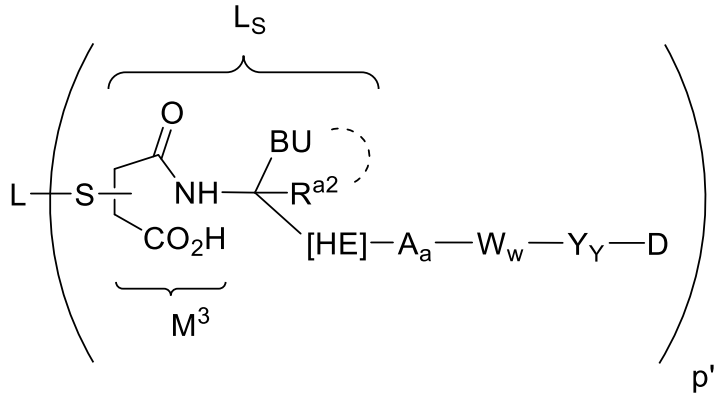


(Formula 2)

in particular, having the structure of:



or



wherein [HE] as A_O is an optional Hydrolysis Enhancing Unit;

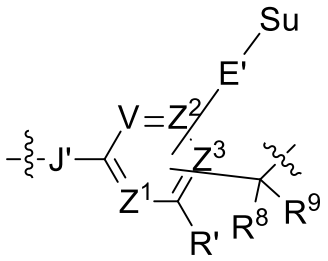
subscript w is 1;

W is Peptide Cleavable Unit; and

wherein the remaining variable groups retain their previous meanings,

wherein protease action on the Peptide Cleavable Unit results in cleavage of the W-J' bond within a drug linker moiety of a Ligand Drug Conjugate compound to initiate release of the NAMPT Drug Unit as NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound, or

W is a Glucuronide Unit of formula –Y(W')- having the structure of:



wherein Su is a carbohydrate moiety and -E'- represents an optionally substituted heteroatom of an glycosidic bond cleavable by a glycosidase so that Su-E' is W' and the remainder of the Glucuronide Unit structure is a self-immolative Spacer Unit bonded to W';

J' is an independently selected heteroatom, optionally substituted, and the wavy line thereto is the site of covalent attachment resistant to enzymatic or non-enzymatic cleavage under normal physiological conditions wherein said site of covalent attachment is to A when subscript a is 1 or to the indicated L_{SS} primary linker when subscript a is 0; and

V, Z^1, Z^2 and Z^3 are independently =N- or =C(R^{24})-, wherein each R^{24} is independently selected from the group consisting of hydrogen and C_1-C_{12} alkyl, C_2-C_{12} alkenyl and C_2-C_{12} alkynyl, optionally substituted, and halogen, an electron withdrawing group, an electron donating group, -E'-Su, and –C(R^8)(R^9)-,

provided that one and only one –C(R^8)(R^9)- moiety and one and only one –E'-Su moiety is present,

wherein one of V, Z^1, Z^2 and Z^3 is =C(R^{24})- in which R^{24} is –C(R^8)(R^9)- and another of V, Z^1, Z^2 and Z^3 is =C(R^{24})- in which R^{24} is –E'-Su,

provided the –C(R^8)(R^9)- and –E'-Su moieties are *ortho* or *para* to each other;

R^8 and R^9 independently are hydrogen, or C_1-C_{12} alkyl, C_2-C_{12} alkenyl or C_2-C_{12} alkynyl, optionally substituted, or C_6-C_{20} aryl or C_5-C_{20} heteroaryl, optionally substituted,

or

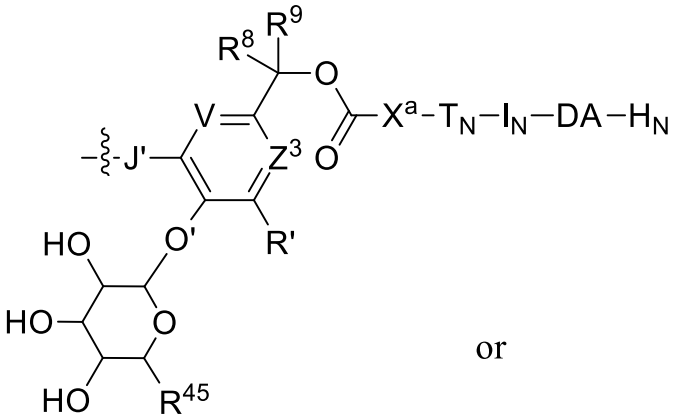
R^8 and R^9 together with the carbon atom to which both are attached define an optionally substituted C_5-C_{20} carbocyclo; and

R’ is hydrogen or -NO_2, or other electron withdrawing group or –OC_1-C_6 alkyl, or other electron donating group; and

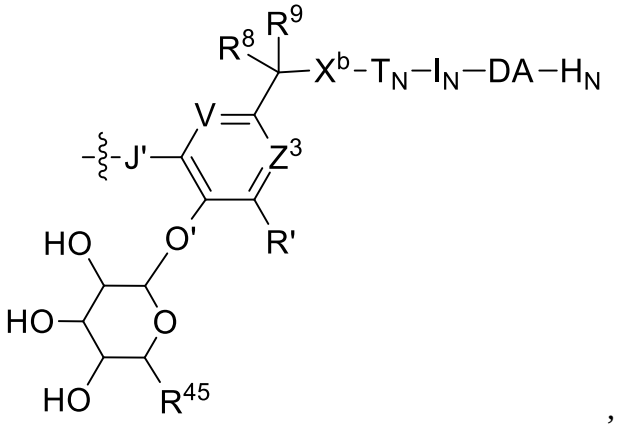
wherein the wavy line adjacent to the –C(R^8)(R^9)- moiety indicates the site of covalent attachment of the Glucuronide Unit to Y’ when subscript y is 2, or to D when subscript y is 1, and

wherein the remaining variable groups of the compound structure are as previously defined for W as a Peptide Cleavable Unit.

11. The Ligand Drug Conjugate compound of claim 10, wherein W is a Glucuronide Unit for which –W-Y_y-D has the structure of:



or



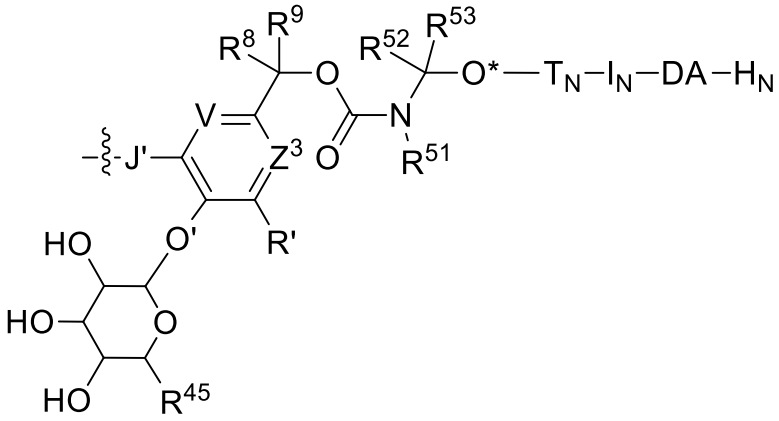
,

or a pharmaceutically acceptable salt thereof, wherein

X^a is a nitrogen atom from a primary or secondary amine functional group of T_N;

X^b is an oxygen atom from an alcohol functional group or a sulfur atom from a thiol functional group of T_N,

or –W-Y_y-D has the structure of:



or a pharmaceutical acceptable salt thereof,

R^{51}, R^{52} and R^{53} independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_6-C_{14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl,

or R^{51} and R^{52} together with the nitrogen and carbon atoms to which both are attached define an azetidine, pyrrolidine, piperidine or homopiperidine heterocyclo, and R^{53} is hydrogen;

and in either –W-Y_y-D structure:

R^{45} is $–CH_2OH$ or $–CO_2H$;

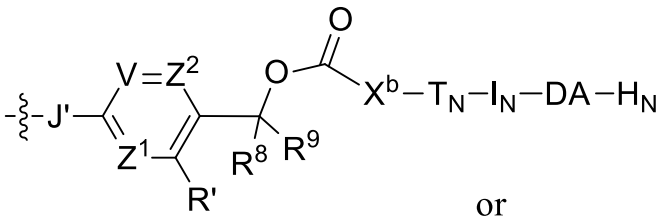
R' is hydrogen or $–NO_2$ or other electron withdrawing group;

J' is an optionally substituted heteroatom, and the wavy line thereto is the site of covalent attachment resistant to enzymatic or non-enzymatic cleavage under normal physiological conditions; and

wherein O* represents the oxygen atom from an alcohol functional group of T_N and O' represents the oxygen atom of an O-glycosidic bond cleavable by a glycosidase, wherein said cleavage within a drug linker moiety of Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative from that Ligand Drug Conjugate compound,

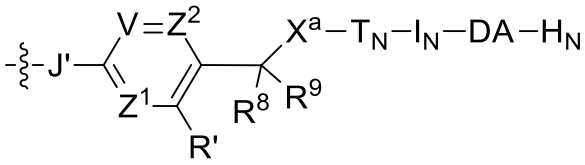
or, wherein

W is a Peptide Cleavable Unit for which –Y_y-D – has the structure of:



or

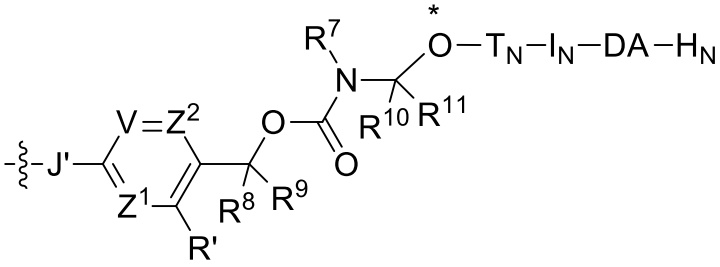
,



or a pharmaceutical acceptable salt thereof, wherein

X^a is an oxygen atom from an alcohol functional group or a sulfur atom of a thiol functional group of T_N;

X^b is a nitrogen atom from a primary or secondary amine functional group of T_N, or has the structure of:



or a pharmaceutical acceptable salt thereof, wherein

R' is hydrogen or $–OC_1$-C_6 alkyl or other electron donating group;

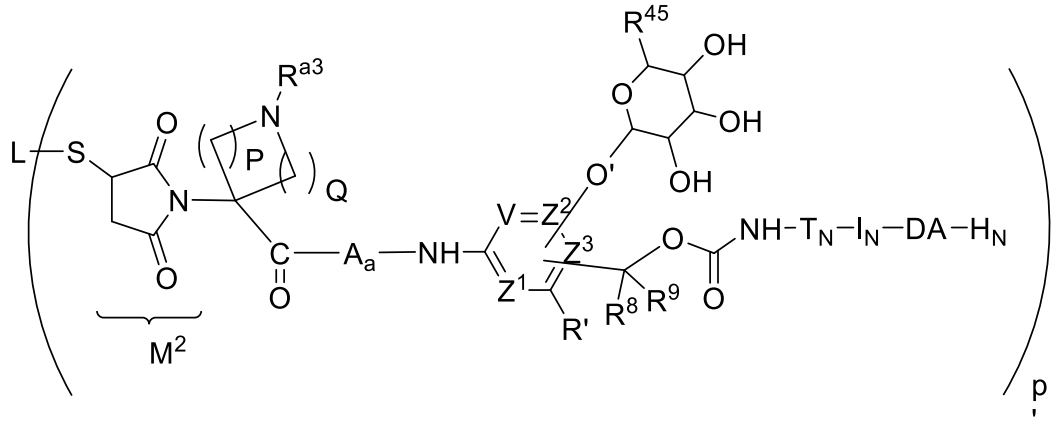
R^7, R^{10} and R^{11} independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_6-C_{14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl,

or R^7 and R^{10} together with the nitrogen and carbon atoms to which both are attached define an azetidine, pyrrolidine, piperidine or homopiperidine heterocyclo, and R^{11} is hydrogen;

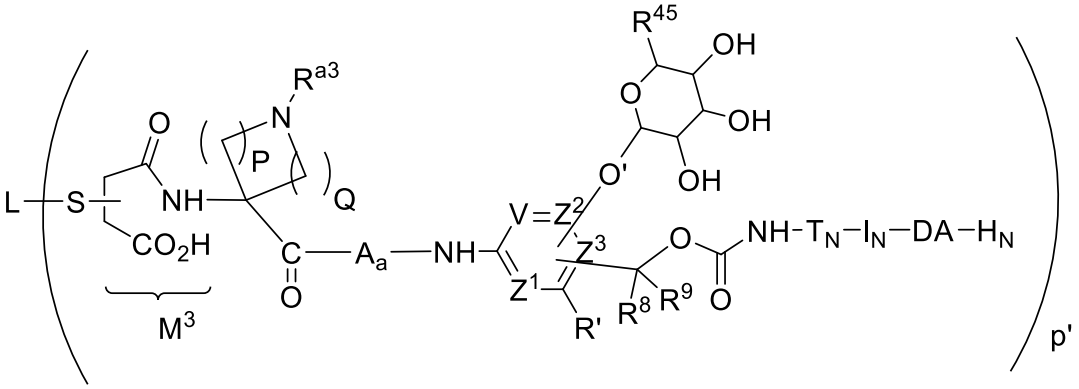
J' is an optionally substituted heteroatom bonded to W as indicated by the wavy line, wherein cleavage of that bond within a drug linker moiety of a Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound; and

the remaining variable groups are as previously defined for W as a Glucuronide Unit.

12. The Ligand Drug Conjugate compound of claim 10, wherein W is a Glucuronide Unit for which the compound is represented by the structure of:



or

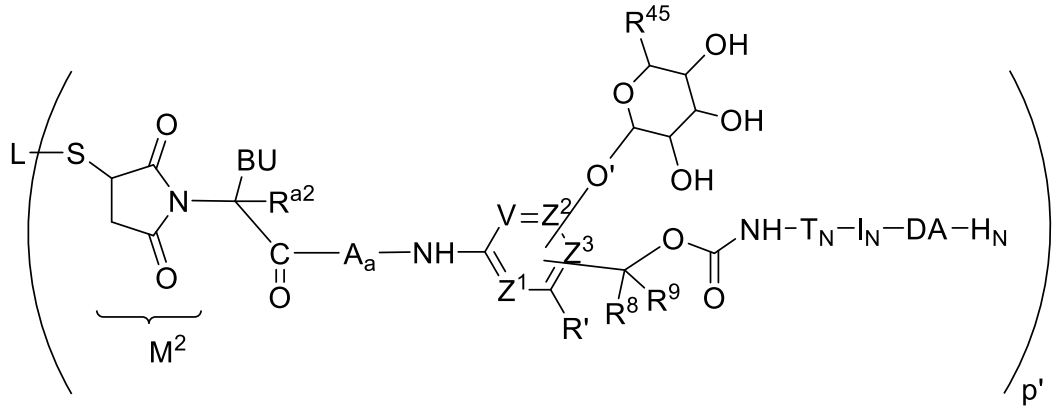


or a pharmaceutical acceptable salt thereof, wherein

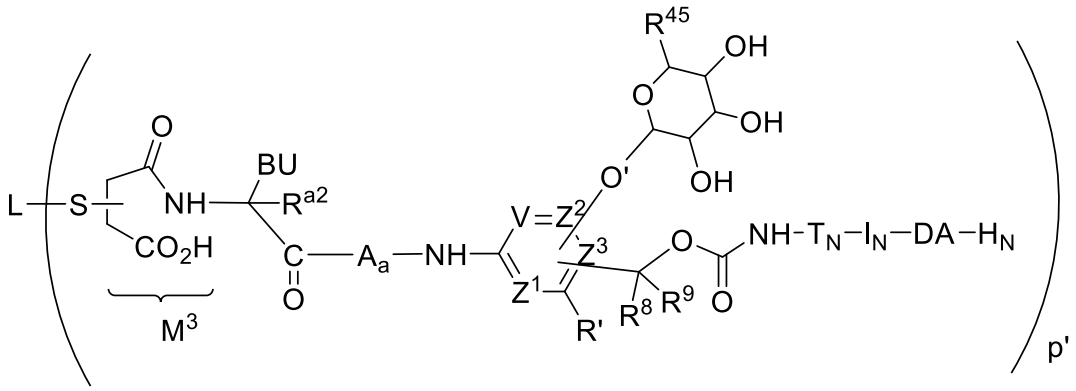
subscript P is 1, 2 or 3; and

subscript Q ranges from 1 to 6,

or by the structure of:



or



or a pharmaceutical acceptable salt thereof, wherein

R^{a2} is hydrogen or C_1-C_6 alkyl;

BU is an acyclic Basic Unit having the structure of $–[C(R^{a1})(R^{a1})]-[C(R^{a1})(R^{a1})]_{0-3}-N(R^{a3})(R^{a3})$, wherein each R^{a1} independently is hydrogen or C_1-C_4 alkyl, C_6-C_{10} aryl, C_5-C_{10} heteroaryl, (C_6-C_{10} aryl)-C_1-C_4 alkyl-, or (C_5-C_{10} heteroaryl)-C_1-C_4 alkyl-, optionally substituted, or two R^{a1} together with the carbon(s) to which they are attached and any intervening carbons define an optionally substituted C_3-C_6 cycloalkyl; and

R^{a3} independently are hydrogen, optionally substituted C_1-C_6 alkyl or R^{a3} together with the nitrogen atom to which both are attached define a C_3-C_6 heterocyclyl in which the basic nitrogen atom is a skeletal atom,

or one of R^{a3} is –H and the other is optionally substituted C_1-C_6 alkyl, optionally substituted -C_1-C_4 alkylene-(C_6-C_{10} aryl), or $-R^{PEG1}-O-(CH_2CH_2O)_{1-36}-R^{PEG2}$, wherein R^{PEG1} is C_1-C_4 alkylene, and R^{PEG2} is –H or C_1-C_4 alkyl; and

the basic nitrogen atom bonded to R^{a3} is optionally protonated; and

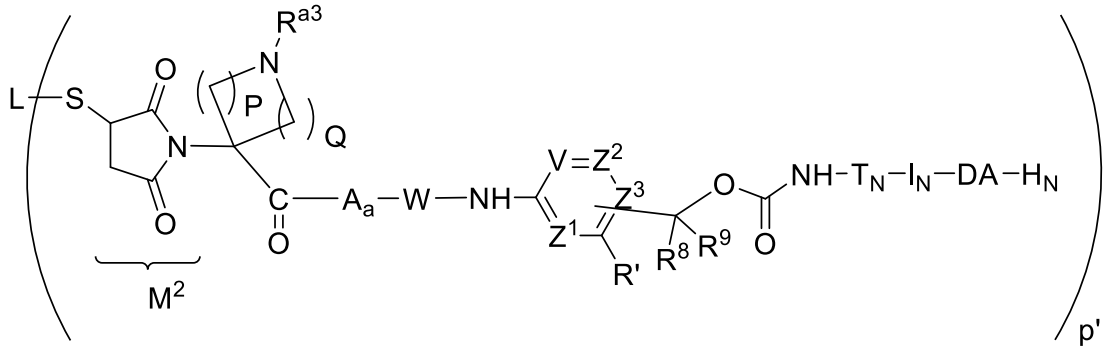
wherein R’ is hydrogen or $–NO_2$ or other electron withdrawing group;

R^{45} is $–CH_2OH$ or $–CO_2H$;

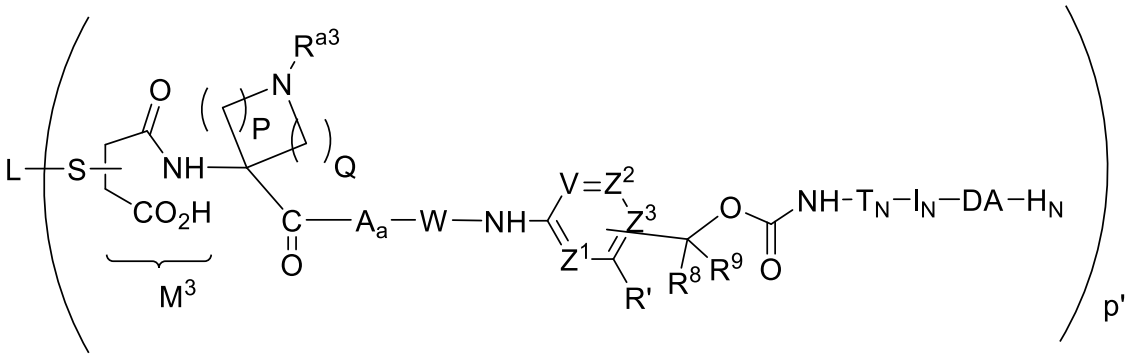
wherein -O’- represents the oxygen atom of an O-glycosidic bond cleavable by a glycosidase, wherein said cleavage within a drug linker moiety of a Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof that Ligand Drug Conjugate compound,

or

wherein the W is a Peptide Cleavable Unit for which the compound is represented by the structure of:



or

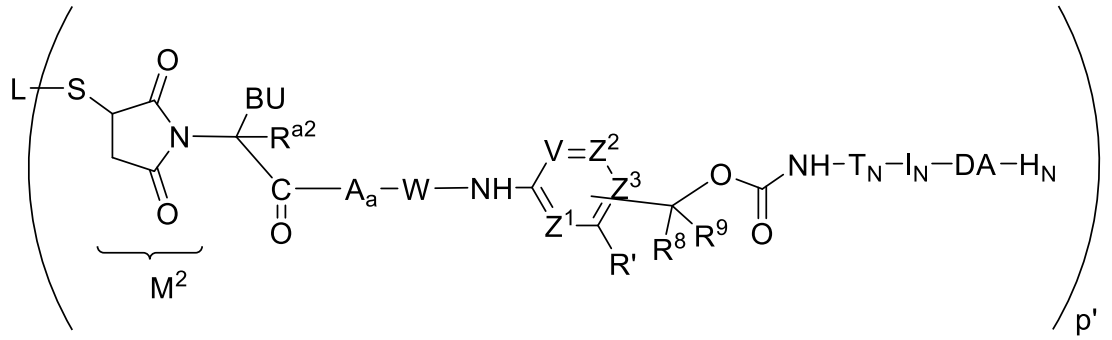


or a pharmaceutical acceptable salt thereof, wherein

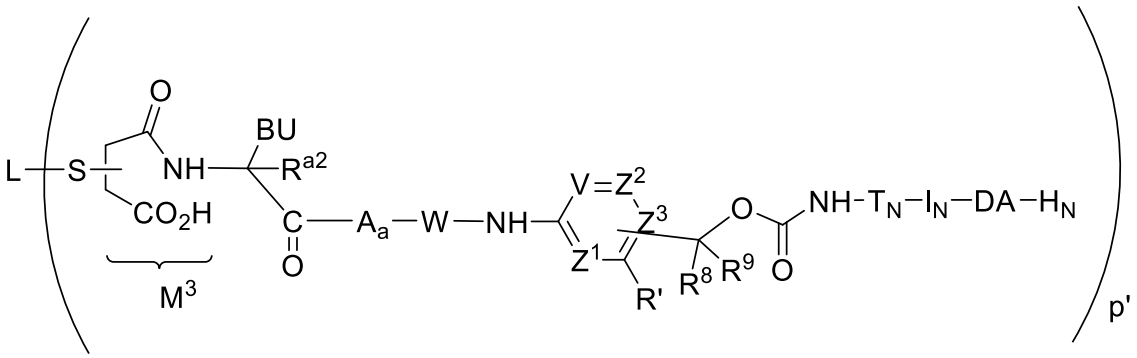
subscript P is 1, 2 or 3; and

subscript Q ranges from 1 to 6,

or is represented by the structure of:



or



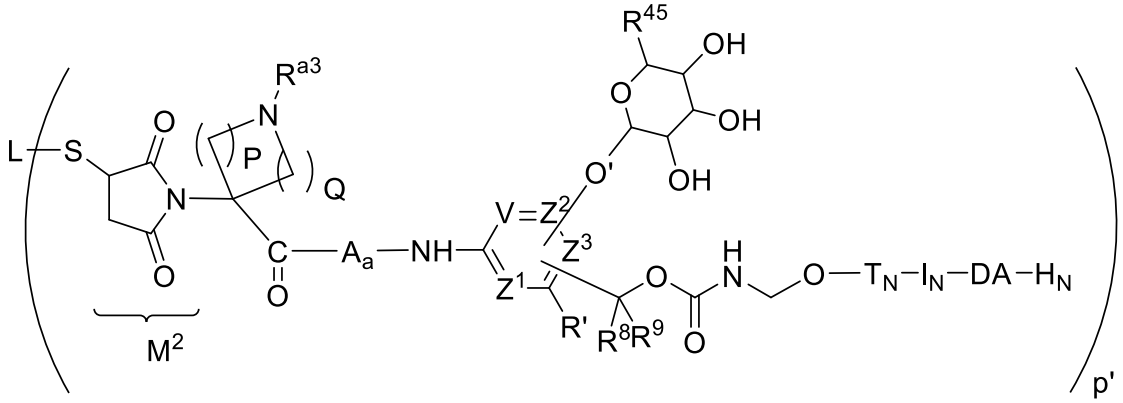
or a pharmaceutical acceptable salt thereof, wherein

R’ is hydrogen or –OC_1-C_6 alkyl or other electron donating group; and

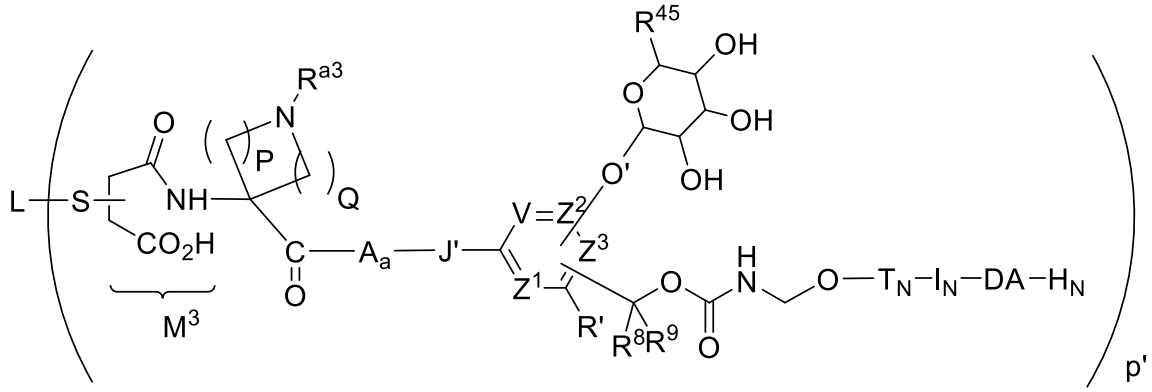
and the remaining variable gropus are as defined by the above structures in which W is a Glucuronide Unit,

wherein protease action on the Peptide Cleavable Unit cleaves the W-NH bond, wherein said cleavage within a drug linker moiety of a Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound.

13. The Ligand Drug Conjugate compound of claim 10, wherein W is a Glucuronide Unit for which the compound is represented by the structure of:



or

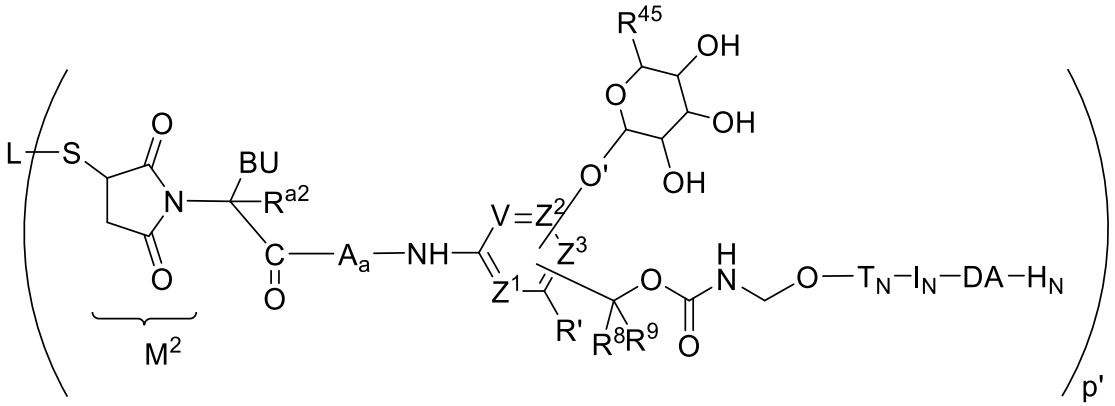


or a pharmaceutical acceptable salt thereof, wherein

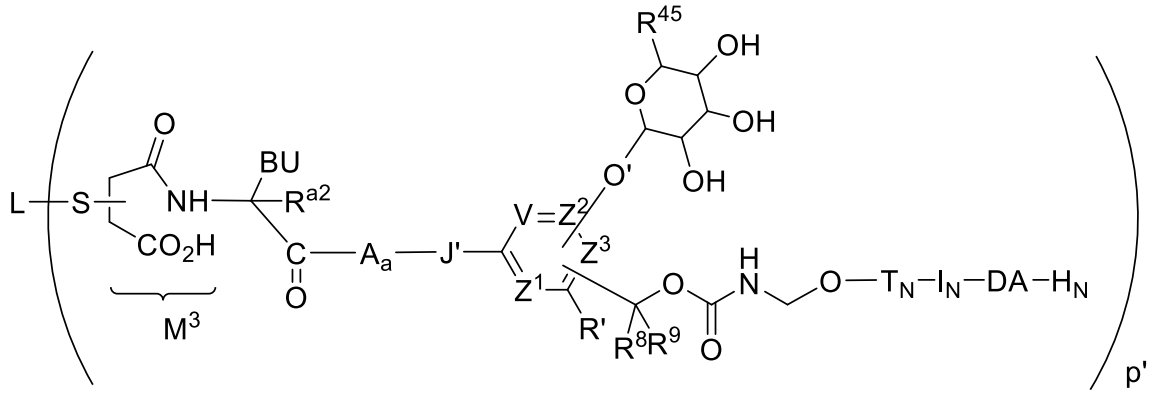
subscript P is 1 or 2 or 3; and

subscript Q ranges from 1 to 6,

or is represented by the structure of:



or



or a pharmaceutical acceptable salt thereof, wherein

R^{a2} is hydrogen or C_1-C_6 alkyl;

BU is an acyclic Basic Unit having the structure of –[C(R^{a1})(R^{a1})]-[C(R^{a1})(R^{a1})]$_{0-3}$-N(R^{a3})(R^{a3}), wherein each R^{a1} independently is hydrogen or C_1-C_4 alkyl, C_6-C_{10} aryl, C_5-C_{10} heteroaryl, (C_6-C_{10} aryl)-C_1-C_4 alkyl-, or (C_5-C_{10} heteroaryl)-C_1-C_4 alkyl-, optionally substituted, or two R^{a1} together with the carbon(s) to which they are attached and any intervening carbons define an optionally substituted C_3-C_6 cycloalkyl; and

R^{a3} independently are hydrogen, optionally substituted C_1-C_6 alkyl or R^{a3} together with the nitrogen atom to which both are attached define a C_3-C_6 heterocyclyl in which the basic nitrogen atom is a skeletal atom,

or one of R^{a3} is –H and the other is optionally substituted C_1-C_6 alkyl, optionally substituted -C_1-C_4 alkylene-(C_6-C_{10} aryl), or -R^{PEG1}-O-(CH_2CH_2O)$_{1-36}$-R^{PEG2}, wherein R^{PEG1} is C_1-C_4 alkylene, and R^{PEG2} is –H or C_1-C_4 alkyl; and

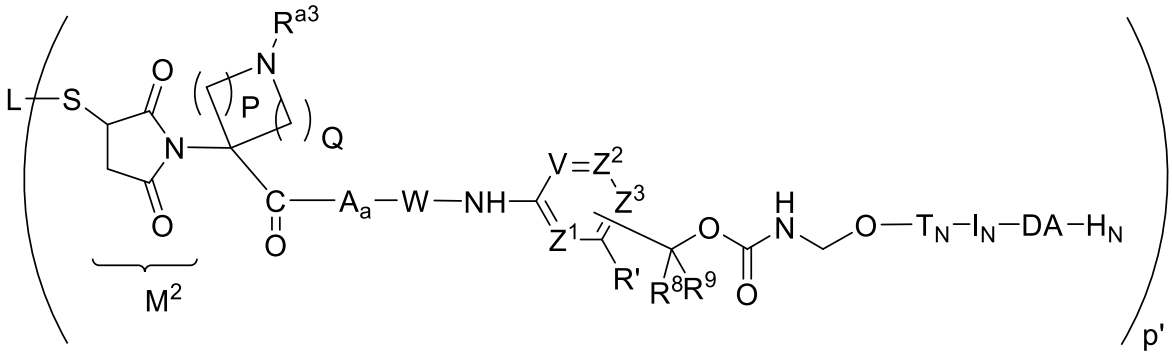
the basic nitrogen atom bonded to R^{a3} is optionally protonated;

R’ is hydrogen or –NO_2 or other electron withdrawing group;

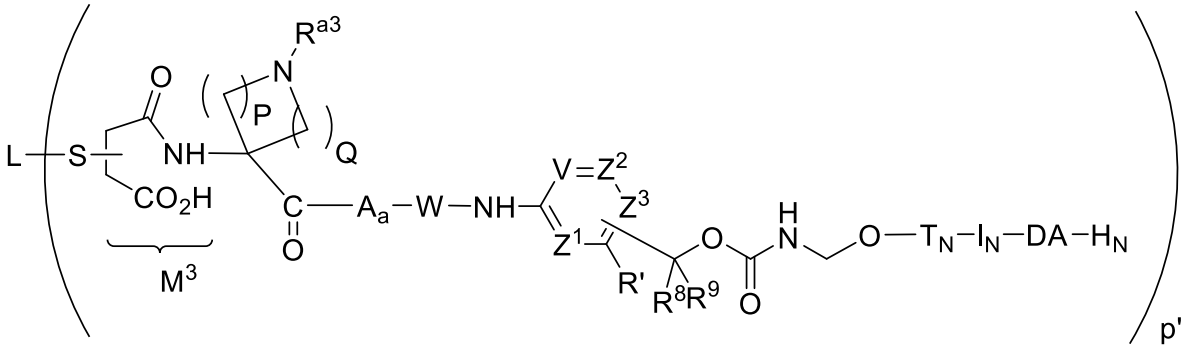
R^{45} is –CH_2OH or –CO_2H; and

-O’- represents the oxygen atom of an O-glycosidic bond cleavable by a glycosidase, wherein said cleavage within a drug linker moiety of a Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound,

or wherein W is a Peptide Cleavable Unit for which the compound is represented by the structure of:



or

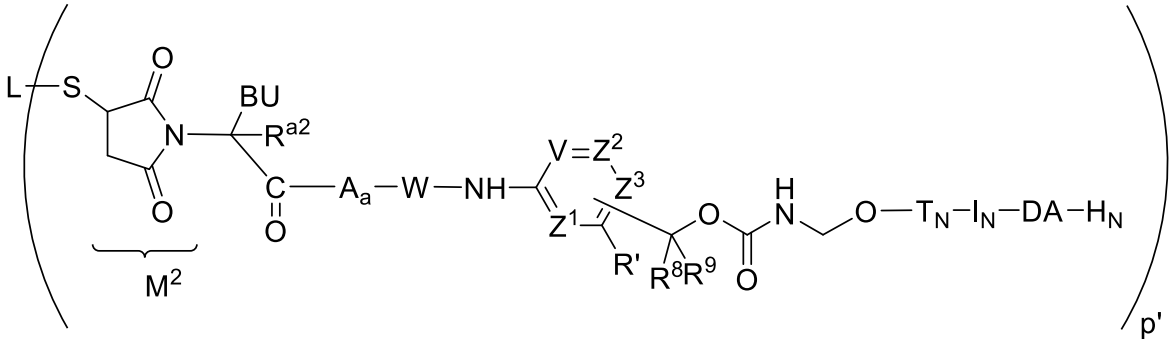


or a pharmaceutical acceptable salt thereof, wherein

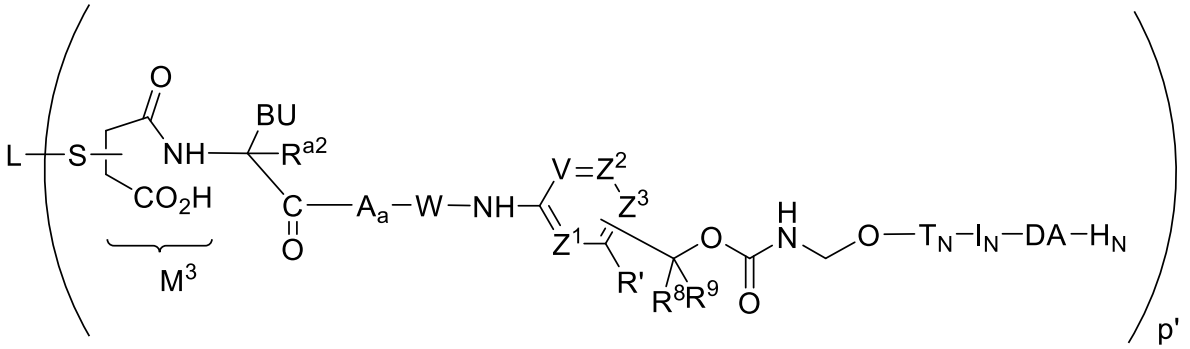
subscript P is 1, 2 or 3;

subscript Q ranges from 1 to 6,

or is represented by the structure of:



or



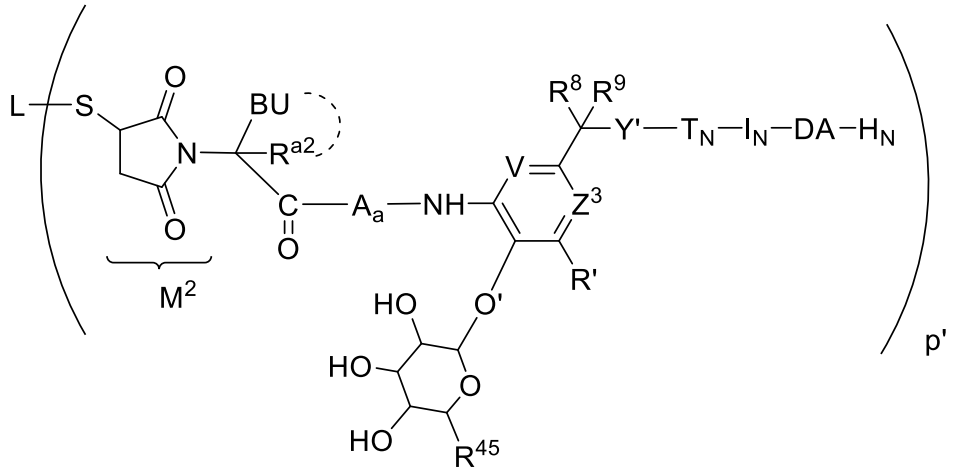
or a pharmaceutical acceptable salt thereof, wherein

R’ is hydrogen or –OC_1-C_6 alkyl or other electron donating group; and

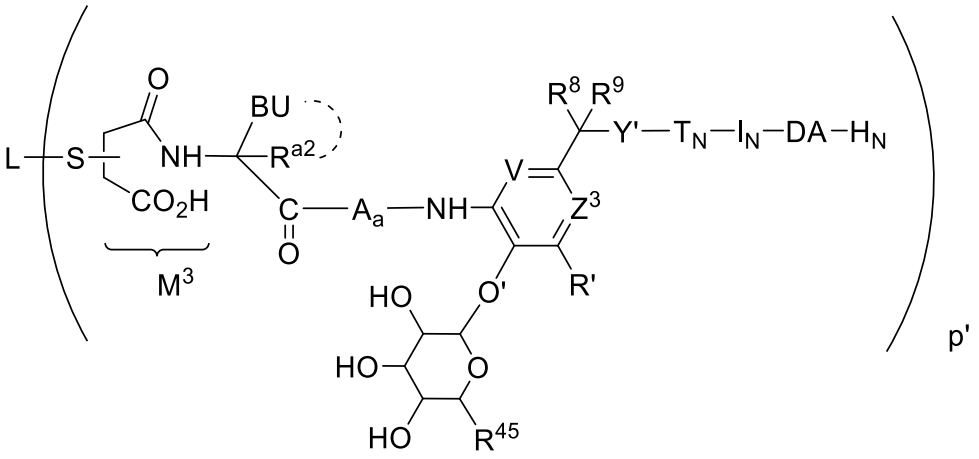
and the remaining variable groups are as defined by the above structures in which W is a Glucuronide Unit,

wherein protease action on the Peptide Cleavable Unit cleaves the W-NH bond, wherein said cleavage within a drug linker moiety of a Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound.

14. The Ligand Drug Conjugate compound of claim 10, wherein W is a Glucuronide Unit for which the compound is represented by the structure of:



or



or a pharmaceutical acceptable salt thereof, wherein

R' is hydrogen or $–NO_2$ or other electron withdrawing group;

R^{a2} is hydrogen or C_1-C_6 alkyl, optionally cyclized to BU, as indicated by the dotted curved line,

BU has the structure of $–[C(R^{a1})(R^{a1})]-[C(R^{a1})(R^{a1})]_{0-3}-N(R^{a3})(R^{a3})$,

wherein in the absence of cyclization to R^{a2}, each R^{a1} independently is hydrogen or C_1-C_4 alkyl, C_6-C_{10} aryl, C_5-C_{10} heteroaryl, (C_6-C_{10} aryl)-C_1-C_4 alkyl-, or (C_5-C_{10} heteroaryl)-C_1-C_4 alkyl-, optionally substituted, or two R^{a1} together with the carbon(s) to which they are attached and any intervening carbons define an optionally substituted C_3-C_6 cycloalkyl; and

R^{a3} independently are hydrogen, optionally substituted C_1-C_6 alkyl or R^{a3} together with the nitrogen atom to which both are attached define a C_3-C_6 heterocyclyl in which the basic nitrogen atom is a skeletal atom,

or one of R^{a3} is –H and the other is optionally substituted C_1-C_6 alkyl, optionally substituted -C_1-C_4 alkylene-(C_6-C_{10} aryl), or -R^{PEG1}-O-$(CH_2CH_2O)_{1-36}$-R^{PEG2}, wherein R^{PEG1} is C_1-C_4 alkylene, and R^{PEG2} is –H or C_1-C_4 alkyl; and

the basic nitrogen atom bonded to R^{a3} is optionally protonated; and

in the presence of cyclization one of R^{a1} or one of R^{a3} is replaced with a bond to a carbon atom of R^{a2} in which R^{a2} is C_1-C_6 alkyl and the remaining R^{a1} and R^{a3} are as previously defined; and

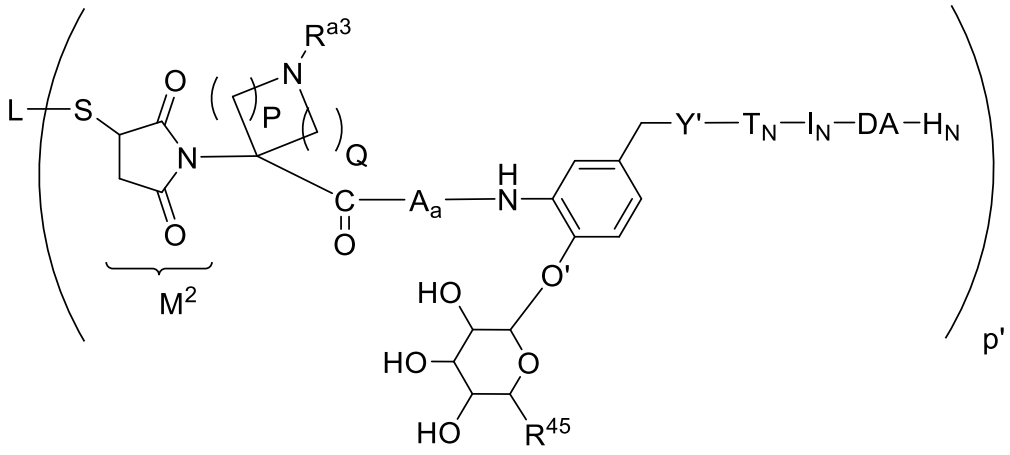
wherein Y’ is -X^a-, -O-C(=O)-X^b- or –OC(=O)NH-CH_2-X^a-,

wherein X^a or X^b are from T_N, wherein –X^a- is O or S and X^b is –NH-; and

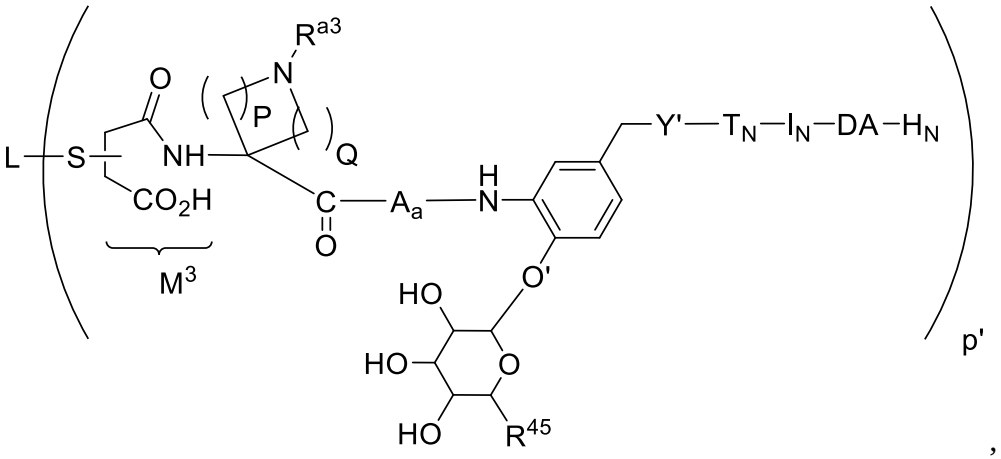
R^{45} is –CH_2OH or –CO_2H; and

wherein -O’- represents the oxygen atom of an O-glycosidic bond cleavable by a glycosidase, wherein said cleavage within a drug linker moiety of a Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound,

in particular, by the structure of:



or



,

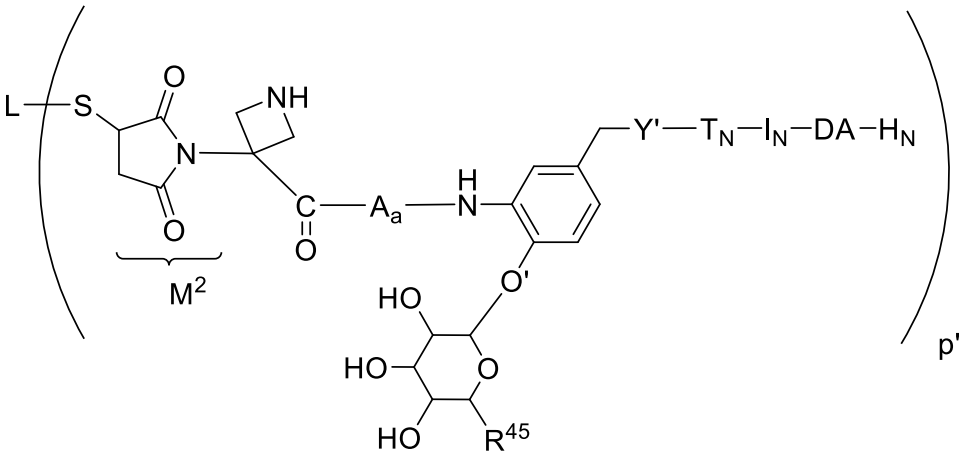
or a pharmaceutically acceptable salt thereof,

subscript P is 1, 2 or 3;

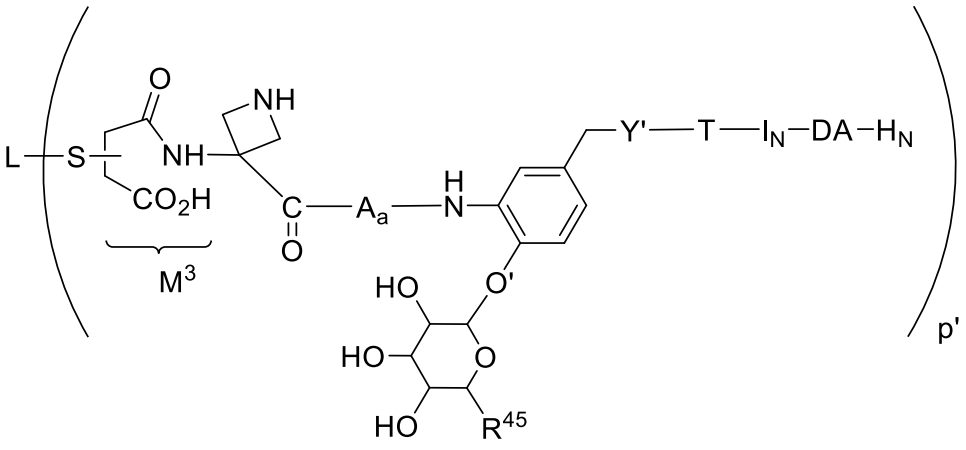
subscript Q ranges from 1 to 6; and

wherein the remaining variable groups are as previously defined,

more particularly, by the structure of:



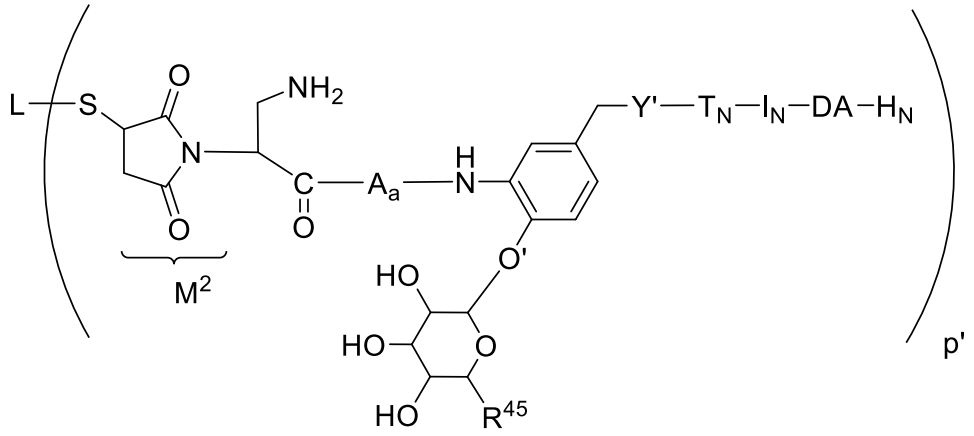
or



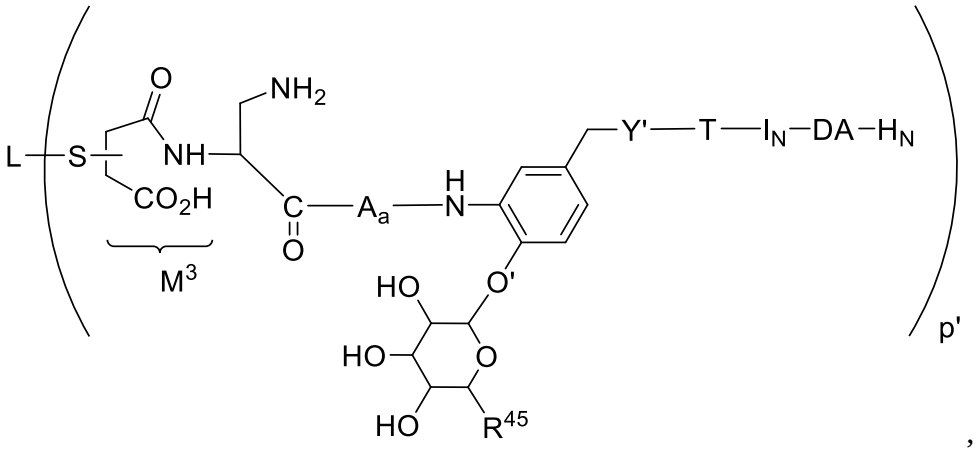
or a pharmaceutically acceptable salt thereof, wherein

the variable groups are as previously defined, or

the compound is represented particularly by the structure of:



or

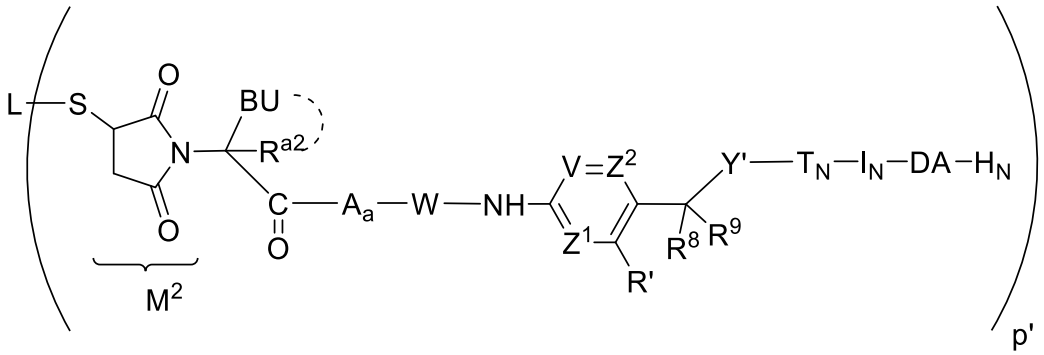


,

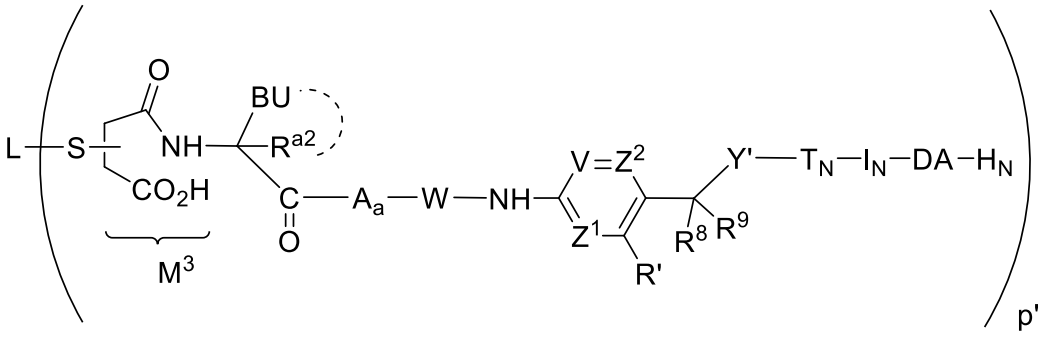
or a pharmaceutical acceptable salt thereof, wherein

the variable groups are as previously defined, or

wherein W is a Peptide Cleavable Unit for which the compound is represented by the structure of:



or



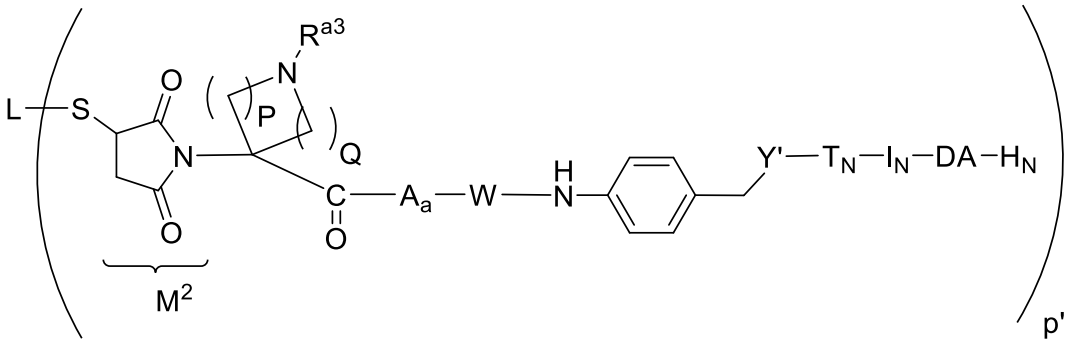
or a pharmaceutically acceptable salt thereof, wherein

R' is hydrogen or $-OC_1$-C_6 alkyl or other electron donating group; and

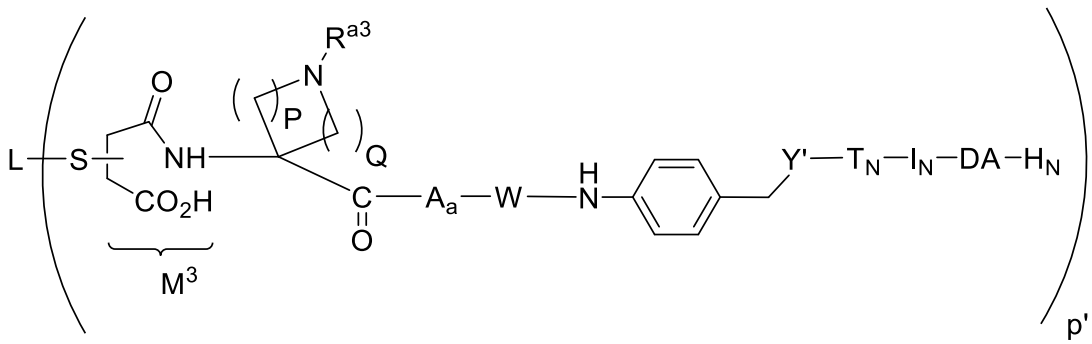
the remaining variable groups are as defined by the above structures in which W is a Glucuronide Unit; and

wherein protease action on the Peptide Cleavable Unit cleaves the W-NH bond, wherein said cleavage within a drug linker moiety of the Ligand Drug Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound,

in particular by the structure of:

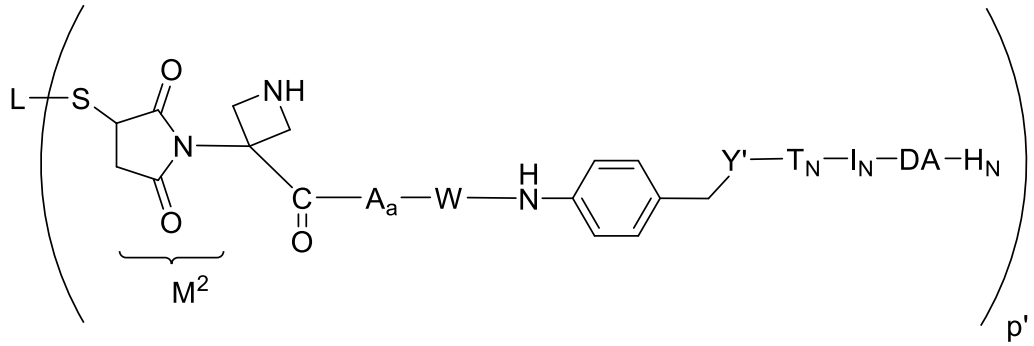


or

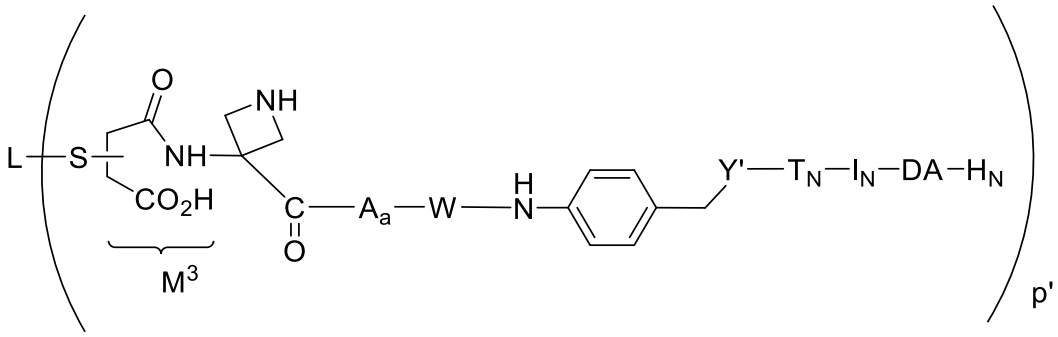


or a pharmaceutically acceptable salt thereof,

more particularly by the structure of:

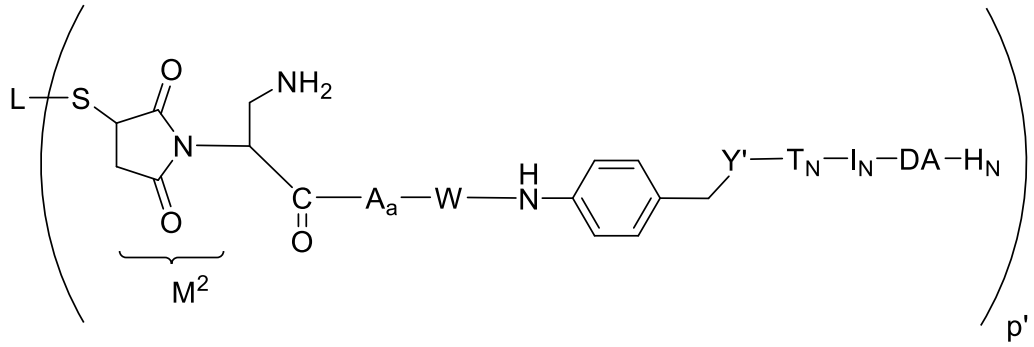


or

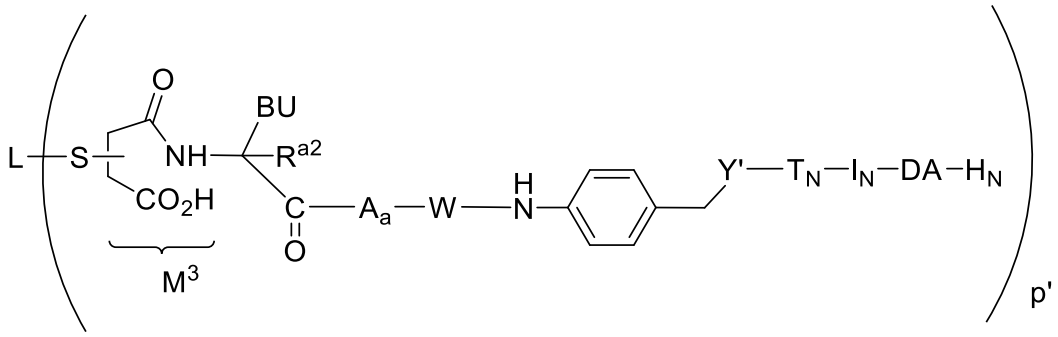


or a pharmaceutically acceptable salt thereof, wherein the variable groups are as previously defined, or

the compound is represented particularly by the structure of:



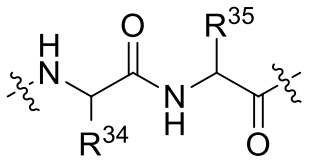
or

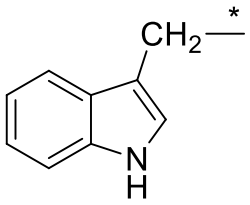


or a pharmaceutically acceptable salt thereof; and wherein the variable groups are as previously defined

15. The Ligand Drug Conjugate compound of any one of claims 10 to 14 in which W is a Peptide Cleavable Unit that comprises a dipeptide wherein the dipeptide provides for a recognition site for a regulatory or lysosomal protease for cleavage by said protease of the W-J' bond or the W-NH bond when J' is -NH within a Ligand Drug Conjugate compound so as to initiate release of the NAMPT Drug Unit as NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound.

16. The Ligand Drug Conjugate compound of claim 15, wherein the W has the structure of:



wherein R^{34} is benzyl, methyl, isopropyl, isobutyl, sec-butyl, -CH(OH)CH_3 or has the structure of  , wherein the asterisk indicates the site of covalent attachment to the dipeptide backbone; and

R^{35} is methyl, –$(CH_2)_4$-NH_2, -$(CH_2)_3$NH(C=O)NH_2, -$(CH_2)_3$NH(C=NH)NH_2, or, -$(CH_2)_2CO_2H$; and

wherein the wavy lines indicate the points of covalent attachment of the dipeptide into the structure representing the Ligand Drug Conjugate compound,

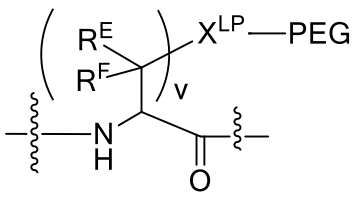
in particular W is selected from the group consisting of -Phe-Lys-, -Val-Ala-, -Val-Lys-, -Ala-Lys-, -Val-Cit-, -Phe-Cit-, -Leu-Cit-, -Ile-Cit-, -Phe-Arg-, and -Trp-Cit-, wherein Cit is citrulline.

17. The Ligand Drug Conjugate compound of any one of claims 1-8 and 10-14, wherein A or a subunit thereof is –L^P(PEG)-,

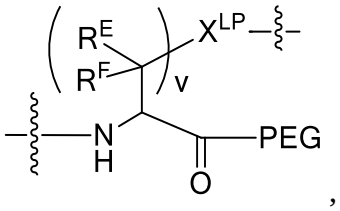
wherein –L^P- or a subunit thereof is a aminoalkanedioic acid, a diaminoalkanoic acid, a sulfur-substituted alkanedioic acid, a sulfur-substituted aminoalkanoic acid, a diaminoalkanol, an aminoalkanediol, a hydroxyl substituted alkanedioic acid, a hydroxyl substituted aminoalkanoic acid or a sulfur-substituted aminoalkanol residue, optionally substituted, wherein the substituted sulfur is in reduced or oxidized form, or

–L^P- or a subunit thereof is an amino acid residue of lysine, arginine, asparagine, glutamine, ornithine, citrulline, cysteine, homocysteine, penicillamine, threonine, serine, glutamic acid, aspartic acid, tyrosine, histidine or tryptophan, wherein the amino acid is in the **D**- or **L**-configuration, or

wherein –L^P(PEG)- has the structure of:



(Formula L^P-3)



(Formula L^P-4)

or a pharmaceutical acceptable salt thereof, wherein

wherein subscript v is an integer ranging from 1 to 4;

X^{LP} is selected from the group consisting of –O-, -NR^{LP}-, -S-, -S(=O)-, -$S(=O)_2$-, -C(=O)-, -C(=O)N(R^{LP})-, -N(R^{LP})C(=O)N(R^{LP})-, -N(R^{LP})C(=NR^{LP})N(R^{LP})-, and C_3-C_8 heterocyclo, in particular –O-, -NH, -S- and -C(=O)-;

wherein each R^{LP} is independently selected from the group consisting of hydrogen and optionally substituted C_1-C_6 alkyl, or two of R^{LP} together along with the carbons atoms to which they are attached and their intervening atoms define a C_5-C_6 heterocyclo and any remaining R^{LP} are as previously defined;

Ar is a C_6-C_{10} arylene or a C_5-C_{10} heteroarylene, optionally substituted;

each R^E and R^F is independently selected from the group consisting of -H, optionally substituted C_1-C_6 alkyl, optionally substituted C_2-C_6 alkylene, optionally substituted C_6-C_{10} arylene and optionally substituted C_5-C_{10} heteroarylene, in particular hydrogen and C_1-C_4 alkyl,

or R^E and R^F together with the carbon atom to which both are attached defines an optionally substituted spiro C_3-C_6 carbocyclo, or R^E and R^F from adjacent carbon atoms

together with these atoms and any intervening carbon atoms defines an optionally substituted C_5-C_6 carbocyclo with any remaining R^E and R^F as previously defined, or

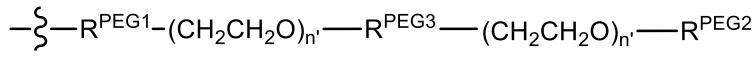
wherein the side chain of $–[C(R^E)(R^F)]_v$-X^{LP}- is provided by a natural or un-natural amino acid side chain; and

wherein the wavy lines indicate the sites of covalent attachments within the remainder of the Ligand Drug Conjugate compound structure;

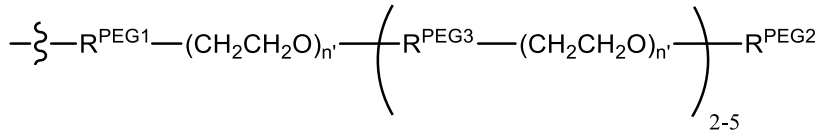
in particular having the PEG Unit respresented by:



,



, and



wherein the wavy line indicates site of attachment to X^{LP} of the Parallel Connector Unit (L_P);

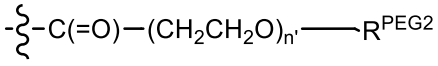
subscript n' independently ranges from 1 to 72;

R^{PEG1} is an optional PEG Attachment Unit;

R^{PEG2} is a PEG Capping Unit; and

R^{PEG3} is an PEG Coupling Unit, or

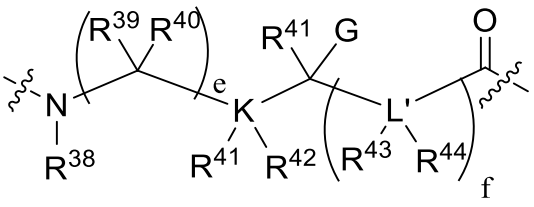
having X^{LP}-PEG with the structure of:



,

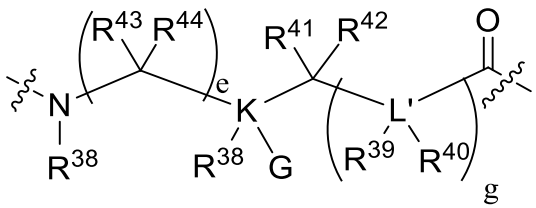
wherein subscript n' is 8, 12 or 24 and R^{PEG2} is H or $–CH_3$.

18. The Ligand Drug Conjugate compound of any one of claims 1-8 and 10-14, wherein A or a subunit thereof has the structure of formula (3) or formula (4):



f

,



g

(3) (4)

wherein the wavy lines indicated covalent attachment within the Ligand Drug Conjugate compound structure;

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

wherein subscripts e and f are independently selected integers that range from 0 to 12, and subscript g is an integer ranging from 1 to 12;

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

G is -$N(R^{PR})(R^{PR})$, wherein R^{PR} are independently a protecting group or R^{PR} together form a suitable protecting group, or

G is -$N(R^{45})(R^{46})$, wherein one of R^{45}, R^{46} is hydrogen or R^{PR}, wherein R^{PR} is a suitable protecting group, and the other is hydrogen or optionally substituted C_1-C_6 alkyl;

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

R^{39}-R^{44} are independently selected from the group consisting of hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl,

or R^{39}, R^{40} together with the carbon atom to which both are attached, or R^{41}, R^{42} together with K to which both are attached when K is a carbon atom, define a C_3-C_6 carbocyclo, and R^{41}-R^{44} are as defined herein,

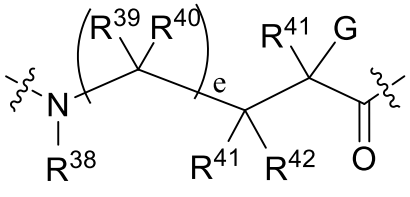
or R^{43}, R^{44} together with L' to which both are attached when L' is a carbon atom define a C_3-C_6 carbocyclo, and R^{39}-R^{42} are as defined herein,

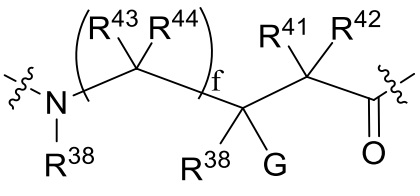
or R^{40} and R^{41}, or R^{40} and R^{43}, or R^{41} and R^{43} to together with the carbon atom or heteroatom to which both are attached and the atoms intervening between those carbon atoms and/or heteroatoms define a C_5-C_6 carbocyclo or a C_5-C_6 heterocyclo, and R^{39}, R^{44} and the remainder of R^{40}-R^{43} are as defined herein,

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

A or a subunit thereof is an alpha-amino, beta-amino or another amine-containing acid residue,

in particular, wherein formula (3) or formula (4) has the structure of formula (3a) or formula (4a):



(3a),


(4a),

wherein subscript e and f are independently 0 or 1.

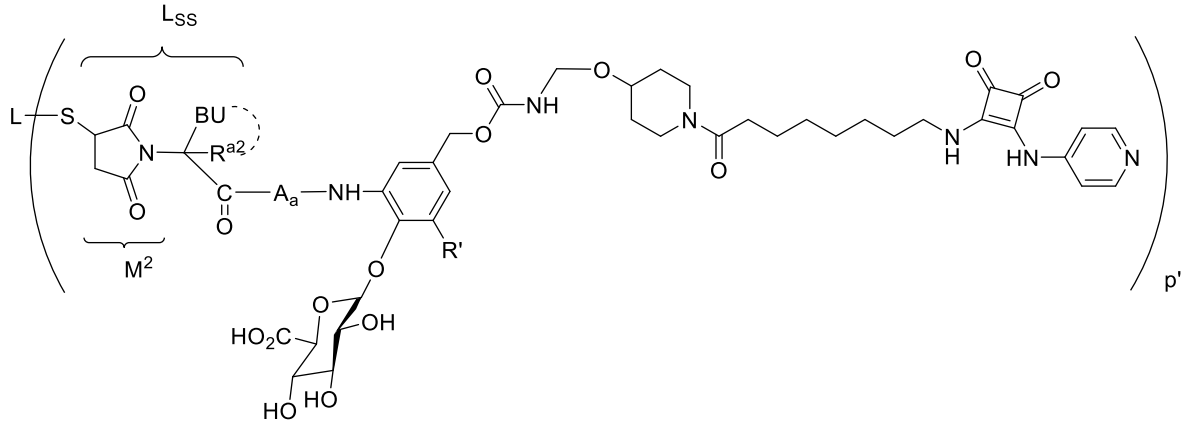
19. The Ligand Drug Conjugate compound of any one of claims 1-8 and 10-14, wherein the Ligand Unit is an antibody or an antigen-binding fragment thereof, thereby defining an antibody Ligand Unit of an antibody drug conjugate (ADC),

wherein the antigen targeted by the antibody Ligand Unit is an accessible cell-surface antigen of abnormal cells that is capable of cellular internalization when bound to an ADC compound and is present in greater copy number on the abnormal cells in comparison to normal cells distant from the site of the abnormal cells, or the antigen is an accessible cell-surface antigen of a vascular epithelial cell in the vicinity of abnormal cells, wherein said antigen is capable of cellular internalization of bound ADC and is present in greater copy number on said cells in comparison to normal epithelial cells distant from the site of the abnormal cells.

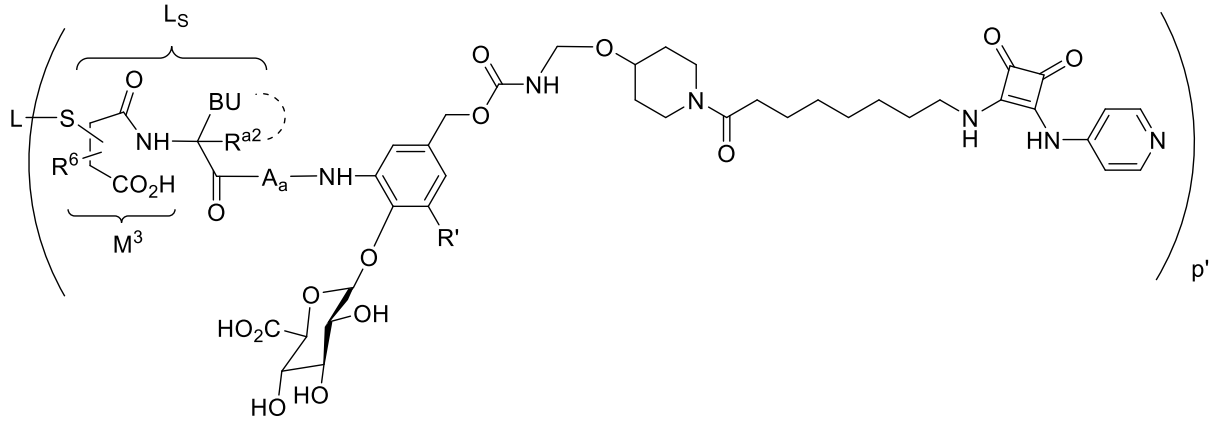
20. The Ligand Drug Conjugate compound of claim 19, wherein subscript p is 2, 4, 8, or 10.

21. The Ligand Drug Conjugate compound of any one of claims 10-14, wherein the sulfur atom attached to the indicated succinimide (M^2) or succinic acid amide (M^3) moeity of a drug linker moiety of the Ligand Drug Conjugate compound is that of an antibody or antigen-binding fragment thereof, thereby defining an antibody Ligand Unit, wherein the sulfur atom of the antibody Ligand Unit bonded to the succinic acid (M^2) moiety or succinic acid amide (M^3) moiety is that of a cysteine residue native to the antibody or antigen-binding fragment thereof or an introduced cysteine residue in the heavy chain or light chain of the antibody or antigen binding-fragment thereof.

22. The Ligand Drug Conjugate compound of claim 1, wherein the compound is represented by the structure of:



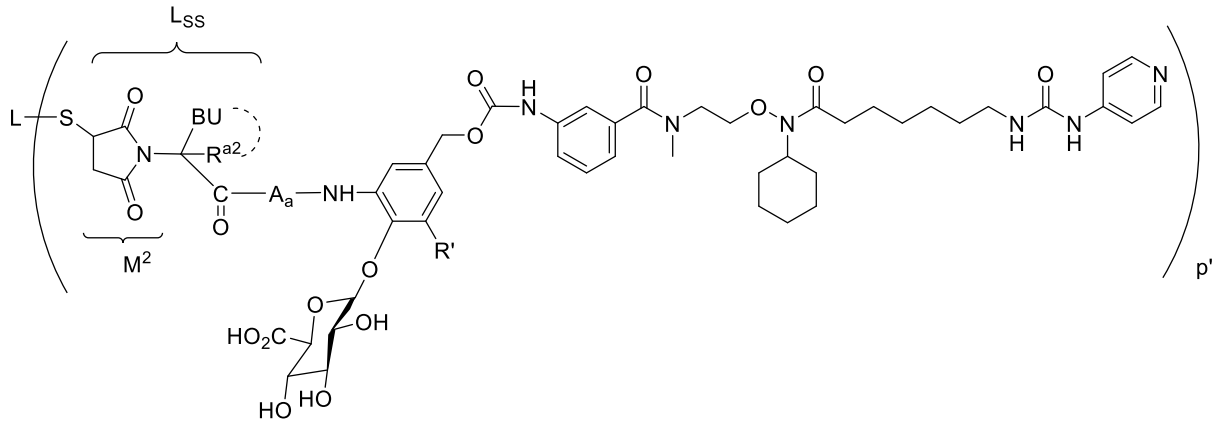
or



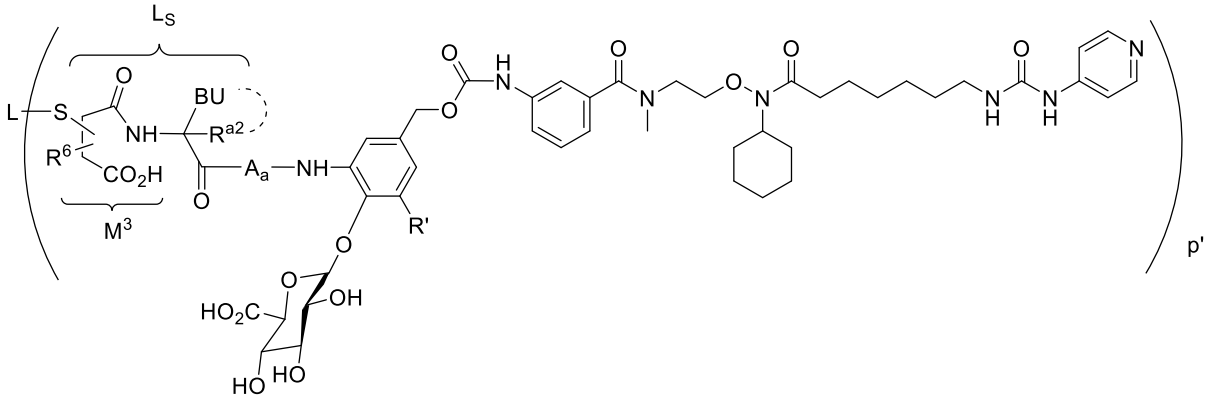
or pharmaceutical acceptable salt(s) thereof, wherein

or

the Ligand Drug Conjugate compound is represented by the structure of:

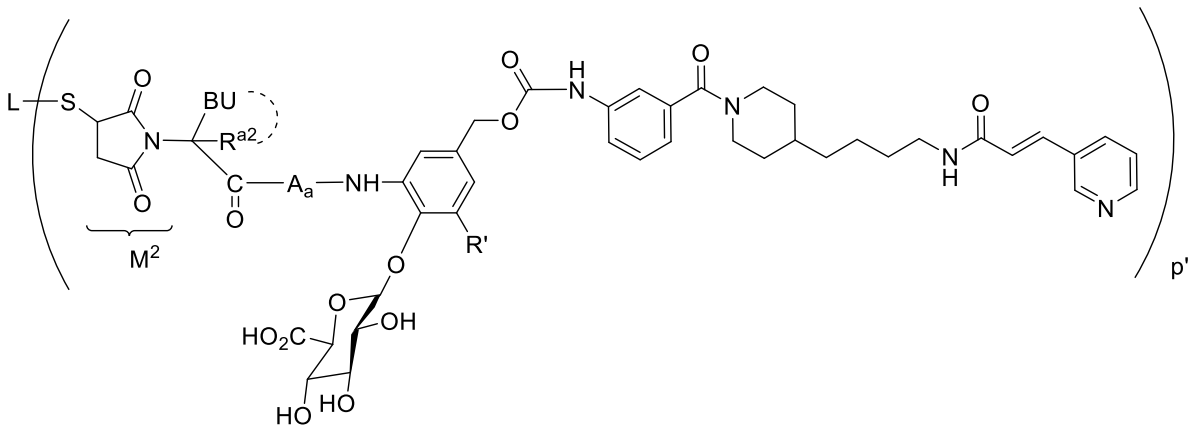


or

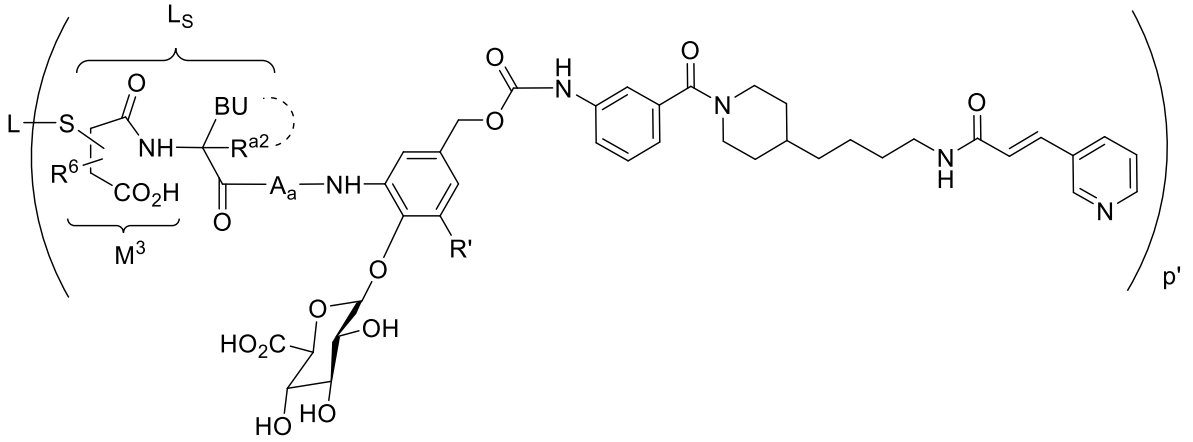


or pharmaceutical acceptable salt(s) thereof,

in particular by:



or



or pharmaceutical acceptable salt(s) thereof,

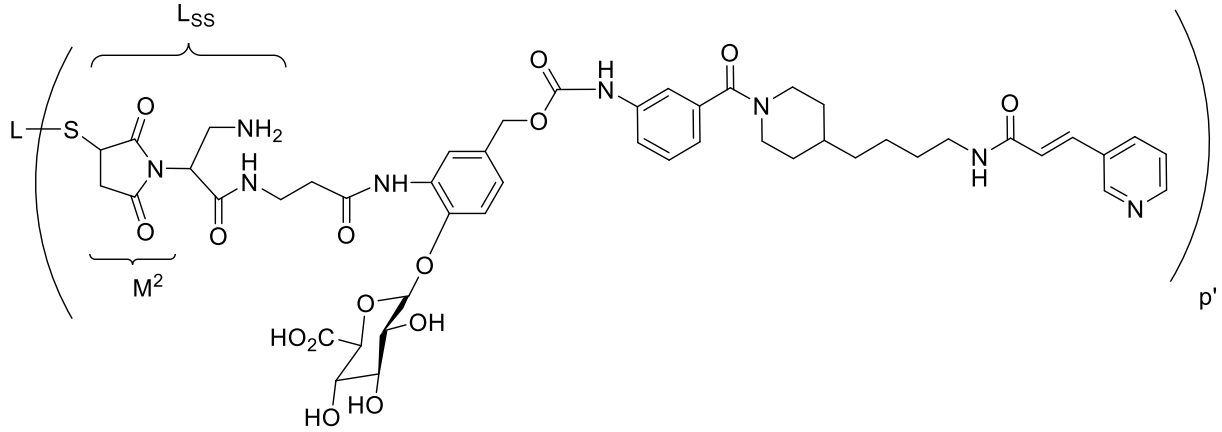
wherein

subscript a is 1 and A is an amino acid residue;

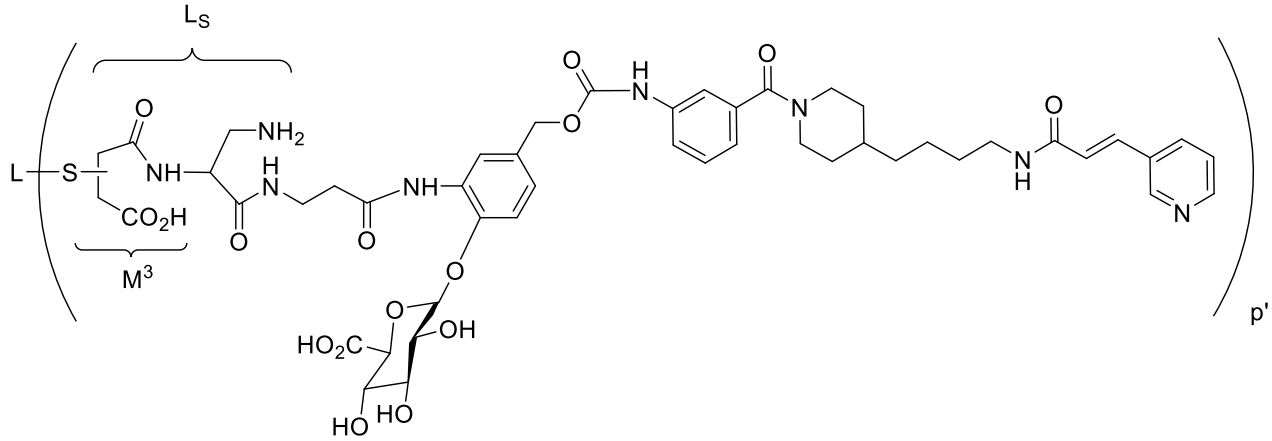
BU is a acyclic Basic Unit so that the dotted curve line is absent, and R^{a2} is hydrogen, or BU together with R^{a2} as C_1-C_6 alkyl and the carbon atom to which both are attached define a cyclic Basic Unit so that the dotted curved line is present; and

R' is hydrogen or $–NO_2$,

more particularly by:

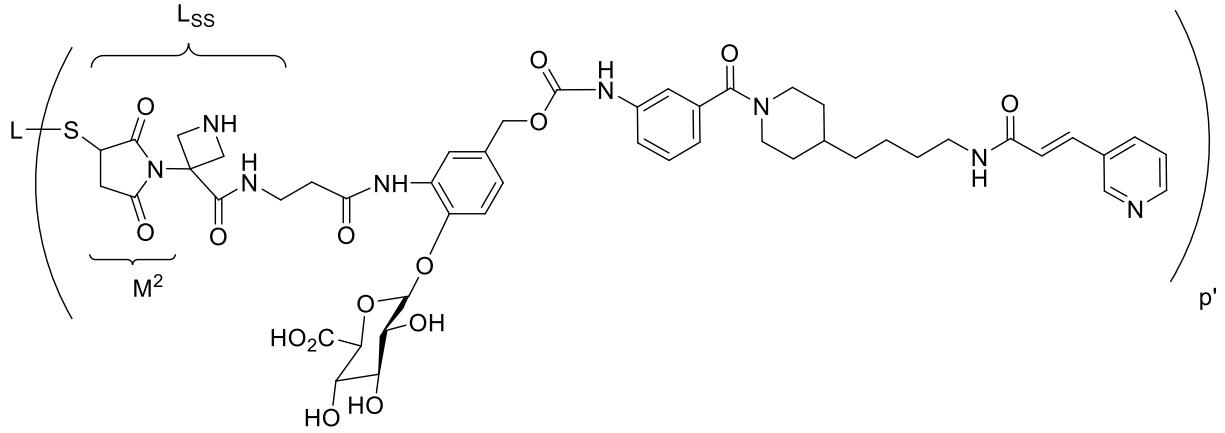


or

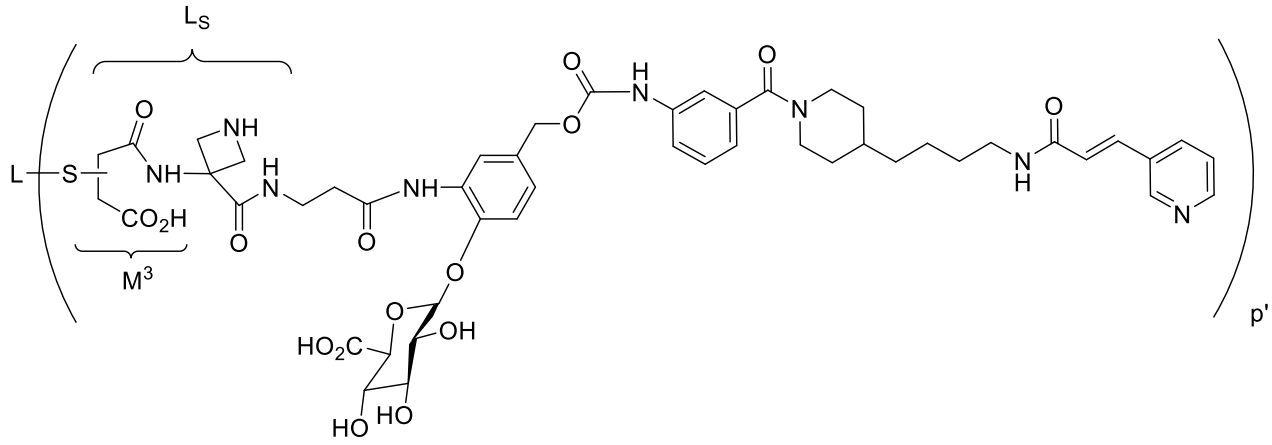


or pharmaceutical acceptable salt(s) thereof,

or by:



or



or pharmaceutical acceptable salt(s) thereof,

wherein

L is an antibody, thereby defining an antibody Ligand Unit of an antibody drug conjugate (ADC), and S is a sulfur atom of the antibody, wherein the antibody is a monoclonal antibody in particular a humanized or chimeric antibody.

23. A formulation comprising a Ligand Drug Conjugate compound of any one of claims 1-8, 10-14, and 22 and at least one, two, three or more excipients,

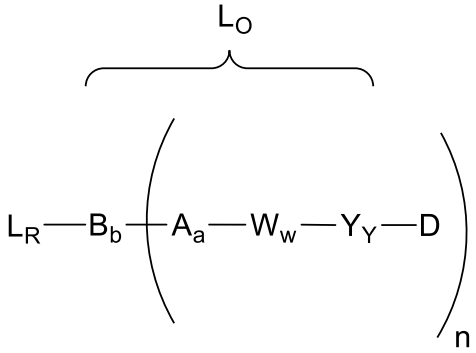
in particular, wherein the formulation is a pharmaceutically acceptable formulation or a precursor thereof, particularly wherein the pharmaceutically acceptable formulation precursor is a solid suitable for reconstitution as a solution for intravenous injection to a subject in need thereof, or the pharmaceutically acceptable formulation is a liquid suitable for intravenous injection to a subject in need thereof, more particularly in which the Ligand Drug

Conjugate compound is present in an effective amount for treatment of a hyperproliferative disease or condition in said solid or liquid formulation.

24. Use of an effective amount of a Ligand Drug Conjugate compound of any one of claims 1-8, 10-14, and 22 in the manufacture of a medicament for treating a hyperproliferative disease or condition in a subject in need thereof having said disease or condition, in particular having a cancer, more particularly a leukemia or lymphoma.

25. A method of inhibiting the multiplication of a tumor cell or cancer cell *in vitro*, or causing apoptosis in a tumor or cancer cell *in vitro* by exposing said cell to an effective amount of a Ligand Drug Conjugate compound of any one of claims 1-8, 10-14, and 22.

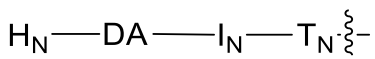
26. A Drug Linker compound, wherein the compound is represented by the structure of:



or a salt thereof, wherein

L_R is a primary linker having a functional group capable interacting with a targeting agent to form a covalent bond to a Ligand Unit corresponding to or incorporating the targeting agent in a Ligand Drug Conjugate compound;

D is a NAMPT Drug Unit represented by the general structure of:

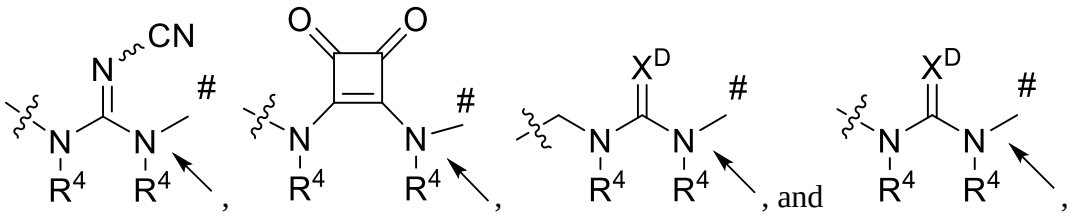


, wherein

the wavy line indicates the site of covalent attachment to L_O, as indicated, which is an optional secondary linker, or L_R, depending on the presence or absence of L_O, respectively;

H_N is a NAMPT Head Unit, wherein the NAMPT Head Unit is pyridin-3-yl or pyridin-4-yl, each of which is optionally substituted;

DA is a Donor-Acceptor Unit selected from the group consisting of:



wherein

X^D is O, S or NR^D, wherein the nitrogen atom is optionally protonated and R^D is hydrogen or optionally substituted C_1-C_4 alkyl;

each R^4 is independently selected from the group consisting of hydrogen and optionally substituted C_1-C_4 alkyl, or both R^4 together with the nitrogen atoms to which they are attached and the intervening carbon atom(s) define an optionally substituted C5-C6 heterocyclo;

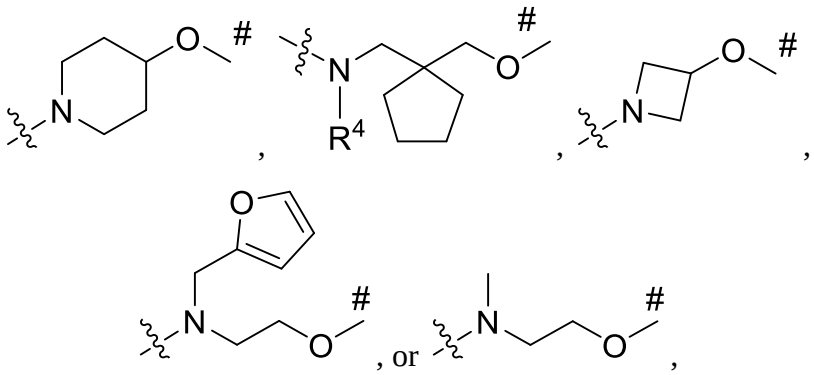
the pound sign (#) indicates the site of covalent attachment to I_N; and the wavy line indicates the site of covalent attachment to H_N;

I_N is an Interconnecting Unit, wherein the Interconnecting Unit is or comprises -X^1-$[C(=O)]_{0,1}$-;

X^1 is optionally substituted C_5-C_7 alkylene;

T_N is a NAMPT Tail Unit, wherein the NAMPT Tail Unit is or comprises an optionally substituted amino-alcohol residue, the –O- of which is the site of covalent attachment to L_O, or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein

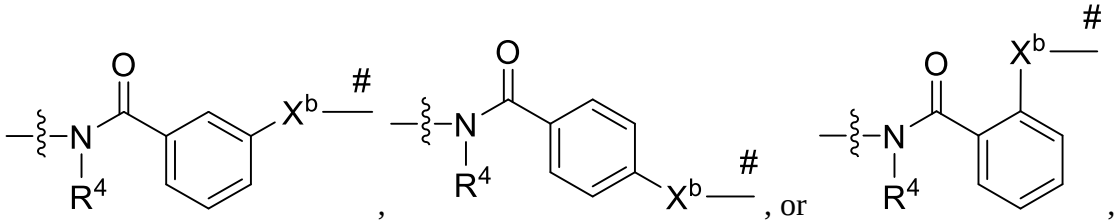
R^4 is hydrogen or optionally substituted C_1-C_4 alkyl;

the wavy line indicates the site of covalent attachment to I_N; and

the pound sign (#) indicates the site of covalent to L_O or L_R, depending on the presence or absence of L_O, respectively, or

T_N is or comprises an optionally substituted benzamide moiety, the amide nitrogen atom of which is bonded to I_N with optional cyclization of that atom back to I_N or to the remainder of T_N, and the aromatic ring of which is at least substituted with a hydroxyl or amino residue, the –O- or optionally substituted nitrogen atom of which is attached is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O,

wherein T_N is selected from the group consisting of:



wherein X^b is –O- or -NH-, optionally substituted; and

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl, wherein

the benzamide moeity is optionally cyclized to I_N, wherein the amide nitrogen atom of the benzamide moiety is the site of said cyclization so that R^4 is replaced by a covalent bond to I_N; subscripts a and b independently are 0 or 1, indicating the absence or presence, respectively, of A or B;

subscript n is 1, 2, 3 or 4;

A is an first optional Stretcher; and

B is a Branching Unit, when subscript b is 1 and subscript n is 2, 3 or 4, or B is absent, so that subscript b is 0, when subscript n is 1,

wherein each of A and B is an independently selected single unit or is optionally comprised or consists of at least two, three or four independently selected subunits;

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

Y is a Spacer Unit; and subscript y is 0, 1 or 2, indicating the absence or presence of one or two of Y, respectively,

provided that when subscript y is 1, Y is a Spacer Unit covalently attached to a heteroatom or moiety thereof of T_N selected from the group consisting of –O-, -S- and optionally substituted nitrogen,

provided that when subscript y is 2 so that Y_y is –Y-Y', Y is a first Spacer Unit and Y' is a second Spacer Unit or a functional group comprising the optionally substituted heteroatom from T_N; and

provided that subscript y is 1 or 2 when W is a Glucuronide Unit of formula Y(W'), in which instance subscript y is inclusive of a first Spacer Unit Y, wherein that Spacer Unit is a required self-immolative Spacer Unit; and

subscript w is 0 or 1, indicating the absence or presence, respectively, of W; wherein

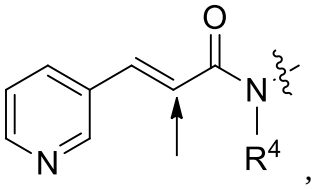
when subscript w is 1, W is a Peptide Cleavable Unit or said Glucuronide Unit in which W' represents a carbohydrate moiety with glycosidic bonding to the required self-immolative Spacer Unit through an optionally substituted heteroatom, enzymatic or non-enzymatic cleavage of that Unit in the Drug Linker Compound, or in a drug linker moiety of a Ligand Drug Conjugate compound or a N-acetyl-cysteine (NAC)conjugate prepared from the Drug Linker compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative therefrom, and

when subscript w is 0, which indicates the absence of a Cleavable Unit, enzymatic or non-enzymatic cleavage of the bond between the indicated L_R and L_O moieties, when L_O is present, or the bond between L_R and D, when L_O is absent, initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from the Drug Linker compound or said drug linker moiety or NAC conjugate, wherein when a derivative of a NAMPTi compound is released, the derivitized NAMPTi compound inhibits NAMPT and/or undergoes further enzymatic or non-enzymatic action(s) to release the parent NAMPTi compound.

27. The Drug Linker compound of claim 26, wherein the Donor Acceptor (DA) Unit comprises an optionally substituted amide functional group or bioisostere thereof.

28. The Drug Linker compound of claim 26, wherein each of the NAMPT homodimers of the enzymatically competent NAMPT homodimer has the amino acid sequence of SEQID 1.

29. The Drug Linker compound of claim 26, wherein H_N-DA- has the structure of:



,

or a salt thereof, wherein

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl; and

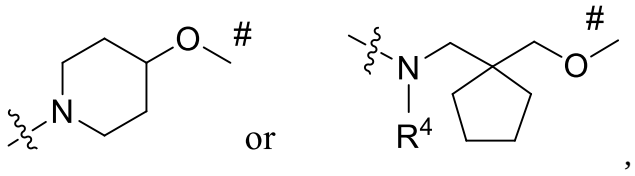
the wavy line indicates the site of covalent attachment to I_N, and

wherein the sp^2 carbon atom proximal to the carbonyl carbon atom is the site (as indicated by an arrow) of optional cyclization to H_N through an introduced optionally substituted non-aromatic carbon atom or an optionally substituted aromatic heteroatom.

30. The Drug Linker compound of any one of claims 26 to 29, wherein the NAMPT Tail Unit is or comprises an optionally substituted amino alcohol moeity,

wherein the oxygen atom of the alcohol is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively,

in particular having the structure of.



,

or a pharmaceutically acceptable salt thereof, wherein

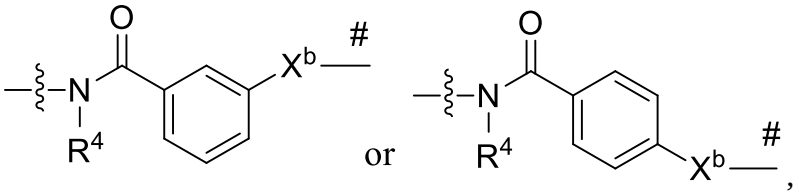
R^4 is hydrogen or optionally substituted C_1-C_4 alkyl;

the wavy line indicates the site of covalent attachment to I_N; and

the pound sign (#) indicates the site of covalent to L_O or L_R, depending on the presence or absence of L_O, respectively, or

wherein the Tail Unit is or comprises an optionally substituted benzamide moeity having a functional group providing a heteroatom that is the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively,

in particular, having the structure of:

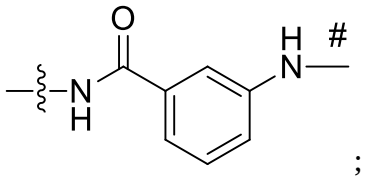


wherein X^b is –S- –O- or -NH-, optionally substituted; and

R^4 is hydrogen or optionally substituted C_1-C_4 alkyl, wherein

the benzamide moeity is optionally cyclized to I_N, wherein the amide nitrogen atom of the benzamide moiety is the site of said cyclization so that R^4 is replaced by a covalent bond to I_N,

more particularly, having the structure of:



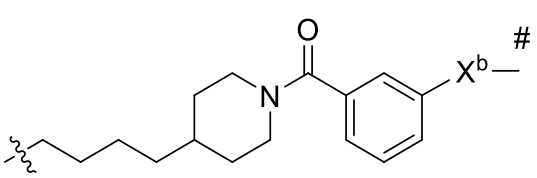
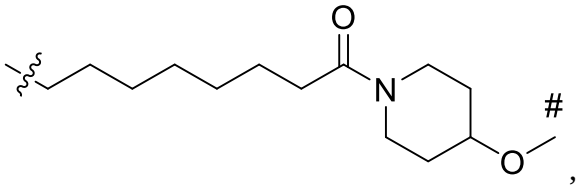
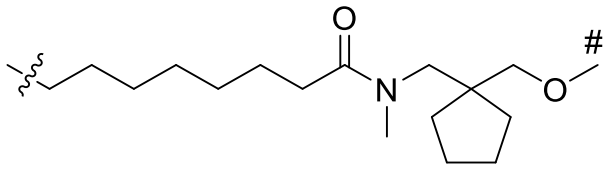
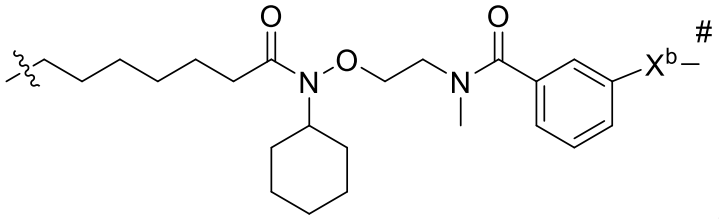
;

wherein the wavy line indicates the site of covalent attachment to I_N;

the pound sign (#) indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively.

31. The Drug Linker compound of claim 30, wherein I_N is -CH_2-$(CH_2)_{3-7}$-CH_2-, -CH_2-$(CH_2)_{3-7}$-CH_2-O-, -CH_2-$(CH_2)_{3-7}$-C(=O)-, -CH_2-$(CH_2)_{3-7}$-$S(=O)_2$- or -CH_2-$(CH_2)_{3-7}$-S(=O)-.

32. The Drug Linker compound of claim 31, wherein –I_N-T_N- has the structure of:

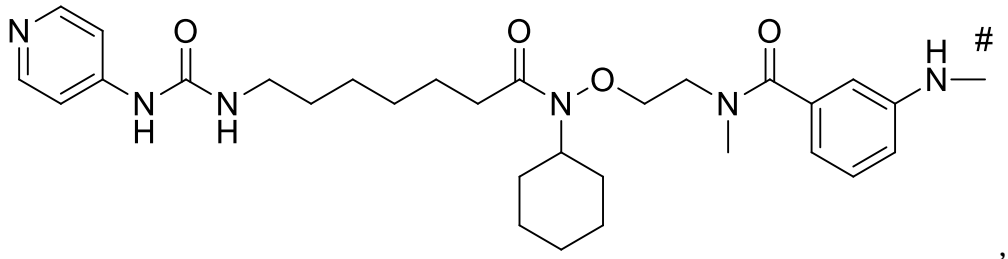
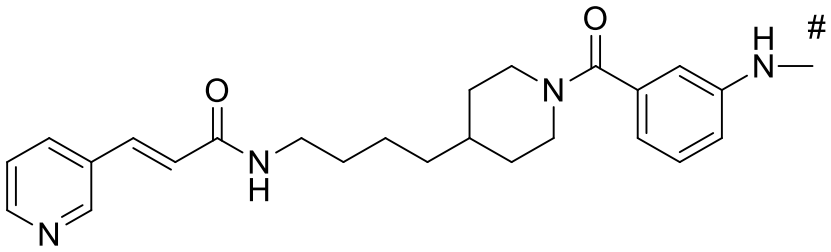



, or

,

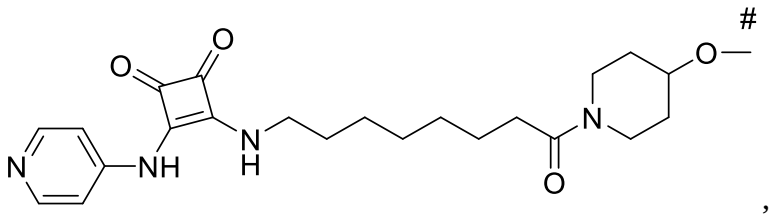
wherein X^b is -NH-, –O- or –S-;

the wavy line indicates the site of covalent attachment to DA; and

the pound sign (#) indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively.

33. The Drug Linker compound of claim 26, wherein the NAMPT Drug Unit has the structure of:


,

, or

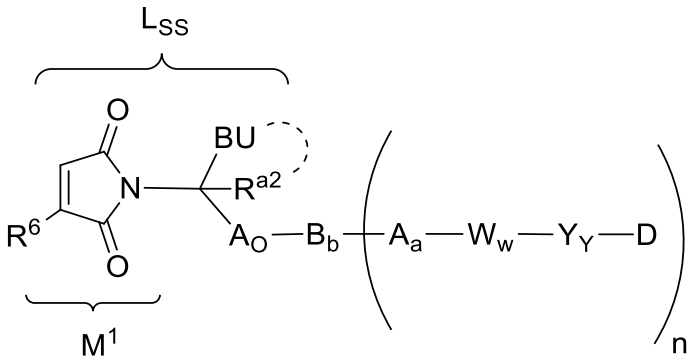


,

or a salt thereof, wherein

the pound sign (#) indicates the site of covalent attachment to L_O or L_R, depending on the presence or absence of L_O, respectively.

34. The Drug Linker compound of claim 26, wherein the Drug Linker compound is represented by the structure of:



or a salt thereof, wherein

R^6 is hydrogen or an optionally substituted C_1-C_6 alkyl, which in Formula 2 is bonded to the saturated carbon atom adjacent to the carbon substituted by L-S-;

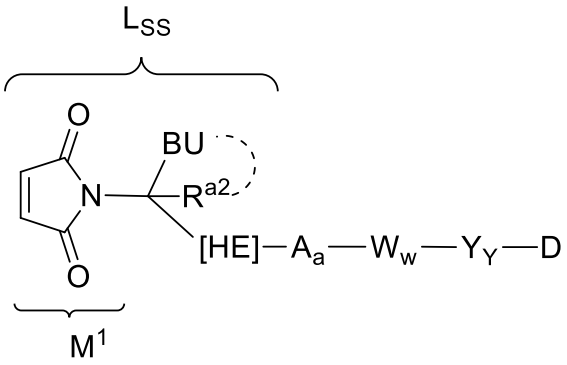
A_O is a second optional Stretcher Unit;

BU is a Basic Unit and R^{a2} is an optionally substituted C_1-C_{12} alkyl group; and

the dotted curved line indicates optional cyclization so that in the absence of said cyclization BU is an acyclic Basic Unit or in the presence of said cyclization BU is a cyclized Basic Unit in which R^{a2} and BU together with the carbon atom to which both are attached, define an optionally substituted spiro C_3-C_{20} heterocyclo containing a skeletal basic nitrogen atom of a secondary or tertiary amine functional group as the basic function group of the cyclic Basic Unit,

wherein the basic nitrogen atom of the acyclic Basic Unit or cyclic Basic Unit is optionally suitably protected by a nitrogen protecting group, dependent on the degree of substitution of the basic nitrogen atom, or is optionally protonated,

in particular, having the structure of:



wherein [HE] as A_O is an optional Hydrolysis Enhancing Unit;

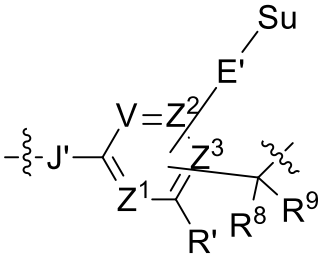
subscript w is 1;

W is Peptide Cleavable Unit; and

the remaining variable groups retain their previous meanings

wherein protease action on the Peptide Cleavable Unit resulting in cleavage of the W-J' bond within the Drug Linker compound, or from the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound initiates release of the NAMPT Drug Unit as NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound, or

W is a Glucuronide Unit of formula –Y(W')- having the structure of:



wherein Su is a carbohydrate moiety and -E'- represents an optionally substituted heteroatom of an glycosidic bond cleavable by a glycosidase so that Su-E' is W' and the remainder of the Glucuronide Unit structure is a self-immolative Spacer Unit bonded to W';

J' is an independently selected heteroatom, optionally substituted, and the wavy line thereto is the site of covalent attachment resistant to enzymatic or non-enzymatic cleavage under normal physiological conditions wherein said site of covalent attachment is to A when subscript a is 1 or to the indicated L_{SS} primary linker when subscript a is 0; and

V, Z^1, Z^2 and Z^3 are independently =N- or =C(R^{24})-, wherein each R^{24} is independently selected from the group consisting of hydrogen and C_1-C_{12} alkyl, C_2-C_{12}

alkenyl and C_2-C_{12} alkynyl, optionally substituted, and halogen, an electron withdrawing group, an electron donating group, -E'-Su, and –C(R^8)(R^9)-,

provided that one and only one –C(R^8)(R^9)- moiety and one and only one –E'-Su moiety is present,

wherein one of V, Z^1, Z^2 and Z^3 is =C(R^{24})- in which R^{24} is –C(R^8)(R^9)- and another of V, Z^1, Z^2 and Z^3 is =C(R^{24})- in which R^{24} is –E'-Su,

provided the –C(R^8)(R^9)- and –E'-Su moieties are *ortho* or *para* to each other;

R^8 and R^9 independently are hydrogen, or C_1-C_{12} alkyl, C_2-C_{12} alkenyl or C_2-C_{12} alkynyl, optionally substituted, or C_6-C_{20} aryl or C_5-C_{20} heteroaryl, optionally substituted,

or

R^8 and R^9 together with the carbon atom to which both are attached define an optionally substituted C_5-C_{20} carbocyclo; and

R' is hydrogen or -NO_2, or other electron withdrawing group or –OC_1-C_6 alkyl, or other electron donating group; and

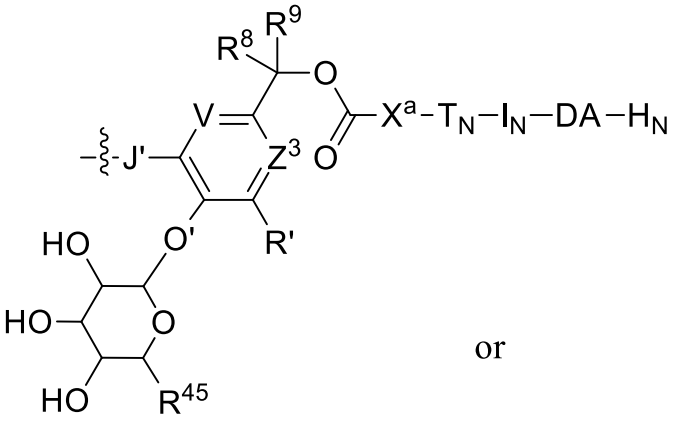
wherein the wavy line adjacent to the –C(R^8)(R^9)- moiety indicates the site of covalent attachment of the Glucuronide Unit to Y' when subscript y is 2, or to D when subscript y is 1, and

wherein the remaining variable groups of the Drug Linker compound are as previously defined for W as a Peptide Cleavable Unit;

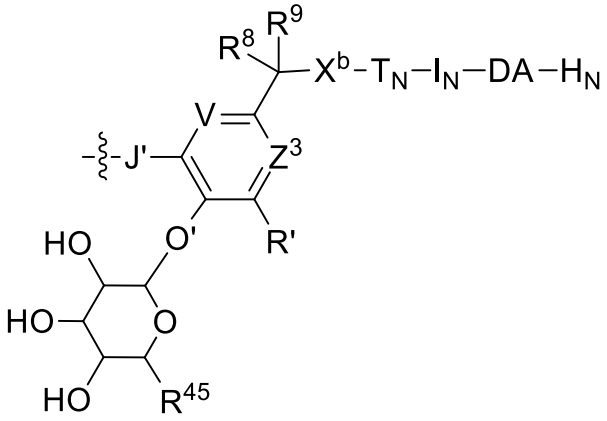
and

wherein glycosidase action on the Glucuronide Unit resulting in cleavage of its glycosidic bond initiates release of the NAMPT Drug Unit as NAMPTi compound or derivative thereof from the Drug Linker compound or from the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound.

35. The Drug Linker compound of claim 34, wherein W is a Glucuronide Unit for which –W-Y_y-D has the structure of:



or



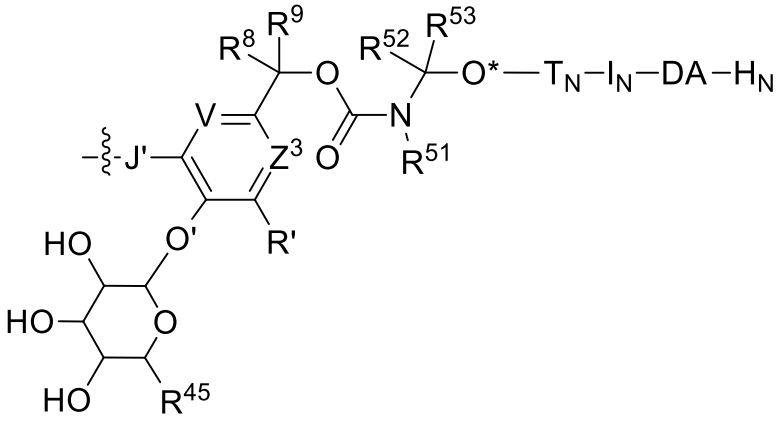
,

or a salt thereof, wherein

X^a is a nitrogen atom from a primary or secondary amine functional group of T_N;

X^b is an oxygen atom from an alcohol functional group or a sulfur atom from a thiol functional group of T_N,

or –W-Y_y-D has the structure of :



or a salt thereof,

R^{51}, R^{52} and R^{53} independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_6-C_{14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl,

or R^{51} and R^{52} together with the nitrogen and carbon atoms to which both are attached define an azetidine, pyrrolidine, piperidine or homopiperidine heterocyclo, and R^{53} is hydrogen;

and in either –W-Y_y-D structure:

R^{45} is $–CH_2OH$ or $–CO_2H$;

R' is hydrogen or $–NO_2$ or other electron withdrawing group;

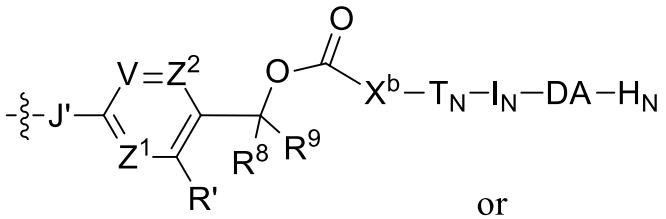
J' is an optionally substituted heteroatom, and the wavy line thereto is the site of covalent attachment resistant to enzymatic or non-enzymatic cleavage under normal physiological conditions; and

wherein O* represents the oxygen atom from an alcohol functional group of T_N and O' represents the oxygen atom of an O-glycosidic bond cleavable by a glycosidase,

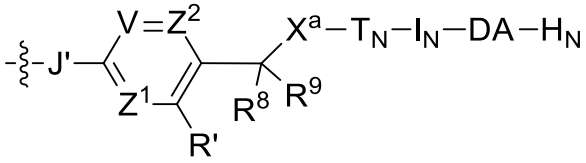
wherein said cleavage initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative from the Drug Linker compound or from the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound,

or wherein

W is a Peptide Cleavable Unit for which –Y_y-D – has the structure of:



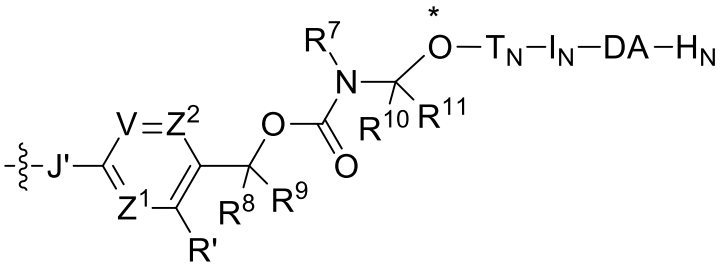
or



or a salt thereof, wherein

X^a is an oxygen atom from an alcohol functional group or a sulfur atom of a thiol functional group of T_N;

X^b is a nitrogen atom from a primary or secondary amine functional group of T_N, or has the structure of:



or a salt thereof, wherein

R' is hydrogen or $–OC_1$-C_6 alkyl or other electron donating group;

R^7, R^{10} and R^{11} independently are hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_6-C_{14} aryl, or optionally substituted C-linked C_3-C_8 heteroaryl,

or R^7 and R^{10} together with the nitrogen and carbon atoms to which both are attached define an azetidine, pyrrolidine, piperidine or homopiperidine heterocyclo, and R^{11} is hydrogen;

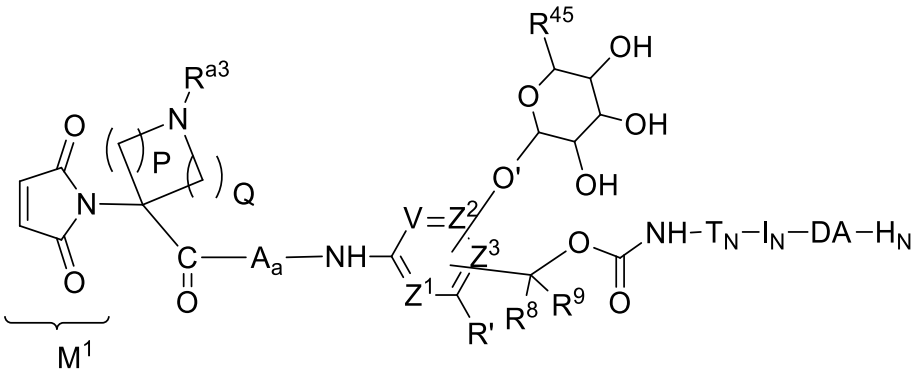
and

R^{45} is $–CH_2OH$ or $–CO_2H$;

O* represents the oxygen atom from an alcohol functional group of T_N; and

J' is an optionally substituted heteroatom bonded to W as indicated by the wavy line, wherein cleavage of that bond initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative from the Drug Linker compound or from the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound.

36. The Drug Linker compound of claim 34, wherein W is a Glucuronide Unit for which the Drug linker compound is represented by the structure of:

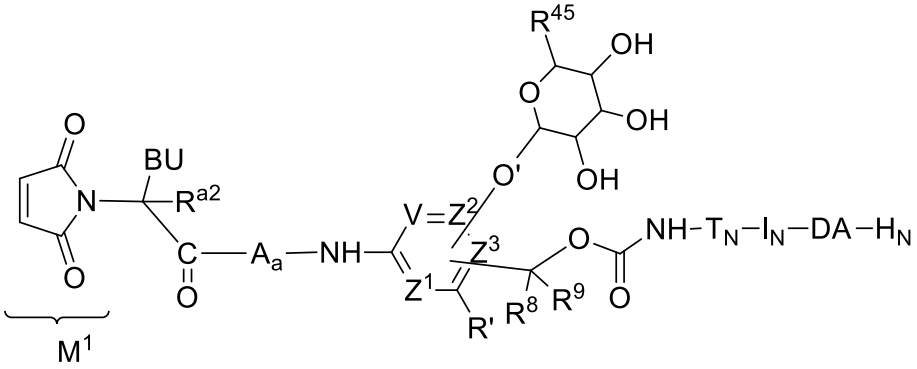


or a salt thereof, wherein

subscript P is 1, 2 or 3; and

subscript Q ranges from 1 to 6,

or by the structure of:



or a pharmaceutical acceptable salt thereof, wherein

R^{a2} is hydrogen or C_1-C_6 alkyl;

BU is an acyclic Basic Unit having the structure of $–[C(R^{a1})(R^{a1})]$-$[C(R^{a1})(R^{a1})]_{0-3}$-$N(R^{a3})(R^{a3})$, wherein each R^{a1} independently is hydrogen or C_1-C_4 alkyl, C_6-C_{10} aryl, C_5-C_{10} heteroaryl, (C_6-C_{10} aryl)-C_1-C_4 alkyl-, or (C_5-C_{10} heteroaryl)-C_1-C_4 alkyl-, optionally substituted, or two R^{a1} together with the carbon(s) to which they are attached and any intervening carbons define an optionally substituted C_3-C_6 cycloalkyl; and

R^{a3} independently are hydrogen, optionally substituted C_1-C_6 alkyl or R^{a3} together with the nitrogen atom to which both are attached define a C_3-C_6 heterocyclyl in which the basic nitrogen atom is a skeletal atom,

or one of R^{a3} is –H and the other is optionally substituted C_1-C_6 alkyl, optionally substituted -C_1-C_4 alkylene-(C_6-C_{10} aryl), or $-R^{PEG1}$-O-$(CH_2CH_2O)_{1-36}$-R^{PEG2}, wherein R^{PEG1} is C_1-C_4 alkylene, and R^{PEG2} is –H or C_1-C_4 alkyl; and

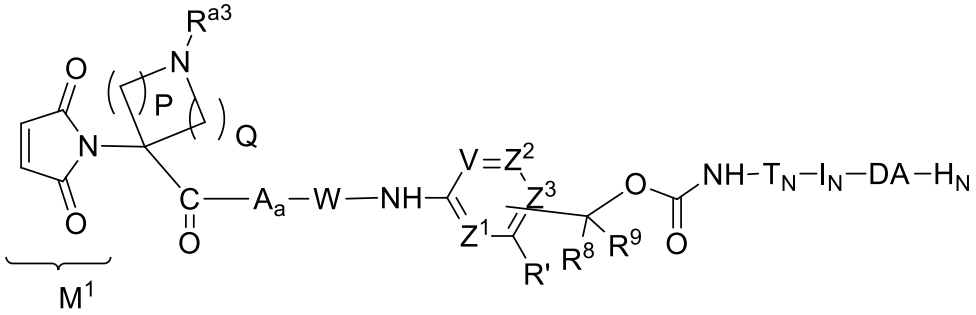
the basic nitrogen atom bonded to R^{a3} is optionally protonated; and

wherein R’ is hydrogen or $–NO_2$ or other electron withdrawing group;

R^{45} is $–CH_2OH$ or $–CO_2H$;

wherein -O’- represents the oxygen heteroatom of an O-glycosidic bond cleavable by a glycosidase, wherein said cleavage within initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative from the Drug Linker compound or from the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound, or

wherein the W is a Peptide Cleavable Unit for which the compound is represented by the structure of:

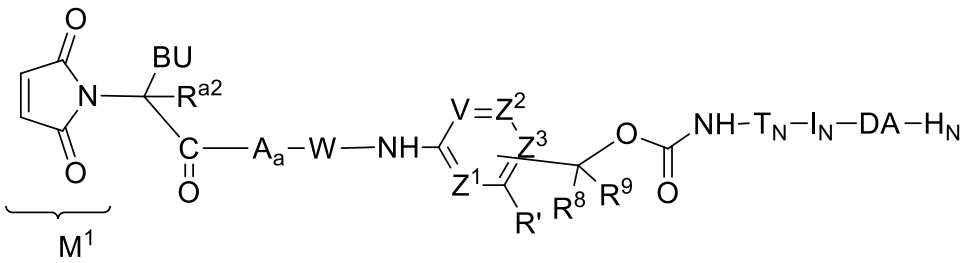


or a salt thereof, wherein

subscript P is 1, 2 or 3; and

subscript Q ranges from 1 to 6,

or is represented by the structure of:



or a salt thereof, wherein

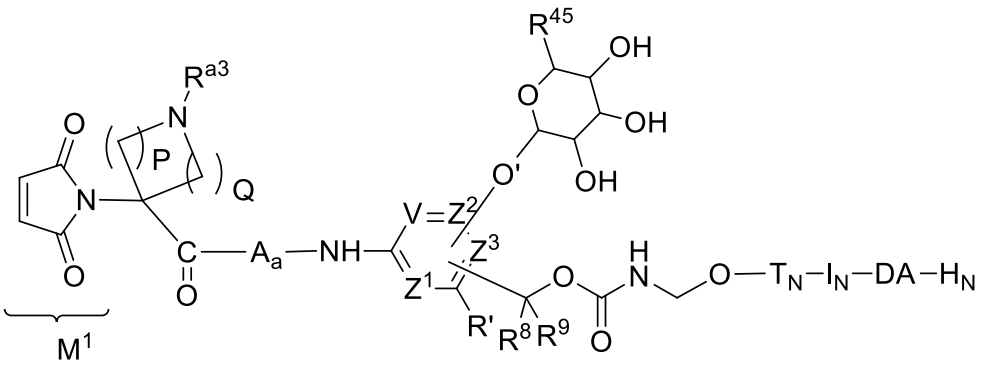
R’ is hydrogen or $–OC_1$-C_6 alkyl or other electron donating group; and

the remaining variable groups are as defined by the above structures in which W is a Glucuronide Unit, and

wherein protease action on the Peptide Cleavable Unit cleaves the W-NH bond, wherein said cleavage initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative from the Drug Linker compound or from the drug linker moiety of the

Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound.

37. The Drug Linker compound of claim 34, wherein W is a Glucuronide Unit for which the Drug Linker compound is represented by the structure of:

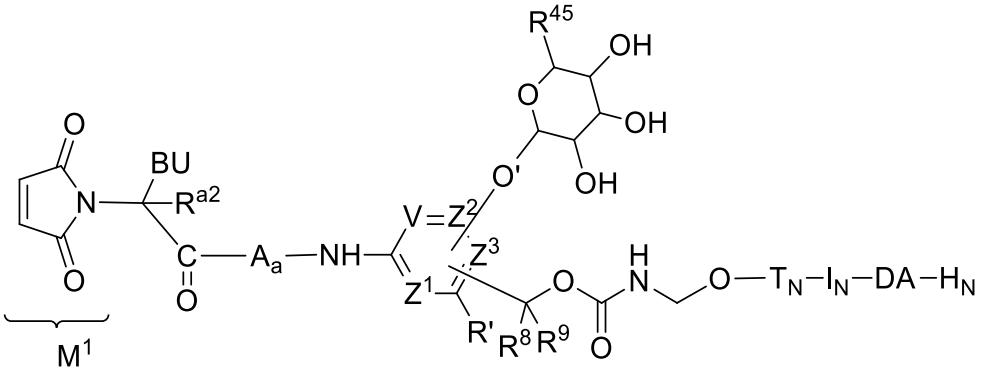


or a salt thereof, wherein

subscript P is 1, 2 or 3; and

subscript Q ranges from 1 to 6,

or is represented by the structure of:



or a salt thereof, wherein

R^{a2} is hydrogen or C_1-C_6 alkyl;

BU is an acyclic Basic Unit having the structure of $–[C(R^{a1})(R^{a1})]$-$[C(R^{a1})(R^{a1})]_{0-3}$-$N(R^{a3})(R^{a3})$, wherein each R^{a1} independently is hydrogen or C_1-C_4 alkyl, C_6-C_{10} aryl, C_5-C_{10} heteroaryl, (C_6-C_{10} aryl)-C_1-C_4 alkyl-, or (C_5-C_{10} heteroaryl)-C_1-C_4 alkyl-, optionally substituted, or two R^{a1} together with the carbon(s) to which they are attached and any intervening carbons define an optionally substituted C_3-C_6 cycloalkyl; and

R^{a3} independently are hydrogen, optionally substituted C_1-C_6 alkyl or R^{a3} together with the nitrogen atom to which both are attached define a C_3-C_6 heterocyclyl in which the basic nitrogen atom is a skeletal atom,

or one of R^{a3} is –H and the other is optionally substituted C_1-C_6 alkyl, optionally substituted -C_1-C_4 alkylene-(C_6-C_{10} aryl), or -R^{PEG1}-O-$(CH_2CH_2O)_{1\text{-}36}$-$R^{PEG2}$, wherein R^{PEG1} is C_1-C_4 alkylene, and R^{PEG2} is –H or C_1-C_4 alkyl; and

the basic nitrogen atom bonded to R^{a3} is optionally protonated;

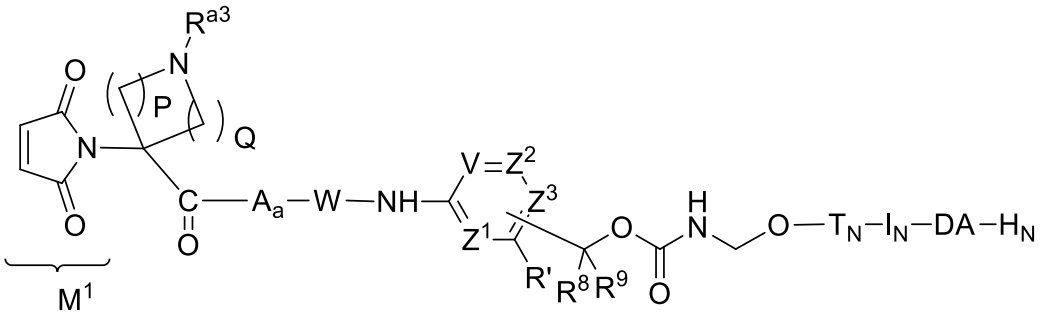
R' is hydrogen or $–NO_2$ or other electron withdrawing group;

R^{45} is $–CH_2OH$ or $–CO_2H$; and

wherein -O'- represents the oxygen atom of an O-glycosidic bond cleavable by a glycosidase, wherein said cleavage initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from the Drug Linker compound or from the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound,

or

wherein W is a Peptide Cleavable Unit for which the Drug Linker compound is represented by the structure of:

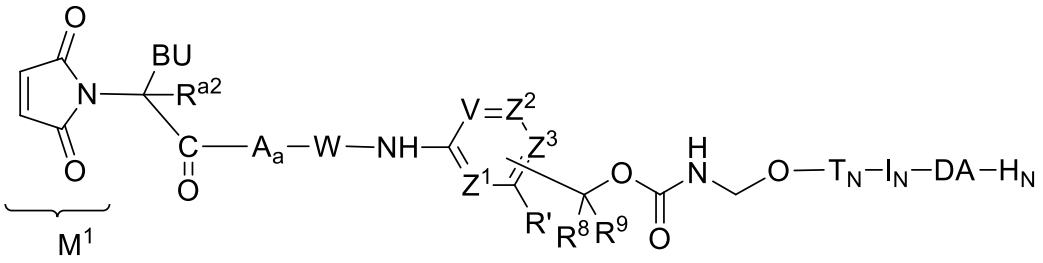


or a salt thereof, wherein

subscript P is 1, 2 or 3;

subscript Q ranges from 1 to 6,

or is represented by the structure of:



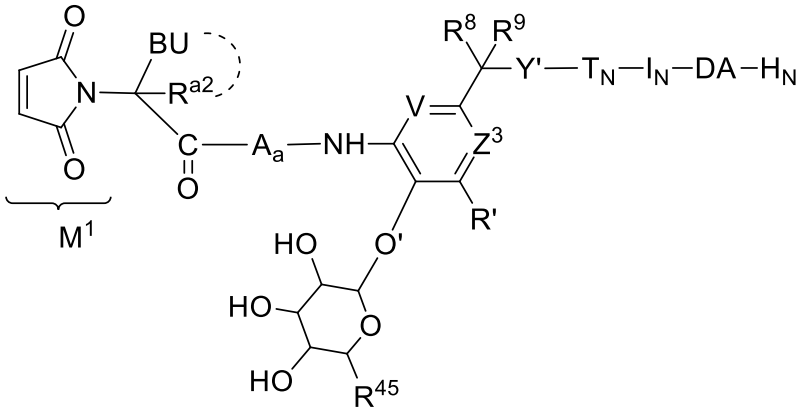
wherein

R’ is hydrogen or –OC_1-C_6 alkyl or other electron donating group; and

and the remaining variable groups are as defined by the above structures in which W is a Glucuronide Unit; and

wherein protease action on the Peptide Cleavable Unit cleaves the W-NH bond, wherein said cleavage initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from the Drug Linker compound or from the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC) conjugate prepared from the Drug Linker compound.

38. The Drug Linker compound of claim 34, wherein W is a Glucuronide Unit for which the Drug Linker compound is represented by the structure of:



or a salt thereof, wherein

or a pharmaceutical acceptable salt thereof, wherein

R’ is hydrogen or –NO_2 or other electron withdrawing group;

R^{a2} is hydrogen or C_1-C_6 alkyl, optionally cyclized to BU, as indicated by the dotted curved line,

BU has the structure of –[$C(R^{a1})(R^{a1})$]-[$C(R^{a1})(R^{a1})]_{0-3}$-$N(R^{a3})(R^{a3})$,

wherein in the absence of cyclization to R^{a2}, each R^{a1} independently is hydrogen or C_1-C_4 alkyl, C_6-C_{10} aryl, C_5-C_{10} heteroaryl, (C_6-C_{10} aryl)-C_1-C_4 alkyl-, or (C_5-C_{10} heteroaryl)-C_1-C_4 alkyl-, optionally substituted, or two R^{a1} together with the carbon(s) to which they are attached and any intervening carbons define an optionally substituted C_3-C_6 cycloalkyl; and

R^{a3} independently are hydrogen, optionally substituted C_1-C_6 alkyl or R^{a3} together with the nitrogen atom to which both are attached define a C_3-C_6 heterocyclyl in which the basic nitrogen atom is a skeletal atom,

or one of R^{a3} is –H and the other is optionally substituted C_1-C_6 alkyl, optionally substituted -C_1-C_4 alkylene-(C_6-C_{10} aryl), or -R^{PEG1}-O-$(CH_2CH_2O)_{1-36}$-R^{PEG2}, wherein R^{PEG1} is C_1-C_4 alkylene, and R^{PEG2} is –H or C_1-C_4 alkyl; and

the basic nitrogen atom bonded to R^{a3} is optionally protonated; and

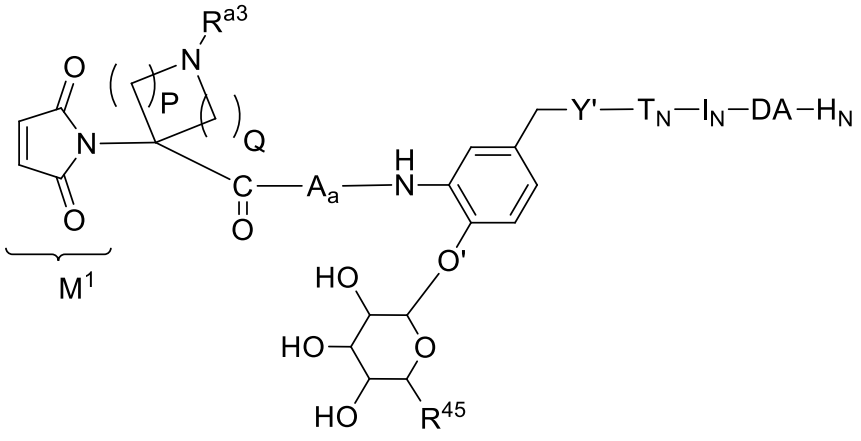
in the presence of cyclization one of R^{a1} or one of R^{a3} is replaced with a bond to a carbon atom of R^{a2} in which R^{a2} is C_1-C_6 alkyl and the remaining R^{a1} and R^{a3} are as previously defined; and

wherein Y' is -X^a-, -O-C(=O)-X^b- or –OC(=O)NH-CH_2-X^a-,

wherein X^a or X^b are from T_N, wherein –X^a- is O or S and X^b is –NH-; and

R^{45} is –CH_2OH or –CO_2H,

in particular, by the structure of:



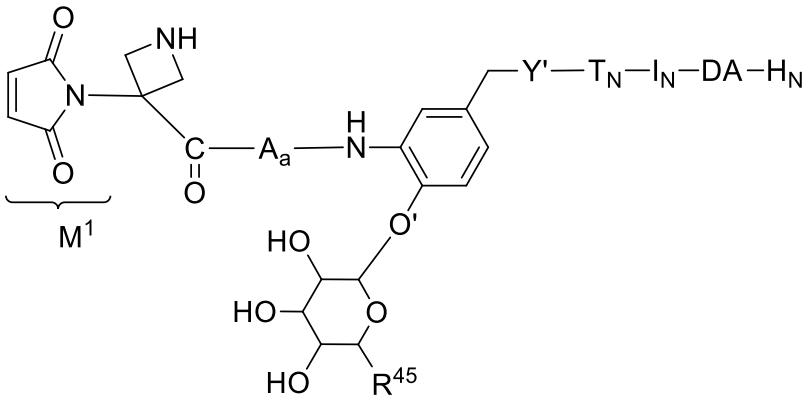
or a salt thereof, wherein

subscript P is 1, 2 or 3;

subscript Q ranges from 1 to 6; and

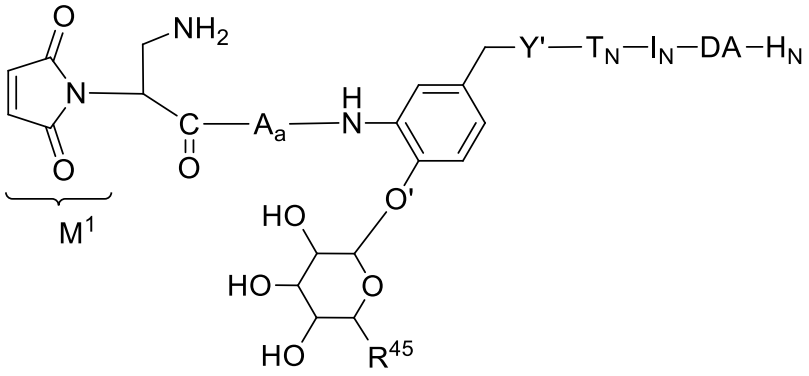
wherein the remaining variable groups are as previously defined,

more particularly, by the structure of:



or a salt thereof,

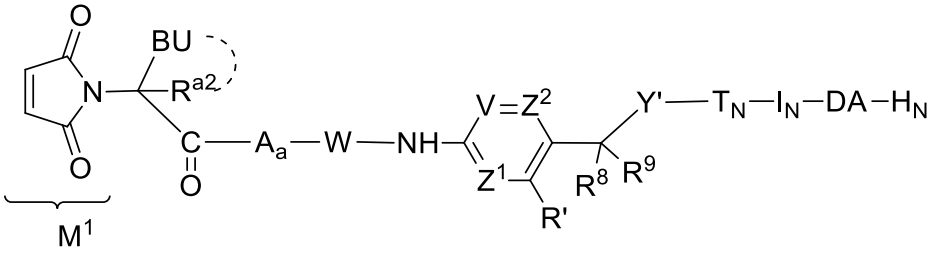
or in particular by the structure of:



or a salt thereof, wherein

the variable groups are as previously defined, or

wherein W is a Peptide Cleavable Unit for which the Drug Linker compound is represented by the structure of:



or a salt thereof, wherein

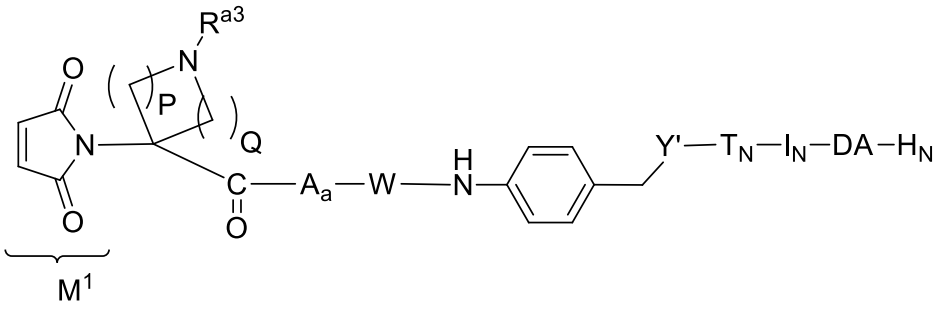
R' is hydrogen or $–OC_1$-C_6 alkyl or other electron donating group; and

the remaining variable groups are as defined by the above structures in which W is a Glucuronide Unit; and

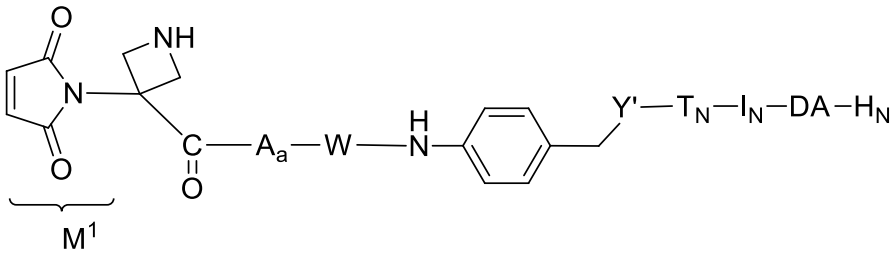
wherein protease action on the Peptide Cleavable Unit cleaves the W-NH bond, wherein said cleavage within a drug linker moiety of a compound of the Ligand Drug

Conjugate compound initiates release of the NAMPT Drug Unit as a NAMPTi compound or derivative thereof from that Ligand Drug Conjugate compound,

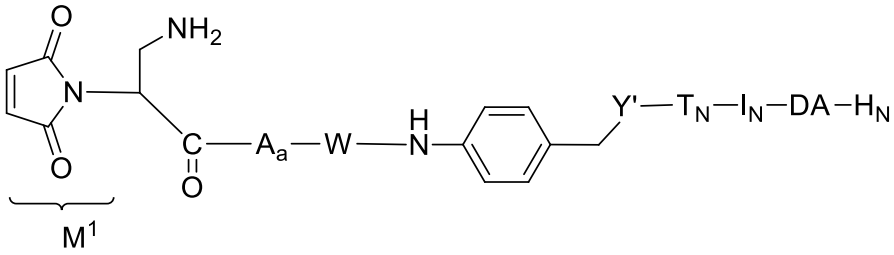
in particular by the structure of:



or a salt thereof, more particularly by the structure of:



or a salt thereof, or particular by the structure of:

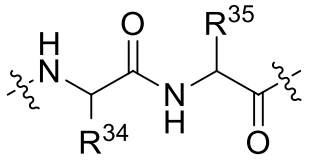


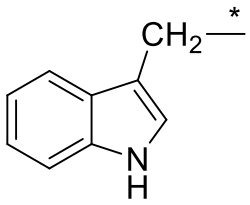
or a salt thereof; and wherein and wherein the variable groups are as previously defined.

39. The Drug Linker compound of any one of claims 34 to 38 in which W is a Peptide Cleavable Unit that comprises a dipeptide wherein the dipeptide provides for a recognition site for a regulatory or lysosomal protease for cleavage by said protease of the W-J' bond or the W-NH bond when J' is -NH within the Drug Linker compound or the drug linker moiety of the Ligand Drug Conjugate compound or N-acetyl-cysteine (NAC)

conjugate prepared from the Drug Linker compound so as to initiate release of the NAMPT Drug Unit as NAMPTi compound or derivative from that Drug Linker compound, drug linker moiety or NAC conjugate.

40. The Drug Linker compound of claim 39, wherein the W has the structure of:



wherein R^{34} is benzyl, methyl, isopropyl, isobutyl, sec-butyl, -CH(OH)CH_3 or has the structure of , wherein the asterisk indicates the site of covalent attachment to the dipeptide backbone; and

R^{35} is methyl, –$(CH_2)_4$-NH_2, -$(CH_2)_3$NH(C=O)NH_2, -$(CH_2)_3$NH(C=NH)NH_2, or, -$(CH_2)_2CO_2H$; and

wherein the wavy lines indicate the points of covalent attachment of the dipeptide into the structure representing the Ligand Drug Conjugate compound,

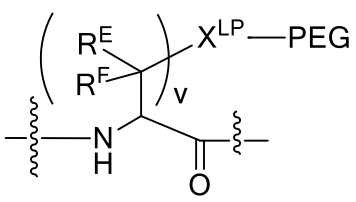
in particular W is selected from the group consisting of -Phe-Lys-, -Val-Ala-, -Val-Lys-, -Ala-Lys-, -Val-Cit-, -Phe-Cit-, -Leu-Cit-, -Ile-Cit-, -Phe-Arg-, and -Trp-Cit-, wherein Cit is citrulline.

41. The Drug Linker compound of any one of claims 26 to 38, wherein A or a subunit thereof is –L^P(PEG)-,

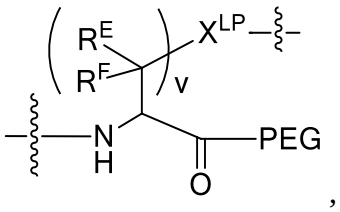
wherein –L^P- or a subunit thereof is a aminoalkanedioic acid, a diaminoalkanoic acid, a sulfur-substituted alkanedioic acid, a sulfur-substituted aminoalkanoic acid, a diaminoalkanol, an aminoalkanediol, a hydroxyl substituted alkanedioic acid, a hydroxyl substituted aminoalkanoic acid or a sulfur-substituted aminoalkanol residue, optionally substituted, wherein the substituted sulfur is in reduced or oxidized form, or

–L^P- or a subunit thereof is an amino acid residue of lysine, arginine, asparagine, glutamine, ornithine, citrulline, cysteine, homocysteine, penicillamine, threonine, serine, glutamic acid, aspartic acid, tyrosine, histidine or tryptophan, wherein the amino acid is in the **D**- or **L**-configuration, or

wherein $–L^P(PEG)-$ has the structure of:



(Formula L^P-3)



(Formula L^P-4)

or a pharmaceutical acceptable salt thereof, wherein

wherein subscript v is an integer ranging from 1 to 4;

X^{LP} is selected from the group consisting of –O-, $-NR^{LP}-$, -S-, -S(=O)-, $-S(=O)_2-$, -C(=O)-, -C(=O)N(R^{LP})-, -N(R^{LP})C(=O)N(R^{LP})-, -N(R^{LP})C(=NR^{LP})N(R^{LP})-, and C_3-C_8 heterocyclo, in particular –O-, -NH, -S- and -C(=O)-;

wherein each R^{LP} is independently selected from the group consisting of hydrogen and optionally substituted C_1-C_6 alkyl, or two of R^{LP} together along with the carbons atoms to which they are attached and their intervening atoms define a C_5-C_6 heterocyclo and any remaining R^{LP} are as previously defined;

Ar is a C_6-C_{10} arylene or a C_5-C_{10} heteroarylene, optionally substituted;

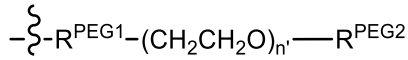
each R^E and R^F is independently selected from the group consisting of -H, optionally substituted C_1-C_6 alkyl, optionally substituted C_2-C_6 alkylene, optionally substituted C_6-C_{10} arylene and optionally substituted C_5-C_{10} heteroarylene, in particular hydrogen and C_1-C_4 alkyl

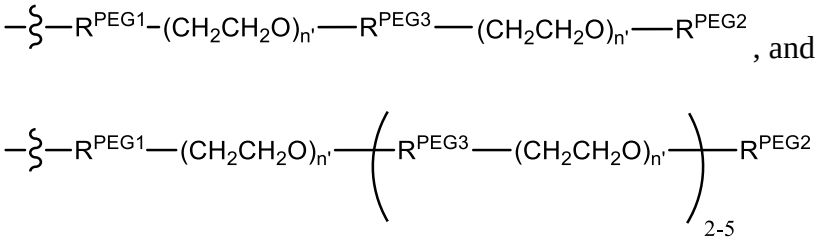
or R^E and R^F together with the carbon atom to which both are attached defines an optionally substituted spiro C_3-C_6 carbocyclo, or R^E and R^F from adjacent carbon atoms together with these atoms and any intervening carbon atoms defines an optionally substituted C_5-C_6 carbocyclo with any remaining R^E and R^F as previously defined, or

wherein the side chain of $–[C(R^E)(R^F)]_v-X^{LP}-$ is provided by a natural or un-natural amino acid side chain; and

wherein the wavy lines indicate the sites of covalent attachments within the remainder of the the Drug Linker Conjugate compound structure;

in particular having the PEG Unit respresented by:





wherein the wavy line indicates site of attachment to X^{LP} of the Parallel Connector Unit (L_P);

subscript n' independently ranges from 1 to 72;

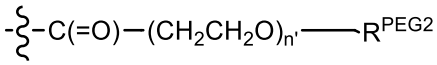
R^{PEG1} is an optional PEG Attachment Unit;

R^{PEG2} is a PEG Capping Unit; and

R^{PEG3} is an PEG Coupling Unit,

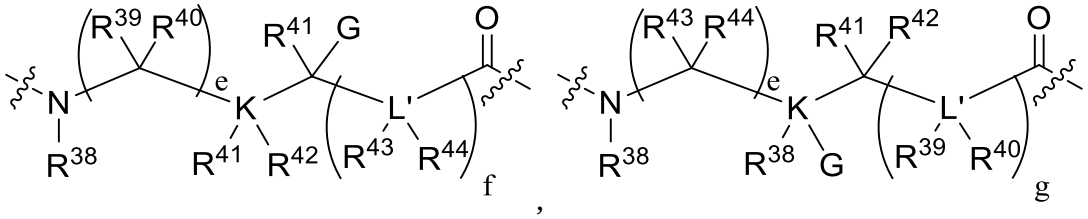
or

having X^{LP}-PEG with the structure of:



wherein subscript n' is 8, 12 or 24 and R^{PEG2} is H or $-CH_3$.

42. The Drug Linker compound of any one of claims 26 to 38, wherein A or a subunit thereof has the structure of formula (3) or formula (4):



(3) (4)

wherein the wavy lines indicated covalent attachment within the compound structure;

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

wherein subscripts e and f are independently selected integers that range from 0 to 12, and subscript g is an integer ranging from 1 to 12;

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

G is -$N(R^{PR})(R^{PR})$, wherein R^{PR} are independently a protecting group or R^{PR} together form a suitable protecting group, or

G is -$N(R^{45})(R^{46})$, wherein one of R^{45}, R^{46} is hydrogen or R^{PR}, wherein R^{PR} is a suitable protecting group, and the other is hydrogen or optionally substituted C_1-C_6 alkyl;

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

R^{39}-R^{44} are independently selected from the group consisting of hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl,

or R^{39}, R^{40} together with the carbon atom to which both are attached, or R^{41}, R^{42} together with K to which both are attached when K is a carbon atom, define a C_3-C_6 carbocyclo, and R^{41}-R^{44} are as defined herein,

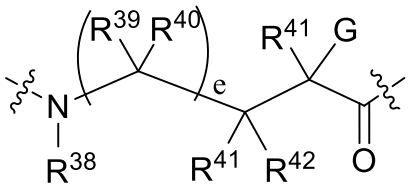
or R^{43}, R^{44} together with L' to which both are attached when L' is a carbon atom define a C_3-C_6 carbocyclo, and R^{39}-R^{42} are as defined herein,

or R^{40} and R^{41}, or R^{40} and R^{43}, or R^{41} and R^{43} to together with the carbon atom or heteroatom to which both are attached and the atoms intervening between those carbon atoms and/or heteroatoms define a C_5-C_6 carbocyclo or a C_5-C_6 heterocyclo, and R^{39}, R^{44} and the remainder of R^{40}-R^{43} are as defined herein,

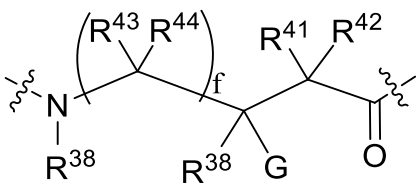
provided that when K is O or S, R^{41} and R^{42} are absent, and when K is N, one of R^{41}, R^{42} is absent, and when L' is O or S, R^{43} and R^{44} are absent, and when L' is N, one of R^{43}, R^{44} is absent, or

A or a subunit thereof is an alpha-amino, beta-amino or another amine-containing acid residue,

in particular, wherein formula (3) or formula (4) has the structure of formula (3a) or formula (4a):



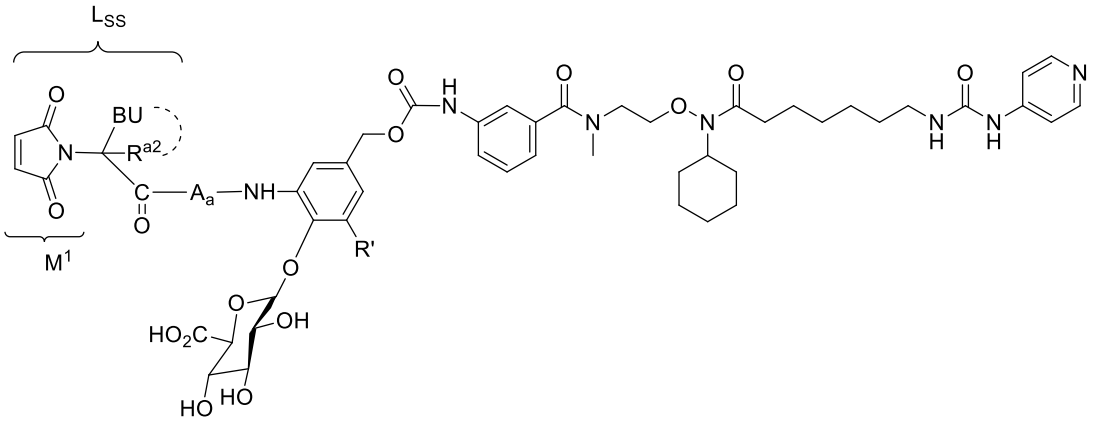
(3a),



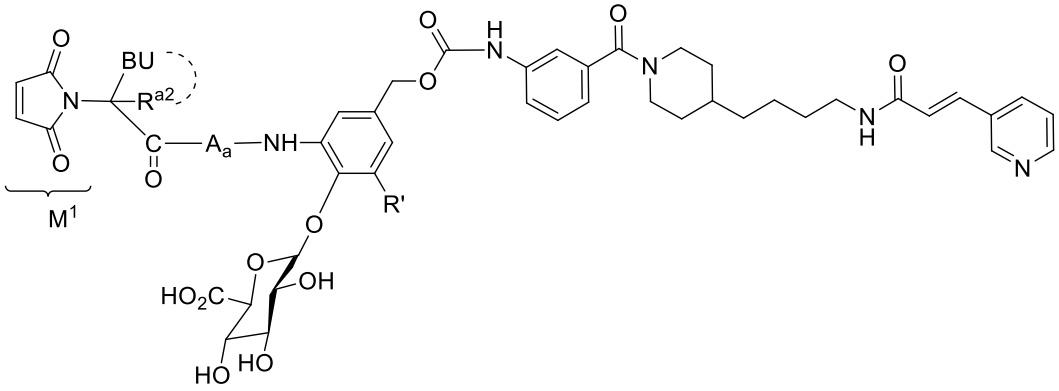
(4a),

wherein subscript e and f are independently 0 or 1.

43. The Drug Linker compound of claim 26, wherein the Drug Linker compound is represented by the structure of:



or



or a salt thereof,

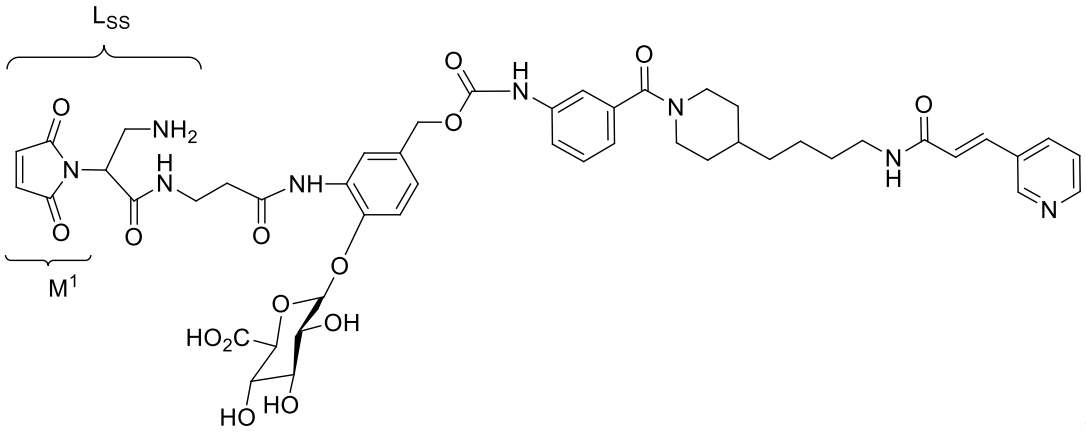
wherein

subscript a is 1 and A is an amino acid residue;

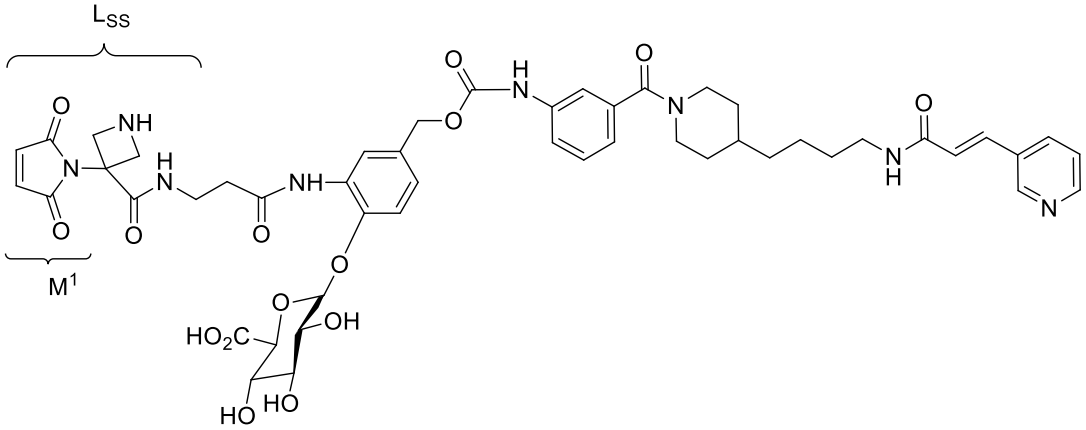
BU is a acyclic Basic Unit so that the dotted curve line is absent, and R^{a2} is hydrogen, or BU together with R^{a2} as C_1-C_6 alkyl and the carbon atom to which both are attached define a cyclic Basic Unit so that the dotted curved line is present; and

R' is hydrogen or $–NO_2$,

in particular by:



or



or a salt thereof.

44. A method of preparing a Ligand Drug Conjugate compound or compound of claim 1, the method comprising the step of: contacting a Drug Linker compound of claim 26 with a targeting agent having a reactive function group capable of interacting with the reactive functional group of the primary linker of the Drug Linker compound so as to form a covalent bond to between the Ligand Unit corresponding to the targeting agent and the primary linker of the Ligand Drug Conjugate compound corresponding in structure to the the primary linker of the Drug Linker compound.

45. The method of claim 44, wherein the reactive functional group of the targeting agent is a cysteine thiol of an antibody, either native to the antibody through interchain disulfide bond reduction or introduced by genetic engineering into the antibody and the reactive functional group of the primary linker of the Ligand Drug Conjugate compound is a maleimide (M^1) moiety comprising the Stretcher Unit of that primary linker, whereby said contacting of said reactive functional groups provides the Ligand Drug Conjugate compound or compound of claim 1 in which L is an antibody Ligand Unit.