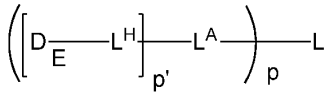
WHAT IS CLAIMED IS:

1. A hydrophilic Drug-Ligand Conjugate Compound having the formula:



I

or a pharmaceutically acceptable salt or solvate thereof,

wherein:

L is a Ligand that specifically binds to a target;

L^A is a Ligand attachment component;

L^H is an optionally branched hydrophilic linker, each branch of L^H having the formula:

$$-AA_1-R^{L1}-R^{L2}-R^{L3}-$$

wherein:

AA_1 is a hydrophilic amino acid that forms a cleavable bond with the D_E to which it is attached;

R^{L1} is optional and is a hydrophilic amino acid or an optionally substituted alkylene, which may share an atom with L^A when R^{L1} is present and R^{L2} and R^{L3} are absent;

R^{L2} is optional and is selected from a hydrophilic amino acid and an optionally substituted alkylene, which may share an atom with L^A when R^{L2} is present and R^{L3} is absent; and

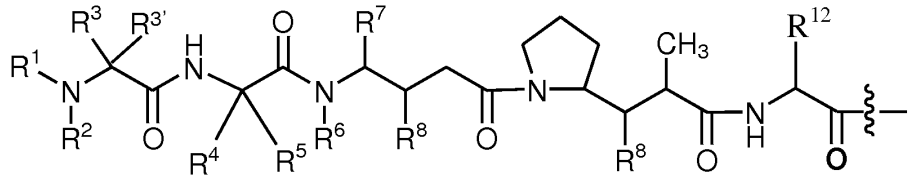
R^{L3} is optional and is selected from a hydrophilic amino acid and an optionally substituted alkylene, which may share an atom with L^A when R^{L3} is present;

the subscript p is an integer of from about 4 to about 20;

the subscript p' is an integer of from 1 to 4;

and

each D_E is an auristatin having the formula:



or a pharmaceutically acceptable salt or solvate thereof,

wherein:

R^1 and R^2 each are independently selected from the group consisting of hydrogen (H) and optionally substituted $-C_1$-C_8 alkyl; with the proviso that both R^1 and R^2 are not H, unless both of $R^3$and $R^{3'}$ are not H;

R^3 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

$R^{3'}$ is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl, and at least one of R^3 and $R^{3'}$ is not H;

R^4 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

R^5 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

or R^4 and R^5 jointly form a carbocyclic ring and have the formula $-(CR^aR^b)_n$-, wherein R^a and R^b are independently selected from the group consisting of H and optionally substituted $-C_1$-C_8 alkyl and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R^6 is selected from the group consisting of H and optionally substituted $-C_1$-C_8 alkyl;

R^7 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

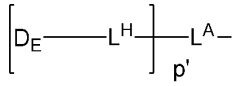
each R^8 is independently selected from the group consisting of H, -OH, optionally substituted -C_1-C_8 alkyl, and optionally substituted –O-(C_1-C_8 alkyl);

R^{12} is selected from the side chains of the group consisting of threonine, serine, asparagine, aspartic acid, glutamine, glutamic acid, homoserine, hydroxyvaline, furyl alanine, threonine(PO_3H_2), pyrazolyl alanine, triazolyl alanine and thiazolyl alanine; or a pharmaceutically acceptable salt or solvate thereof;

wherein the left and right lines of L^H indicate covalent attachments to the D_E unit and L^A, respectively; and

wherein the Drug-Ligand Conjugate has a hydrophilicity index of less than two.

2. A Drug-Linker Compound having the formula:



IV'

or a pharmaceutically acceptable salt or solvate thereof,

wherein:

L^A is a Ligand attachment component;

L^H is an optionally branched hydrophilic linker having the formula:

$$- AA_1 - R^{L1} - R^{L2} - R^{L3} -$$

wherein:

AA_1 is a hydrophilic amino acid that forms a cleavable bond with the D_E unit to which it is attached;

R^{L1} is optional and is selected from a hydrophilic amino acid or an optionally substituted alkylene, which may share an atom with L^A when R^{L3} and R^{L3} are not present;

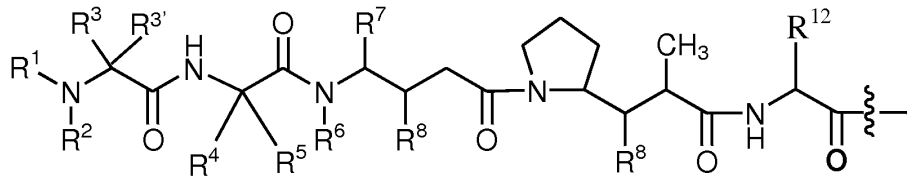
R^{L2} is optional and is selected from a hydrophilic amino acid and an optionally substituted alkylene, which may share an atom with L^A when R^{L2} is present and R^{L3} is not present; and

R^{L3} is optional and is selected from a hydrophilic amino acid and an optionally substituted alkylene, which may share an atom with L^A when R^{L3} is present;

L^A is a Ligand attachment component;

the subscript p' is an integer of from 1 to 4; and

each D_E is an auristatin (Aur) having the formula:



or a pharmaceutically acceptable salt or solvate thereof,

wherein:

R^1 and R^2 each are independently selected from the group consisting of hydrogen (H) and optionally substituted –C_1-C_8 alkyl; with the proviso that both R^1 and R^2 are not H, unless both of $R^3$and $R^{3'}$ are not H;

R^3 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

$R^{3'}$ is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl, and at least one of R^3 and $R^{3'}$ is not H;

R^4 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

R^5 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

or R^4 and R^5 jointly form a carbocyclic ring and have the formula –$(CR^aR^b)_n$-, wherein R^a and R^b are independently selected from the group consisting of H and optionally substituted –C_1-C_8 alkyl and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R^6 is selected from the group consisting of H and optionally substituted –C_1-C_8 alkyl;

R^7 is selected from the group consisting of H and optionally substituted -C_1-C_8 alkyl;

each R^8 is independently selected from the group consisting of H, -OH, optionally substituted -C_1-C_8 alkyl, and optionally substituted –O-(C_1-C_8 alkyl);

R^{12} is selected from the side chains of the group consisting of threonine, serine, asparagine, aspartic acid, glutamine, glutamic acid, homoserine, hydroxyvaline, furyl alanine, threonine(PO_3H_2), pyrazolyl alanine, triazolyl alanine and thiazolyl alanine; or a pharmaceutically acceptable salt or solvate thereof;

wherein the left and right lines of L^H indicate covalent attachments to the D_E unit and L^A, respectively.

3. The Compound of any of the preceding claims, wherein L^H comprises a modified peptide, wherein at least one R^{L1}, R^{L2} and R^{L3} is an amino acid that is covalently linked by a reactive group on its side chain to an adjacent group; or a pharmaceutically acceptable salt or solvate thereof.

4. The Compound of any of the preceding claims, wherein R^{12} is the side chain of L-threonine; or a pharmaceutically acceptable salt or solvate thereof.

5. The Drug-Ligand Conjugate Compound of any of claims 1 and 3-4, wherein p of the Drug-Ligand Conjugate is at least 8; or a pharmaceutically acceptable salt or solvate thereof.

6. The Compound of claim 5, wherein p of the Drug-Ligand Conjugate is at least 10; or a pharmaceutically acceptable salt or solvate thereof.

7. The Compound of claim 5, wherein p of the Drug-Ligand Conjugate is at least 16; or a pharmaceutically acceptable salt or solvate thereof.

8. The Compound of any of the preceding claims, wherein L^A is a succinimide or a hydrolyzed succinimide; or a pharmaceutically acceptable salt or solvate thereof.

9. A Compound having the formula:

(a) $(L^H)_{p'} - L^A$

or a pharmaceutically acceptable salt or solvate thereof, wherein:

L^H is an optionally branched hydrophilic linker, each branch of L^H having the formula:

$$- AA_1 – R^{L1} – R^{L2} – R^{L3} – \quad ;$$

L^A is a Ligand Attachment component; and

p' is an integer from 1 to 4; and

wherein the left and right lines of L^H indicate attachment sites for a D_E unit and L^A, respectively; or

(b) $([L^H]_{p'} - L^A)_p - L$

or a pharmaceutically acceptable salt or solvate thereof;

wherein:

L is a Ligand that specifically binds to a target;

L^H is an optionally branched hydrophilic linker, each branch of L^H having the formula:

$$- AA_1 - R^{L1} - R^{L2} - R^{L3} - \quad ;$$

L^A is a Ligand Attachment component;

the subscript p is an integer from about 4 to 20; and

the subscript p' is an integer from 1 to 4;

wherein the left and right lines of L^H indicate attachment sites to the D_E Unit and L^A, respectively;

wherein in (a) or (b):

AA_1 is a hydrophilic amino acid that can form a cleavable bond with a D_E unit when it is attached;

R^{L1} is a hydrophilic amino acid or an optionally substituted alkylene, which may share an atom with L^A when R^{L2} and R^{L3} are not present;

R^{L2} is optional and is selected from a hydrophilic amino acid and an optionally substituted alkylene, which may share an atom with L^A when R^{L2} is present and R^{L3} is not present; and

R^{L3} is optional and is selected from a hydrophilic amino acid and an optionally substituted alkylene, which may share an atom with L^A when R^{L3} is present.

10. The Compound of any of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein:

(a) AA_1 is a hydrophilic amino acid selected from the group consisting of Glycine and L forms of Aspartate, Glutamate, Asparagine, Glutamine, Histidine, Lysine, Arginine, Serine and Alanine;

(b) when R^{L1} is present, it is selected from the group consisting of:

Glycine; L or D forms of Aspartate, Glutamate, Asparagine, Glutamine, Histidine, Lysine, Arginine, Serine and Alanine; $-NH-CH(R^a)-CO-$; and $-NH-CH(COOH)-R^b-$; wherein R^a is selected from $-CH_2NH_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2OH$, $-CH_2CH_2CH_2CO_2H$, $-CH_2CH_2CH_2CO_2H$

and -$CH_2CH_2CH_2CH_2CO_2H$; and R^b is selected from -CH_2NH-, -CH_2CH_2NH-, -$CH_2CH_2CH_2NH$-, -$CH_2CH_2CH_2CH_2NH$-, -CH_2CH_2CO-, -$CH_2CH_2CH_2CO$-, -$CH_2CH_2CH_2CO$- and -$CH_2CH_2CH_2CH_2CO$ -; and

a $C_1 – C_6$ alkylene, optionally substituted with 1-4 substituents selected from –NH-, -C(O)-, -COOH, -N($C_1 – C_3$ alkyl), - NH_2 or –NH($C_1 – C_3$ alkyl);

(c) when R^{L2} is present, it is selected from the group consisting of:

Glycine; L or D forms of Aspartate, Glutamate, Asparagine, Glutamine, Histidine, Lysine, Arginine, Serine and Alanine; –NH – CH(R^a) – CO-; and –NH – CH(COOH) – R^b –; wherein R^a is selected from -CH_2NH_2, -$CH_2CH_2NH_2$, -$CH_2CH_2CH_2NH_2$, -$CH_2CH_2CH_2CH_2NH_2$, -CH_2CH_2OH, -$CH_2CH_2CH_2CO_2H$, -$CH_2CH_2CH_2CO_2H$ and -$CH_2CH_2CH_2CH_2CO_2H$; and R^b is selected from -CH_2NH-, -CH_2CH_2NH-, -$CH_2CH_2CH_2NH$-, -$CH_2CH_2CH_2CH_2NH$-, -CH_2CH_2CO-, -$CH_2CH_2CH_2CO$-, -$CH_2CH_2CH_2CO$- and -$CH_2CH_2CH_2CH_2CO$ -; and

a $C_1 – C_6$ alkylene, optionally substituted with 1-4 substituents selected from –NH-, -C(O)-, -COOH, -N($C_1 – C_3$ alkyl), - NH_2 or –NH($C_1 – C_3$ alkyl); and

(d) when R^{L3} is present, it is selected from the group consisting of:

Glycine; L or D forms of Aspartate, Glutamate, Asparagine, Glutamine, Histidine, Lysine, Arginine, Serine and Alanine; –NH – CH(R^a) – CO-; and –NH – CH(COOH) – R^b –; wherein R^a is selected from -CH_2NH_2, -$CH_2CH_2NH_2$, -$CH_2CH_2CH_2NH_2$, -$CH_2CH_2CH_2CH_2NH_2$, -CH_2CH_2OH, -$CH_2CH_2CH_2CO_2H$, -$CH_2CH_2CH_2CO_2H$ and -$CH_2CH_2CH_2CH_2CO_2H$; and R^b is selected from -CH_2NH-, -CH_2CH_2NH-, -$CH_2CH_2CH_2NH$-, -$CH_2CH_2CH_2CH_2NH$-,

-CH_2CH_2CO-, -$CH_2CH_2CH_2CO$-, -$CH_2CH_2CH_2CO$-
and -$CH_2CH_2CH_2CH_2CO$ -; and

an $C_1 - C_6$ alkylene, optionally substituted with 1-4 substituents selected from –NH-, -C(O)-, -COOH, -N($C_1 - C_3$ alkyl), - NH_2 or –NH($C_1 - C_3$ alkyl).

11. The Compound of any of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein:

(a) $\mathbf{AA_1}$ is present and R^{L1}, R^{L2} and R^{L3} are absent;

(b) $\mathbf{AA_1}$ is present, R^{L1} is present and R^{L2} and R^{L3} are absent;

(c) $\mathbf{AA_1}$ is present, R^{L1} is present, R^{L2} is present and R^{L3} is absent;

(d) $\mathbf{AA_1}$ is present, R^{L1} is present, R^{L2} is present and R^{L3} is present;

(e) $\mathbf{AA_1}$ is present and at least one of R^{L1}, R^{L2} and R^{L3} is present and is an optionally substituted alkylene;

(f) $\mathbf{AA_1}$ is Glutamate and at least one of R^{L1}, R^{L2} and R^{L3} is present and is an optionally substituted alkylene;

(g) $\mathbf{AA_1}$ is Glutamate, $\mathbf{R^{L1}}$ is a hydrophilic amino acid and at least one of R^{L2} and R^{L3} is present and is an optionally substituted alkylene;

(h) $\mathbf{AA_1}$ and R^{L1} are hydrophilic amino acids and at least one of R^{L2} and R^{L3} is present and is an optionally substituted alkylene;

(i) $\mathbf{AA_1}$ is a hydrophilic amino acid and R^{L1} and optionally R^{L2} are an optionally substituted alkylene;

(j) $\mathbf{AA_1}$ is present and at least one of R^{L1}, R^{L2} and R^{L3} is present and is an optionally substituted alkylene selected from the group consisting of ethylenediamine, -NH – CH(COOH) – CH_2 –NH – and–CO – CH(CH_2NH_2) -;

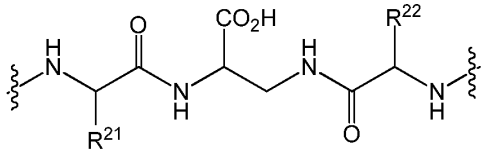
(k) $\mathbf{AA_1}$ is Glutamate, R^{L1} is a hydrophilic amino acid and at least one of R^{L2} and R^{L3} is present and is an optionally substituted alkylene selected from the

group consisting of ethylenediamine, -NH – CH(COOH) – CH_2 –NH – and–CO – $CH(CH_2NH_2)$ -;

(l) **AA_1** and R^{L1} are hydrophilic amino acids and at least one of R^{L2} and R^{L3} is present and is an optionally substituted alkylene selected from the group consisting of ethylenediamine, -NH – CH(COOH) – CH_2 –NH – and–CO – $CH(CH_2NH_2)$ -; or

(m) **AA_1** is a hydrophilic amino acid and R^{L1} and optionally R^{L2} are an optionally substituted alkylene selected from the group consisting of ethylenediamine, -NH – CH(COOH) – CH_2 –NH – and–CO – $CH(CH_2NH_2)$ -.

12. The Compound of any of the preceding claims, wherein -L^H- has the formula:



or a pharmaceutically acceptable salt or solvate thereof,

wherein:

R^{21} is selected from the group consisting

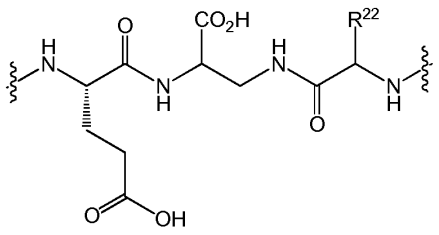
of -CH_2NH_2, -$CH_2CH_2NH_2$, -CH_2OH, -CH_2CH_2OH,

-CH_2CO_2H, -$CH_2CH_2CO_2H$, -$CH_2CH_2CH_2CO_2H$,

and -$CH_2CH_2CH_2CH_2CO_2H$; and

R^{22} is selected from the group consisting of -CH_2NH_2, -$CH_2CH_2NH_2$, -CH_2OH; and the left and right wavy lines indicate attachment to D_E, H or a protecting group, and L^A, respectively.

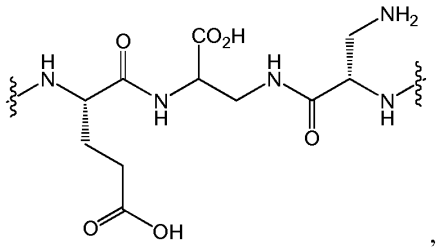
13. The Compound of any of the preceding claims, wherein -L^H- has the formula:



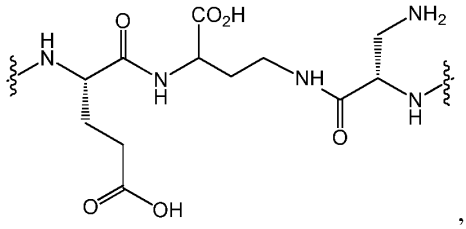
or a pharmaceutically acceptable salt or solvate thereof,

wherein R^{22} is selected from $-CH_2NH_2$, $-CH_2CH_2NH_2$, $-CH_2OH$, and $-CH_2CH_2OH$; and the left and right wavy lines indicate attachments to D_E, H or a protecting group, and L^A, respectively.

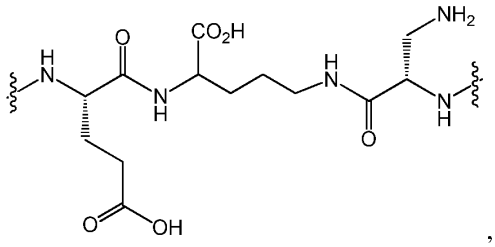
14. The Compound of any of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein $-L^H-$ has the formula selected from the group consisting of:



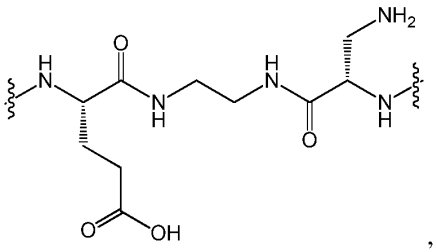
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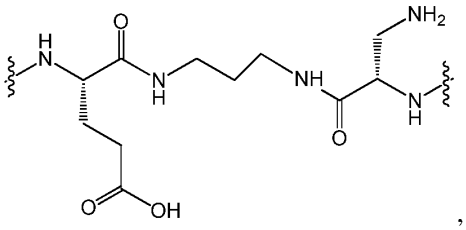
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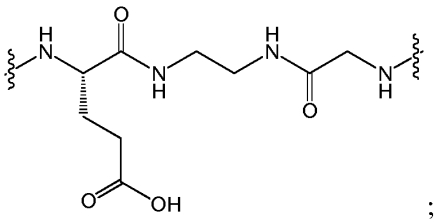
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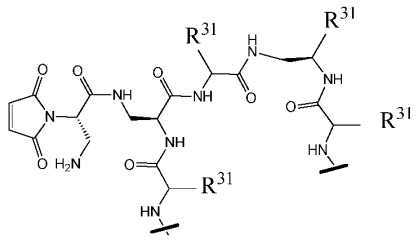


;

wherein the left and right wavy lines indicate attachments to D_E, H or a protecting group, and L^A, respectively.

15. The Compound of any of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein;

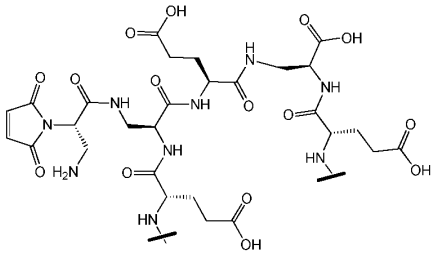
(a) the L^A-L^H of the Drug-Linker Compound has the formula:



wherein each R^{31} is independently selected from the group consisting of $-CH_2NH_2$, $-CH_2CH_2NH_2$, $-CH_2OH$, $-CH_2CH_2OH$, $-CH_2CO_2H$, $-CH_2CH_2CO_2H$, $-CH_2CH_2CH_2CO_2H$, and $-CH_2CH_2CH_2CH_2CO_2H$; and each of the bars indicates an attachment site for a D_E unit; or

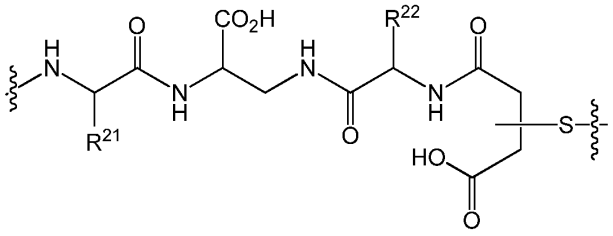
(b) the L^A-L^H of (a) wherein the maleimide group is covalently attached to a thiol group of a Ligand unit.

16. The Compound of any of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein the L^A-L^H of the Drug-Linker Compound have the formula:



and each of the bars indicates attachment site for a D_E unit, wherein the maleimide group is optionally covalently attached to a thiol group of a Ligand unit.

17. The Compound of any of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein the $-L^A$-L^H of the Drug-Ligand Conjugate Compound have the formula:



wherein

R^{21} is selected from the group consisting of $-CH_2NH_2$, $-CH_2CH_2NH_2$, $-CH_2OH$, $-CH_2CH_2OH$,

$-CH_2CO_2H$, $-CH_2CH_2CO_2H$, $-CH_2CH_2CH_2CO_2H$,

and $-CH_2CH_2CH_2CH_2CO_2H$; and

R^{22} is selected from the group consisting of $-CH_2NH_2$, $-CH_2CH_2NH_2$, $-CH_2OH$;

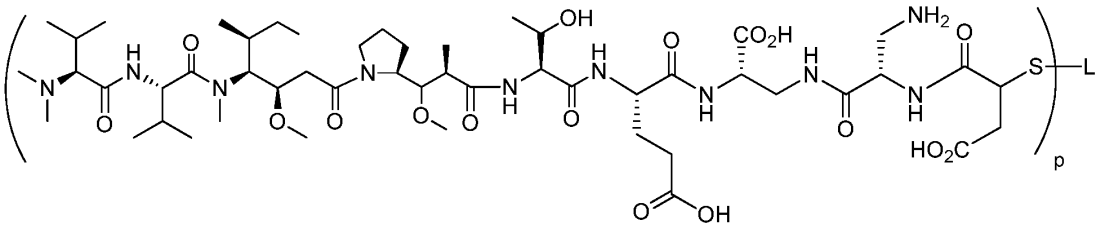
and the left and right wavy lines indicate attachment to the D_E and the Ligand unit (L), respectively; and the sulfur atom is from the Ligand unit.

18. The Compound of any of the preceding claims, wherein the Ligand unit (L) of the Drug-Ligand Conjugate or the Ligand-Linker Compound is a protein, polypeptide or peptide.

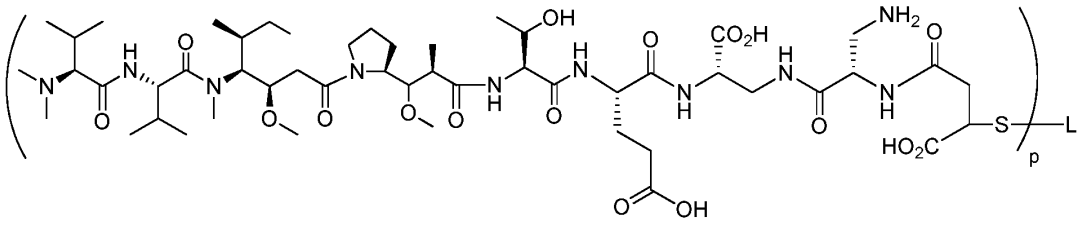
19. The Compound of any of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein the Ligand unit (L) of the Drug-Ligand Conjugate or the Ligand-Linker Compound is an antibody.

20. The Compound of any of one of the preceding claims, or a pharmaceutically acceptable salt or solvate thereof, wherein L^A is selected from the group consisting of maleimide or maleimido diaminopropionic acid.

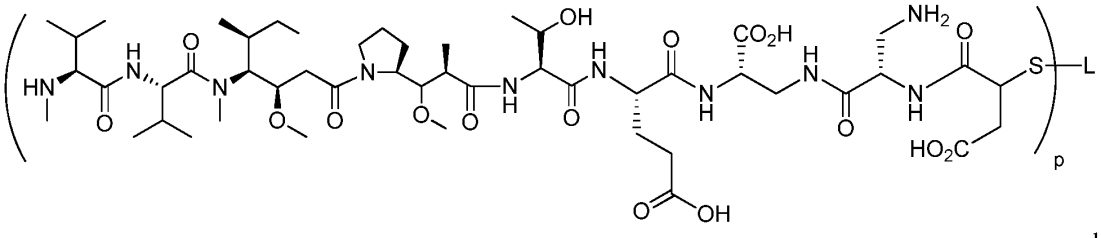
21. The hydrophilic Drug-Ligand Conjugate of claim 1 having a formula selected from:



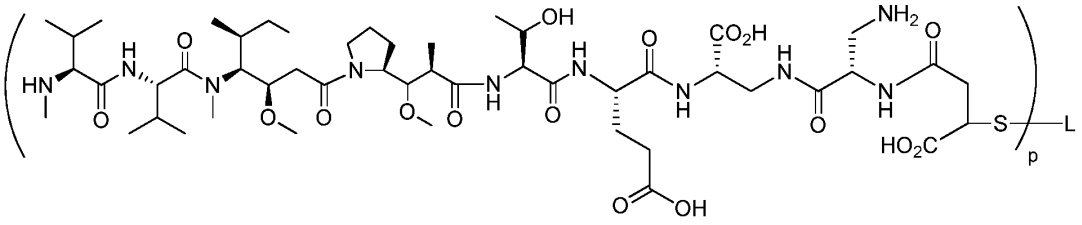
,



,



, and



;

wherein S is a sulfur atom of the Ligand; or a pharmaceutically acceptable salt or solvate thereof.

22. A method of treating a patient in need thereof, comprising administering to the patient a Drug-Ligand Conjugate Compound of any of the preceding claims, wherein the patient has cancer, an autoimmune disease or an infectious disease and wherein the Ligand of the Drug-Ligand Conjugate Compound specifically binds to a target cell associate with the cancer, autoimmune disease or infectious disease.

23. The method of claim 22, wherein the Drug-Ligand Conjugate Compound is administered at a dose of from 0.1 to 10 mg/kg.

24. The method of any of claims 22-23, wherein:

(a) p is at least 8 and the dose of the Drug-Ligand Conjugate compound administered to the patient is the same or less than that of a two loaded conjugate having the same drug linker;

(b) p is at least 8 and the dose of the Drug-Ligand Conjugate compound administered to the patient is the same or less than that of a four loaded conjugate having the same drug linker;

wherein the Drug-Ligand Conjugate compound and the two or four loaded conjugate are administered on a comparable schedule.

25. The method of any one of claims 22-24, wherein the patient is human.

26. A pharmaceutical composition comprising an effective amount of the Drug-Ligand Conjugate Compound of any of claims 1 and 2-21, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent carrier or excipient.

27. The pharmaceutical composition of claim 26 for use in a method of treatment of cancer, an autoimmune disease or an infectious disease, wherein optionally:

(a) the Drug-Ligand Conjugate Compound is formulated in a unit dosage injectable form;

(b) the amount of Drug-Ligand Conjugate Compound administered to a patient is in the range of about 0.1 to about 10 mg/kg of the patient's weight; or

(c) the Drug-Ligand Conjugate Compound is administered intravenously.