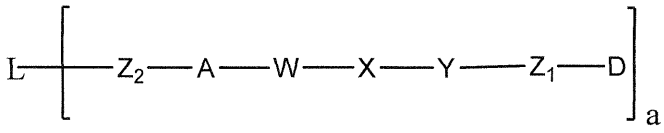
enhanced permeability and retention mechanism. However, barriers of using such targeted deliveries include fast clearance of foreign particles from the blood, and technological hindrances in obtaining highly standardized, pharmaceutically acceptable drug delivery systems with the necessary specificity and selectivity for binding tumor cells.

[0005] Thus, a need exists for targeted anti-proliferative compounds.

SUMMARY

[0006] The present invention refers to subject matter as defined in the attached set of claims. The present disclosure ~~relates to~~ describes conjugate compounds represented by the following structural formula (I):



(I)

wherein:

L is absent or a ligand;

further wherein:

when L is a ligand, L is capable of binding to a cell or cell population;

a is an integer from 1 to 10;

Z_2 and Z_1 are each independently absent or a spacer;

D is a Biologically Active Molecule;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is absent, -O-, -S-, $-CR_5R_6-$, $-NR_4-$;

further wherein: R_4, R_5, and R_6 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

X is absent, aryl, heteroaryl, cycloalkyl, heterocyclyl, wherein aryl, heteroaryl, cycloalkyl, and heterocyclyl are optionally substituted; and

Y is absent, or a spacer.

[0006a] In one ~~aspect~~example, there is ~~provided~~ described a compound of the following formula

-C(=O)-N(R_4)-C(=O)-, or -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, and CR_5R_6 ;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} ismethyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100; and

x is 0, 1 or 2.

[0007] The present disclosure also ~~provides~~ describes linker-biologically active compounds represented by the following structural formula (V):

$$Z_2—A—W—X—Y—Z_1—D \qquad (V)$$

wherein:

Z_2 and Z_1 are each independently absent or a spacer;

D is a Biologically Active Molecule;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is absent, -O-, -S-, -CR_5R_6-, -NR_4-;

further wherein: R_4, R_5, and R_6 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

X is absent, aryl, heteroaryl, cycloalkyl, heterocyclyl, wherein aryl, heteroaryl, cycloalkyl, and heterocyclyl are optionally substituted; and

Y is absent, or a spacer.

[0008] The present disclosure also ~~provides~~ describes linkers represented by the following structural formula (VI).

[0009] In one ~~embodiment~~example, the linker compounds is represented by formula (VI):

Z_2——A——W——X——Y——Z_1 (VI)

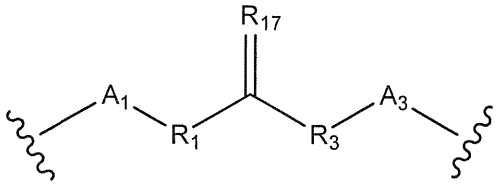
wherein:

Z_2 and Z_1 are each independently absent or a spacer;

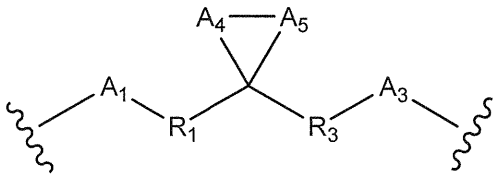
A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is absent, -O-, -S-, -CR_5R_6-, -NR_4-;

X is absent, aryl, heteroaryl, cycloalkyl, heterocyclyl, wherein aryl, heteroaryl, cycloalkyl, and heterocyclyl are optionally substituted;

Y is absent, 

, or



,

wherein A_1, A_3, R_1 and R_3 are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$-, -C(=O)-O-$(CH_x)_{p1}$-, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -$(O\text{-}(CH_2)_{p2}\text{-})_{p3}$-, -$((CH_2)_{p2}\text{-O-})_{p3}$-, -C(=S)-, -C(=S)-S-, -S-C(=S)-, -C(=S)-NH-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-

$N(R_4)$-C(=O)-, -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

A_4 and A_5 are each independently –O-, -S-, -NR_{18}-, -CR_5R_6-;

R_{17} is selected from the group consisting of O, S, NR_{18}, CR_5R_6;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

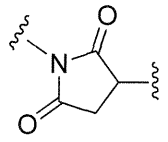
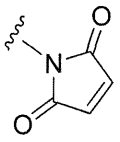
p1, p2 and p3 are each independently 0, or an integer from 1 to 100; and

x is 0, 1 or 2.

[0010] In one ~~aspect~~example, the disclosure ~~provides~~ describes compounds of formula (VI), wherein Z_2 is represented by the following structural formula:

-Z_{2A}-Z_{2B}-Z_{2C}-Z_{2D}-,

wherein:

Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$, -C(=O)-O-$(CH_x)_{p1}$, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-$)_{p3}$-, -(($(CH_2)_{p2}$-O-$)_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -$N(R_4)$-C(=O)-$N(R_8)$-, -$N(R_4)$-C(=O)O-, -$N(R_4)$-C(=O)-, -C(=O)-$N(R_4)$-, -C(=O)-$N(R_4)$-C(=O)-, -O-C(=O)-$N(R_4)$, -O-C(=S)-$N(R_4)$-, -C(=S)-$N(R_4)$-, -N=C=S, -N=C=O,  or ,

wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted and R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl.

[0011] In another ~~aspect~~example, the present disclosure also ~~relates to~~ describes a pharmaceutical composition comprising a therapeutically effective amount of a compound as disclosed above or a pharmaceutically

acceptable salt thereof and one or more pharmaceutically acceptable carriers, diluents, or excipients.

[0012] In another ~~aspect~~example, the present disclosure also ~~provides~~ describes an *ex vivo* method of reducing, retarding or stopping an abnormal cell growth comprising contacting the abnormalcell with a compound as disclosed above, in an amount sufficient to retard, reduce or stop the abnormal cell growth, and wherein the abnormal cell growth is retarded, reduced or stopped.

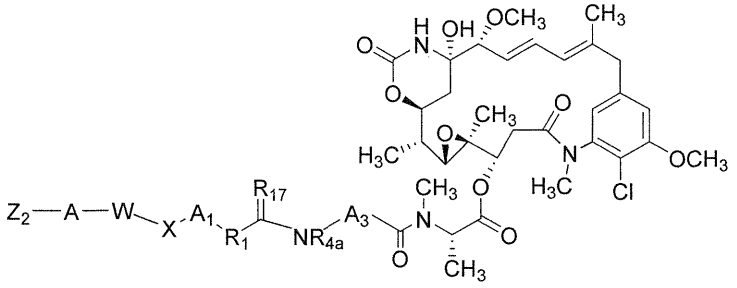
[0013] In another ~~aspect~~example, the present disclosure also ~~provides~~ describes an *ex vivo* method of killing a cell, comprising contacting the cell with a compound as disclosed above, in an amount sufficient to kill the cell, and wherein the cell is killed.

[0014] The present disclosure also ~~provides~~ describes a method of treatment of a medical disorder in an individual suffering from the medical disorder, comprising administering to the individual an effective amount of a composition comprising a compound of formula (I). **[0014a]** In another ~~aspect~~ example there is ~~provided~~ disclosed use of a composition comprising a compound as disclosed above in the manufacture of a medicament for treating a medical disorder in an individual suffering from the medical disorder.

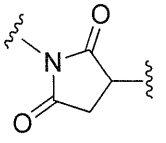
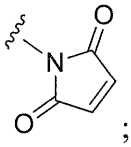
[0015] The present disclosure also ~~provides~~ describes a method of reducing tumor size, stopping tumor size increase, reducing tumor proliferation, or preventing tumor proliferation in an individual in need thereof comprising administering to the individual an effective amount of a composition to reduce tumor size, stop tumor size increase, reduce tumor proliferation, or prevent tumor proliferation, wherein the composition comprises a compound of formula (I). **[0015a]** In another ~~aspect~~example, there is ~~provided~~ disclosed use of a composition comprising a compound as disclosed above in the manufacture of a medicament for reducing tumor size, stopping tumor size increase, reducing tumor proliferation, or preventing tumor proliferation in an individual in need thereof comprising administering to the individual an effective amount of a composition to reduce tumor size, stop tumor size increase, reduce tumor proliferation, or prevent tumor proliferation.

[0016] The present disclosure also ~~relates to~~describes precursor Biologically Active Molecule-linker compounds as represented by formula (V). Compounds of formula (V) provide building blocks for conjugate compounds of formula (I). In addition, compounds of formula (V) may be provided as compositions, pharmaceutical compositions and pharmaceutically acceptable salts thereof.

[0016a] In another ~~aspect~~example, there is ~~provided~~ disclosed a compound of the following formula



wherein:

Z_2 is represented by the following structural formula: $-Z_{2A}$-Z_{2B}-Z_{2C}-Z_{2D}, wherein Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$, -C(=O)-O-$(CH_x)_{p1}$, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-$)_{p3}$-, -($(CH_2)_{p2}$-O-$)_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -$N(R_4)$-C(=O)-$N(R_8)$-, -$N(R_4)$-C(=O)O-, -$N(R_4)$-C(=O)-, -C(=O)-$N(R_4)$-, -C(=O)-$N(R_4)$-C(=O)-, -O-C(=O)-$N(R_4)$, -O-C(=S)-$N(R_4)$-, -C(=S)-$N(R_4)$-, -N=C=S, -N=C=O,  or ;

;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is -O-, -S-, -CR_5R_6-, or -NR_4-;

X isa substituted or unsubstituted: aryl, heteroaryl, cycloalkyl, or heterocyclyl; ~~and~~

wherein A_1, A_3, and R_1 are each independently~~,~~ an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$-, -C(=O)-O-$(CH_x)_{p1}$-, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-$)_{p3}$-, -($(CH_2)_{p2}$-O-$)_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -$N(R_4)$-C(=O)-$N(R_8)$-, -$N(R_4)$-C(=O)O-, -$N(R_4)$-C(=O)-, -C(=O)-$N(R_4)$-, -C(=O)-$N(R_4)$-

C(=O)-, or -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl is optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, or CR_5R_6;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

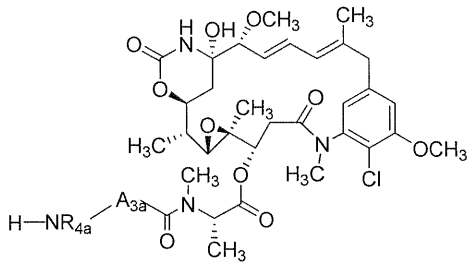
R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} is methyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100; and

x is 0, 1 or 2.

[0016b] In another ~~aspect~~example, there is ~~provided~~ disclosed a compound of the following formula:



wherein:

A_{3a} is each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$-,-C(=O)-O-$(CH_x)_{p1}$-, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-)$_{p3}$-, -($(CH_2)_{p2}$-O-)$_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-,-N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-N(R_4)-C(=O)-, or -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted; and

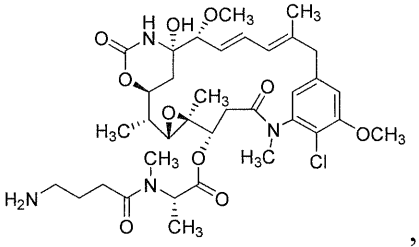
p1, p2 and p3 are each independently 0, or an integer from 1 to 100;

x is 0, 1 or 2;

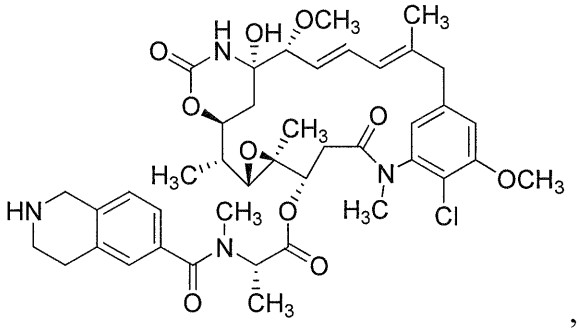
R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl; and

R_{4a} is methyl.

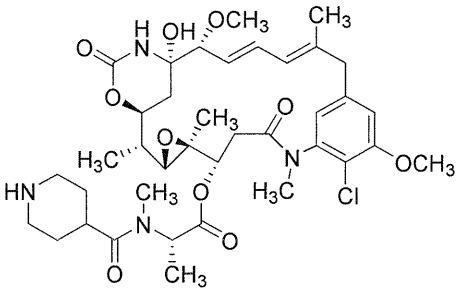
[0016c] In another ~~aspect~~example, there is ~~provided~~ disclosed a compound having a structure selected from one member of the group consisting of



,

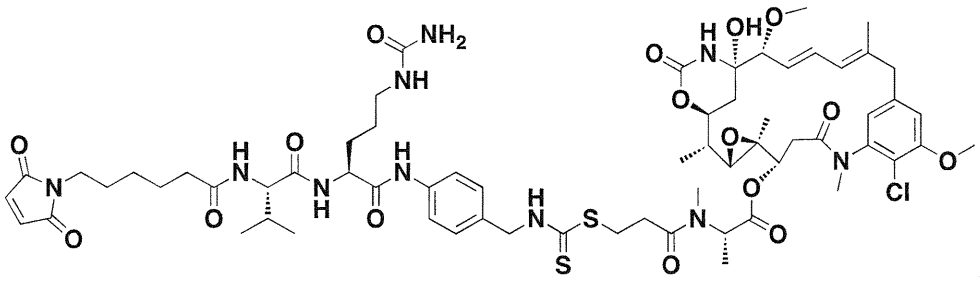


, and



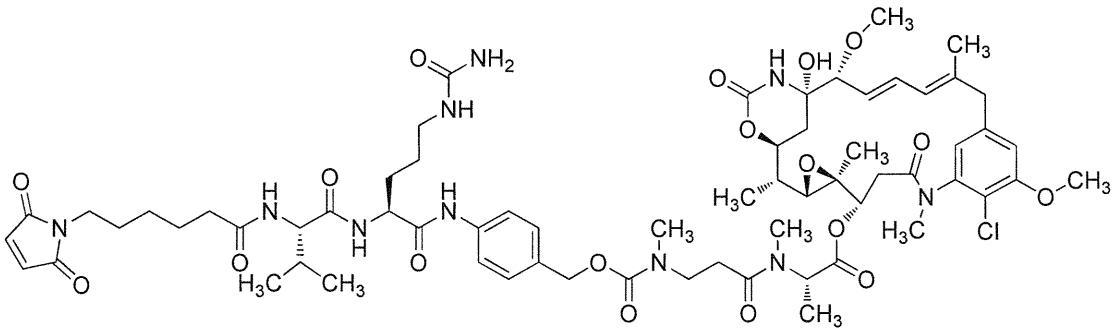
.

[0016d] In another ~~aspect~~example, there is ~~provided~~ disclosed a compound having the following structure:



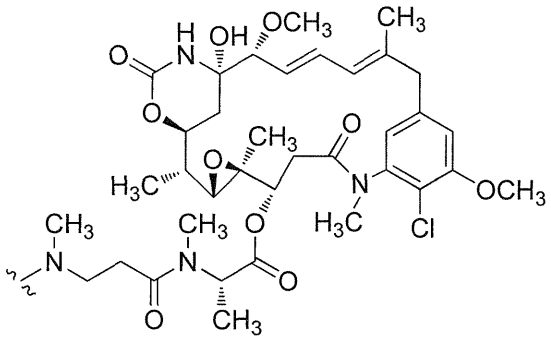
.

[0016e] In another ~~aspect~~example, there is ~~provided~~ disclosed a compound having the following structure:



.

[0016f] In another ~~aspect~~example, there is ~~provided~~ disclosed an antibody-drug conjugate comprising an antibody or antigen-binding fragment thereof conjugated to a payload of the following formula:



[0017] The present disclosure further includes the use of any of the compositions comprising compounds of formula (I) and/or pharmaceutical formulations in the manufacture of a medicament for the treatment, prevention and/or amelioration of a medical disorder.

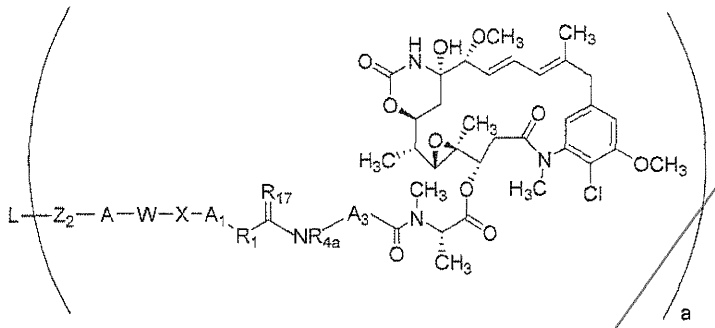
[0018] The present disclosure further includes the use of any of the compositions comprising compounds of formula (I) and/or pharmaceutical formulations in the manufacture of a medicament for the treatment, prevention and/or amelioration of a tumor.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1-8 depict the results of cell viability assays in which various cancer cell lines were grown *in vitro* and treated with serial dilutions of antibodies, free drug, or

Claims:

1. A compound of the following formula



wherein:

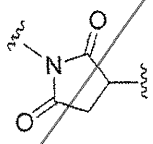
L is a Ligand,

wherein:

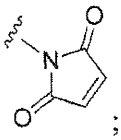
L is capable of binding to a cell or cell population;

a is an integer from 1 to 10;

Z_2 is represented by the following structural formula: $-Z_{2A}-Z_{2B}-Z_{2C}-Z_{2D}$, wherein Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}$, $-C(=O)-O-(CH_x)_{p1}$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, $-O-C(=O)-N(R_4)$, $-O-C(=S)-N(R_4)-$, $-C(=S)-N(R_4)-$, -N=C=S, -N=C=O,



or



;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is -O-, -S-, $-CR_5R_6-$, or $-NR_4-$;

X is aryl, heteroaryl, cycloalkyl, or heterocyclyl, wherein aryl, heteroaryl, cycloalkyl, and heterocyclyl are optionally substituted;

wherein A_1, A_3, and R_1 are each independentlyan amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$-, -C(=O)-O-$(CH_x)_{p1}$-, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-)$_{p3}$-, -($(CH_2)_{p2}$-O-)$_{p3}$-, -C(=S)-, -C(=S)-S-, -S-C(=S)-, -C(=S)-NH-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-N(R_4)-C(=O)-, or -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, and CR_5R_6 ;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} ismethyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100; and

x is 0, 1 or 2.

2. The compound of claim 1, wherein X, A_1, A_3, and R_1 are unsubstituted .

3. The compound of claim 1, wherein A_3 is methyl, ethyl, 1-propyl, 2-propyl, or 1-butyl.

4. The compound of claim 1, wherein L is capable of binding to a specifically targeted cell population.

5. The compound of claim 1, wherein L is selected from the group consisting of proteins, antibodies, fragments of antibodies, nucleic acids, antigen binding scaffolds, and carbohydrates.

6. The compound of claim 5, wherein L is an antibody or a fragment thereof.

7. The compound of claim 6, wherein L is an antibody or fragment thereof that specifically binds a tumor associated antigen.

8. The compound of claim 6, wherein the antibody or a fragment thereof comprises a sulfur group that is covalently attached with Z_2.

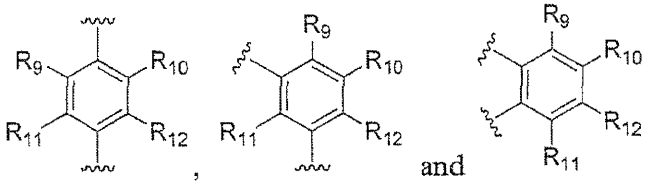
9. The compound of claim 8, wherein the antibody or a fragment thereof comprises a sulfur group that is covalently attached with Z_{2A}.

10. The compound of claim 1, wherein R_1 and R_{17} are O.

11. The compound of claim 1, wherein A is an amino acid selected from the group consisting of alanine, aspartic acid, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, glutamine, arginine, serine, threonine, valine, tryptophan, tyrosine, cysteine, and citrulline.

12. The compound of claim 1, wherein A is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine.

13. The compound of claim 1, wherein X is an aryl selected from the group consisting of



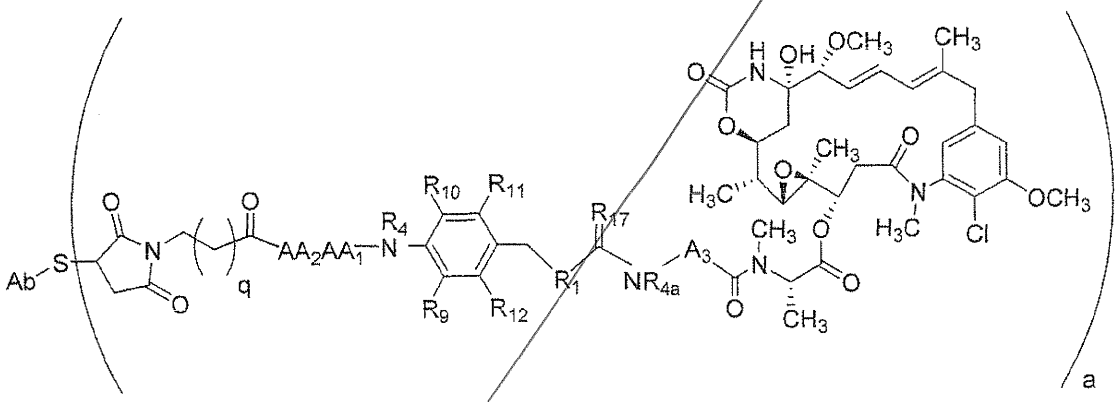
and

wherein R_9, R_{10}, R_{11}, and R_{12} are each independently H, an alkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, -O-C(=O)-R_{15}, -C(=O)-R_{15}, -C(=O)-O-R_{15}, C(=O)-NR_{13} R_{14}; and

further wherein, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl.

14. The compound of claim 9 having the following formula :



wherein:

Ab is an antibody or a fragment thereof;

AA_1-AA_2 is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine;

a is an integer from 1 to 10;

q is 0 or an integer from 1 to 5;

A_3 and R_1 are each independently, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -

C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$-, -C(=O)-O-$(CH_x)_{p1}$-, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-)$_{p3}$-, -($(CH_2)_{p2}$-O-)$_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-N(R_4)-C(=O)-, -O- C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, and CR_5R_6;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} is methyl;

R_9, R_{10}, R_{11}, and R_{12} are each independently H, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, -O-C(=O)-R_{15}, -C(=O)-R_{15}, -C(=O)-O-R_{15}, -C(=O)-NR_{13} R_{14}, or substituted or unsubstituted: alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl;

R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100;

x is 0, 1 or 2

.

15. The compound of claim 14, wherein:

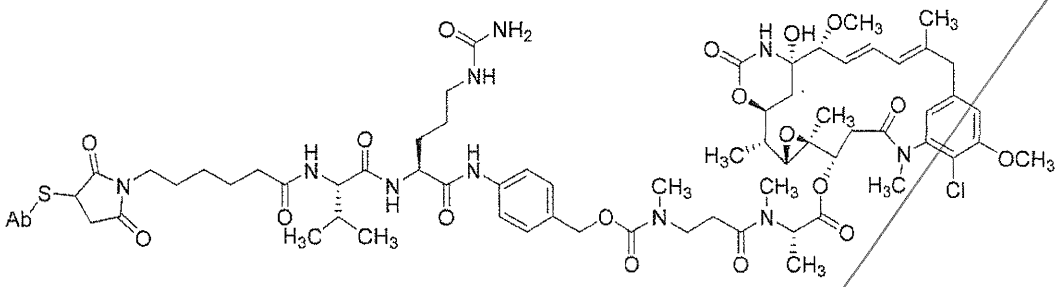
q is 4;

R_1 and ~~R_3~~ are each independently –O-, -S-, NR_4, or -CR_5R_6-;

R_4, R_5, R_6, R_9, R_{10}, R_{11}, and R_{12} are each independently H or alkyl; and

A_3 is an alkyl.

16. The compound of claim 14, represented by the following structure:



wherein Ab is an antibody or a fragment thereof.

17. The compound of claim 1, wherein A is a peptide cleavable by a protease.

18. The compound of claim 1, wherein A is a peptide cleavable by a protease expressed in tumor tissue.

19. The compound of claim 18, wherein the protease is a cathepsin or a plasmin.

20. The pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers, diluents, or excipients.

21. An *ex vivo* method of reducing, retarding or stopping an abnormal cell growth comprising contacting the abnormal cell with a compound of claim 1, in an amount sufficient to retard, reduce or stop the abnormal cell growth, and wherein the abnormal cell growth is retarded, reduced or stopped.

22. An *ex vivo* method of killing a cell, comprising contacting the cell with a compound of claim 1, in an amount sufficient to kill the cell, and wherein the cell is killed.

23. The method of claim 22, wherein the cell is a tumor cell.

24. Use of a composition comprising a compound of claim 1 in the manufacture of a medicament for treating a medical disorder in an individual suffering from the medical disorder.

25. The use of claim 24, wherein the individual is a mammal.

26. The use of claim 24, further comprising administering sequentially or consecutively an additional therapy.

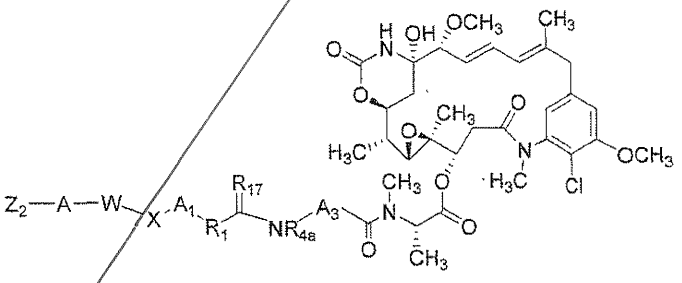
27. The use of claim 26, wherein additional therapy is radiation therapy, chemotherapy, or a combination of both.

28. The use of claim 24, further comprising administering at least one additional therapeutic agent.

29. The use of claim 24, wherein the medical disorder is selected from the group consisting of tumors, cancers, infectious diseases, neurodegenerative diseases, bone disorders, and cardiovascular diseases.

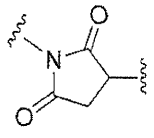
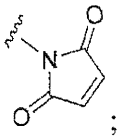
30. Use of a composition comprising a compound of claim 1 in the manufacture of a medicament for reducing tumor size, stopping tumor size increase, reducing tumor proliferation, or preventing tumor proliferation in an individual in need thereof comprising administering to the individual an effective amount of a composition to reduce tumor size, stop tumor size increase, reduce tumor proliferation, or prevent tumor proliferation.

31. A compound of the following formula



wherein:

Z_2 is represented by the following structural formula: $-Z_{2A}$-Z_{2B}-Z_{2C}-Z_{2D}, wherein Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino

acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}$, $-C(=O)-O-(CH_x)_{p1}$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, $-O-C(=O)-N(R_4)$, $-O-C(=S)-N(R_4)-$, $-C(=S)-N(R_4)-$, -N=C=S, -N=C=O,  or ;

;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is -O-, -S-, $-CR_5R_6-$, or $-NR_4-$;

X isa substituted or unsubstituted: aryl, heteroaryl, cycloalkyl, or heterocyclyl; ~~and~~

wherein A_1, A_3, and R_1 are each independently, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}-$, $-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or $-O-C(=O)-NR_4-$, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl is optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, or CR_5R_6;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} is methyl;

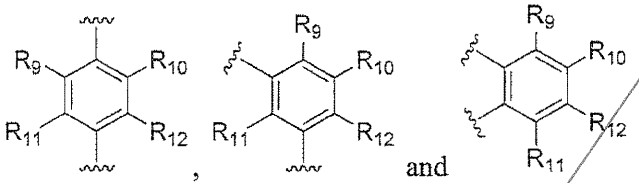
p1, p2 and p3 are each independently 0, or an integer from 1 to 100; and

x is 0, 1 or 2.

32. The compound of claim 31, wherein:

A is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine;

X is an aryl selected from the group consisting of



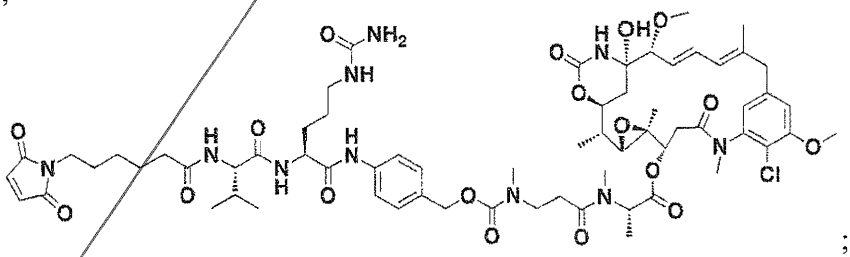
wherein R_9, R_{10}, R_{11}, and R_{12} are each independently H, an alkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, -O-C(=O)-R_{15}, -C(=O)-R_{15}, -C(=O)-O-R_{15}, or -C(=O)-$NR_{13}R_{14}$,

further wherein, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl; and

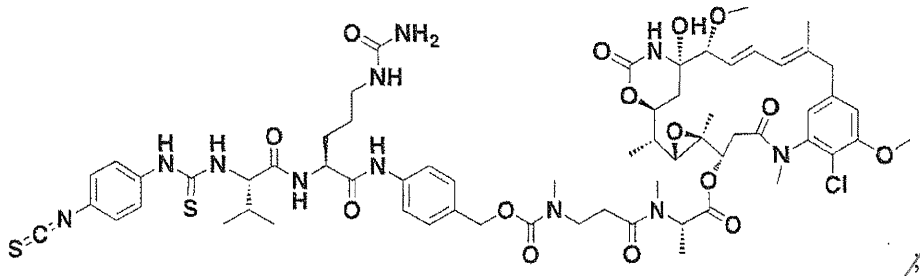
33. The compound of claim 31, having a structure selected from one member of the group consisting of

;

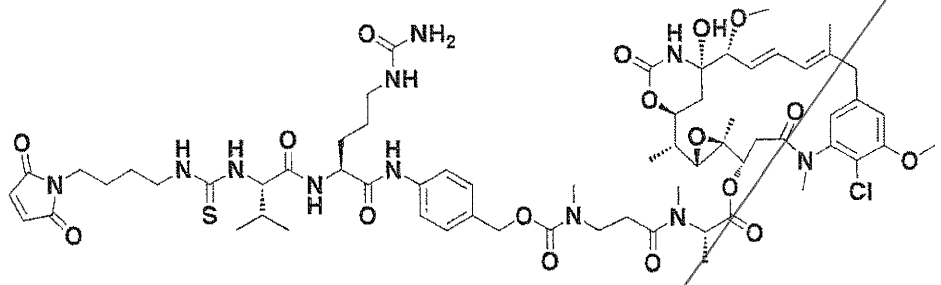


;

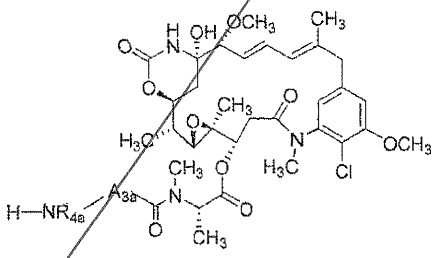
;



; and



34. A compound of the following formula :



wherein:

A_{3a} is each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}-$,$-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$,$-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or $-O-C(=O)-NR_4-$, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted; and

p1, p2 and p3 are each independently 0, or an integer from 1 to 100;

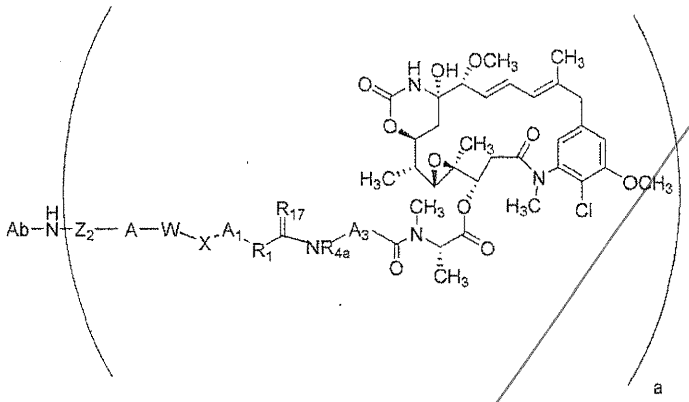
x is 0, 1 or 2;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl; and

R_{4a} is methyl.

35. The compound of claim 34 wherein the compound is about 10 fold less cytotoxic than the corresponding compound of claim 1.

36. A compound of formula (X):



wherein:

Ab is an antibody or a fragment thereof;

a is an integer from 1 to 10;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is, -O-, -S-, $-CR_5R_6-$,or $-NR_4-$;

X is aryl, heteroaryl, cycloalkyl, or heterocyclyl, wherein aryl, heteroaryl, cycloalkyl, and heterocyclyl are optionally substituted;

wherein A_1, A_3, and R_1 are each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}-$, $-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or -O-C(=O)-NR_4-,

wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, or CR_5R_6;

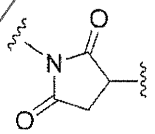
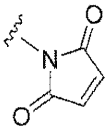
R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

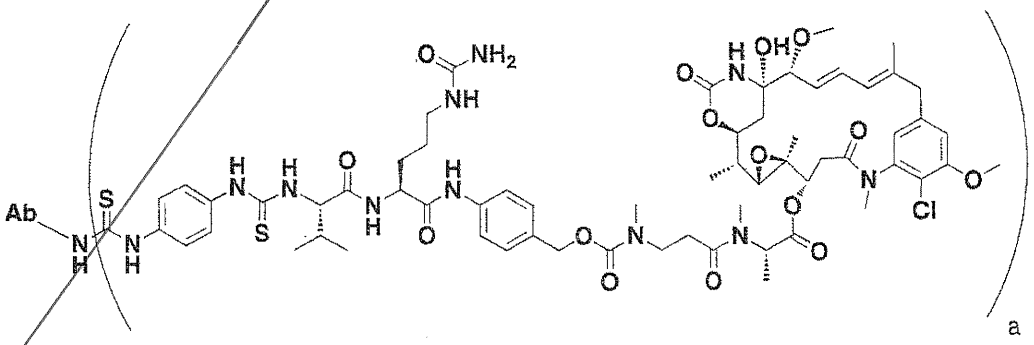
R_{4a} is methyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100;

x is 0, 1 or 2; and

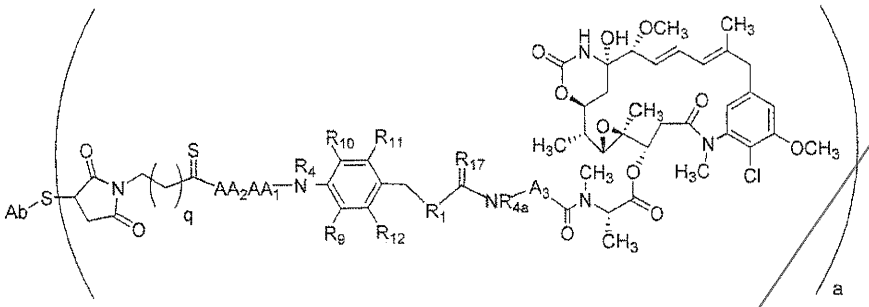
Z_2 is represented by the following structural formula: $-Z_{2A}-Z_{2B}-Z_{2C}-Z_{2D}$, wherein Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}$, $-C(=O)-O-(CH_x)_{p1}$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, $-O-C(=O)-N(R_4)$, $-O-C(=S)-N(R_4)-$, $-C(=S)-N(R_4)-$, -N=C=S, -N=C=O,  or .

37. The compound of claim 36 represented by the following structure:



wherein a is an integer from 1 to 10.

38. The compound of claim 9 having the following formula :



wherein:

Ab is an antibody or a fragment thereof;

AA_1-AA_2 is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine;

a is an integer from 1 to 10;

q is 0 or an integer from 1 to 5;

A_3, and R_1 are each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclylheterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$-, -C(=O)-O-$(CH_x)_{p1}$-, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-)$_{p3}$-, -($(CH_2)_{p2}$-O-)$_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-N(R_4)-C(=O)-, or -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, or CR_5R_6;

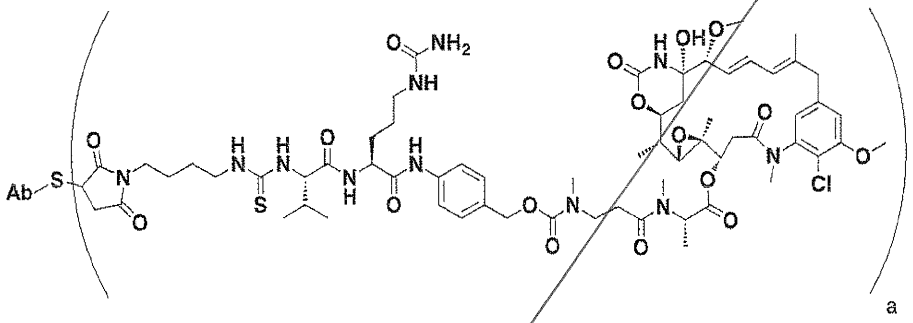
R_4, R_5, R_6, and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, and heterocyclyl;

R_{4a} is methyl;

R_9, R_{10}, R_{11}, and R_{12} are each independently H, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, -O-C(=O)-R_{15}, -C(=O)-R_{15}, -C(=O)-O-R_{15}, -C(=O)-NR_{13} R_{14}, or substituted or unsubstituted: alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl;

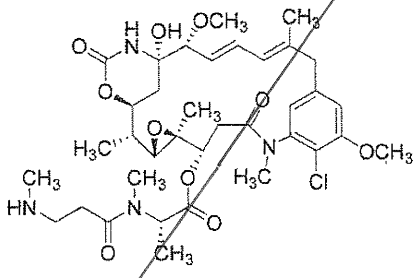
R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl.

39. The compound of claim 38 represented by the following structure:

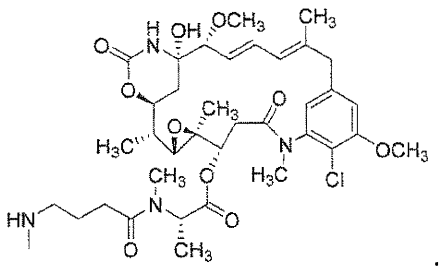


wherein a is an integer from 1 to 10.

40. The compound of claim 34, having a structure selected from one member of the group consisting of

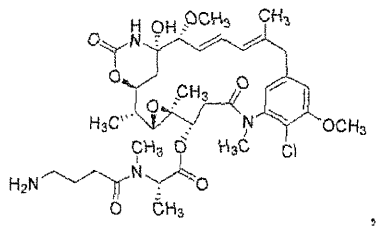


, and

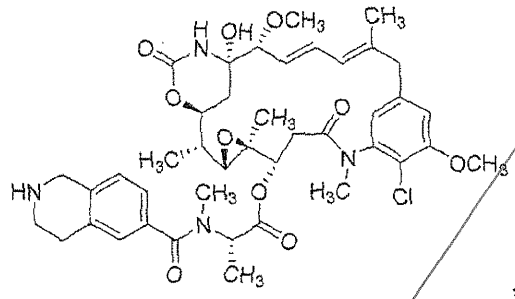


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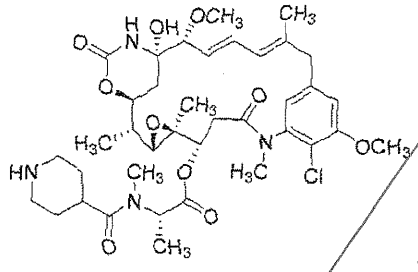
41. A compound having a structure selected from one member of the group consisting of



,

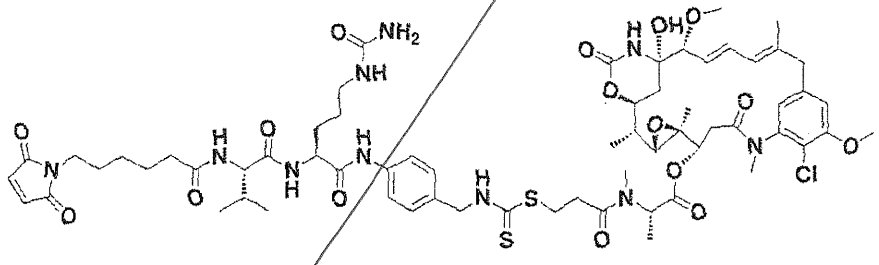


, and



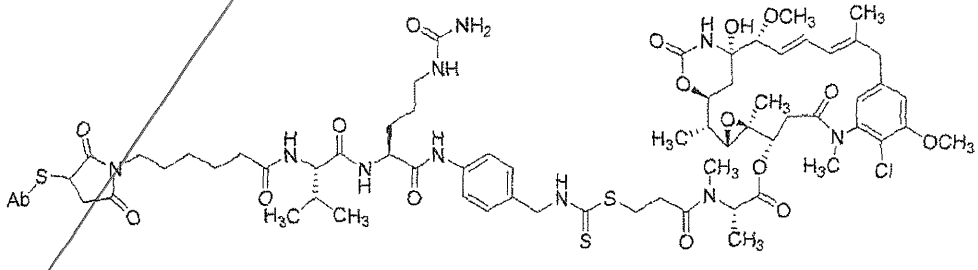
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42. A compound having the following structure:



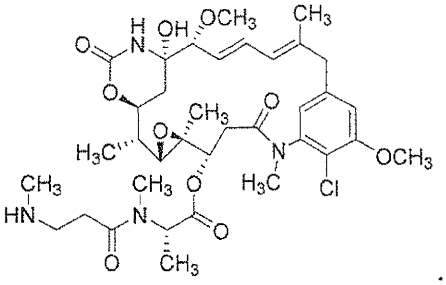
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43. A compound having the following structure:

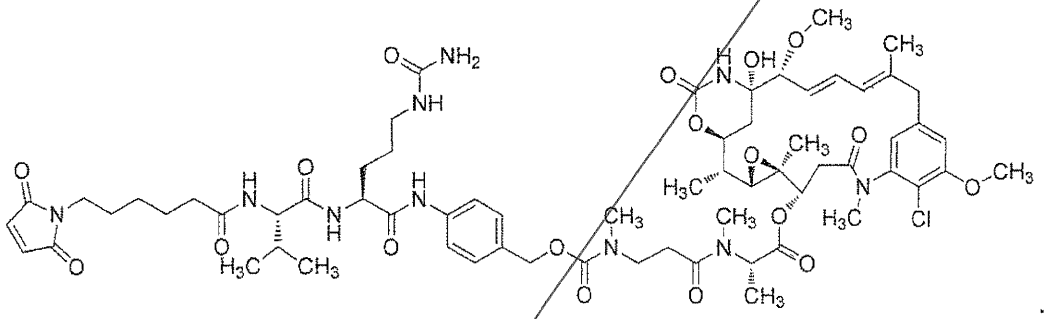


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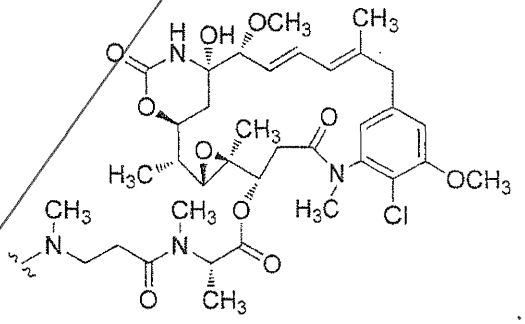
44. A compound having the following structure:

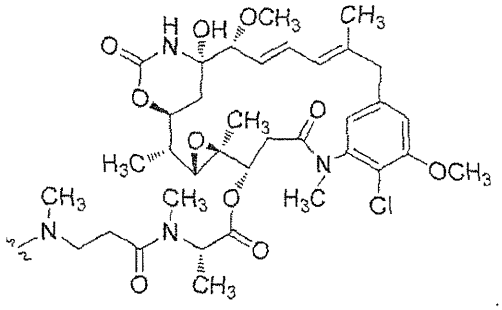


45. A compound having the following structure:



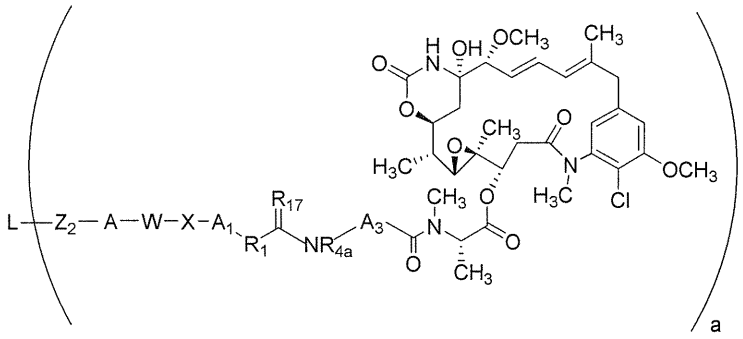
46. An antibody-drug conjugate comprising an antibody or antigen-binding fragment thereof conjugated to a payload of the following formula:





Claims:

1. A compound of the following formula



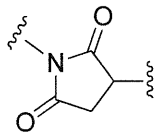
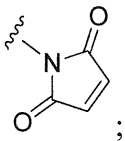
,

wherein:

L is a Ligand, and

L is capable of binding to a cell or cell population;

a is an integer from 1 to 10;

Z_2 is represented by the following structural formula: $-Z_{2A}$-Z_{2B}-Z_{2C}-Z_{2D}, wherein Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$, -C(=O)-O-$(CH_x)_{p1}$, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-)$_{p3}$-, -(($(CH_2)_{p2}$-O-)$_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-N(R_4)-C(=O)-, -O-C(=O)-N(R_4), -O-C(=S)-N(R_4)-, -C(=S)-N(R_4)-, -N=C=S, -N=C=O,  or  ;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is -O-, -S-, -CR_5R_6-, or -NR_4-;

X is aryl, heteroaryl, cycloalkyl, or heterocyclyl, wherein aryl, heteroaryl, cycloalkyl, and heterocyclyl are optionally substituted;

A_1, and R_1 are each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}-$, $-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -S-C(=S)-, -C(=S)-NH-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or $-O-C(=O)-NR_4-$, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

A_3 is methyl, ethyl, 1-propyl, 2-propyl, or 1-butyl;

R_{17} is selected from the group consisting of O, S, NR_{18}, and CR_5R_6 ;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} is methyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100; and

x is 0, 1 or 2.

2. The compound of claim 1, wherein each of X, A_1, A_3, and R_1 is unsubstituted.

3. -The compound of claim 1, wherein L is capable of binding to a specifically targeted cell population.

4. The compound of claim 1, wherein L is selected from the group consisting of proteins, antibodies, fragments of antibodies, nucleic acids, antigen binding scaffolds, and carbohydrates.

5. The compound of claim 4, wherein L is an antibody or a fragment thereof.

6. The compound of claim 5, wherein L is an antibody or fragment thereof that specifically binds a tumor associated antigen.

7. The compound of claim 5, wherein the antibody or a fragment thereof comprises a sulfur group that is covalently attached with Z_2.

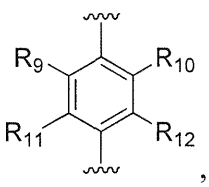
8. The compound of claim 7, wherein the antibody or a fragment thereof comprises a sulfur group that is covalently attached with Z_{2A}.

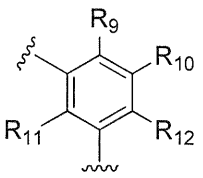
9. The compound of claim 1, wherein each of R_1 and R_{17} is O.

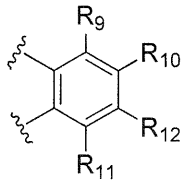
10. The compound of claim 1, wherein A is an amino acid selected from the group consisting of alanine, aspartic acid, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, glutamine, arginine, serine, threonine, valine, tryptophan, tyrosine, cysteine, and citrulline.

11. The compound of claim 1, wherein A is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine.

12. The compound of claim 1, wherein X is an aryl selected from the group consisting of



,


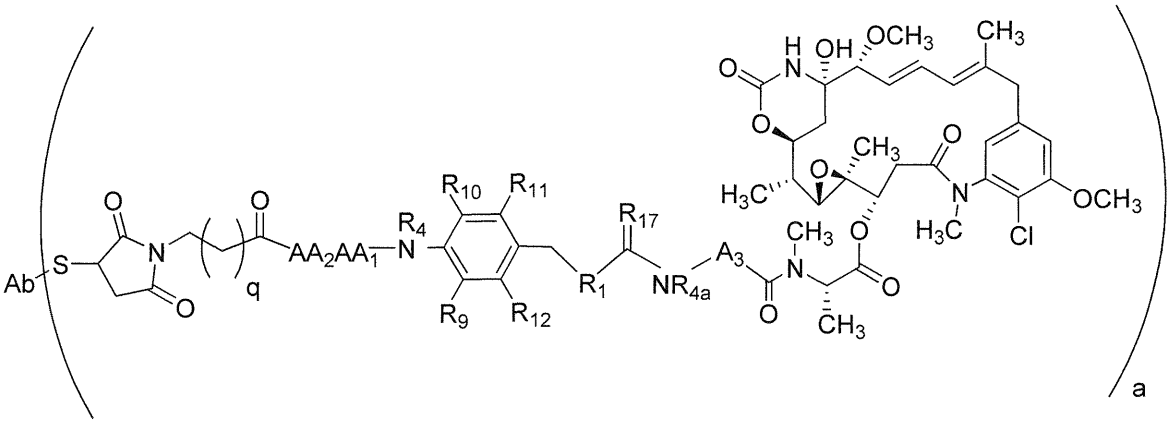
and


wherein R_9, R_{10}, R_{11}, and R_{12} are each independently H, an alkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, -O-C(=O)-R_{15}, -C(=O)-R_{15}, -C(=O)-O-R_{15}, or C(=O)-NR_{13} R_{14}; and

further wherein, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl.

13. The compound of claim 8 having the following formula :



wherein:

Ab is an antibody or a fragment thereof;

AA_1-AA_2 is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine;

a is an integer from 1 to 10;

q is 0 or an integer from 1 to 5;

A_3, and R_1 are each independently, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}-$, $-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or -O- $C(=O)-NR_4-$, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, and CR_5R_6;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} is methyl;

R_9, R_{10}, R_{11}, and R_{12} are each independently H, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, -O-C(=O)-R_{15}, -C(=O)-R_{15}, -C(=O)-O-R_{15}, -C(=O)-NR_{13} R_{14}, or substituted or unsubstituted: alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl;

R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100;

x is 0, 1 or 2.

14. The compound of claim 13, wherein:

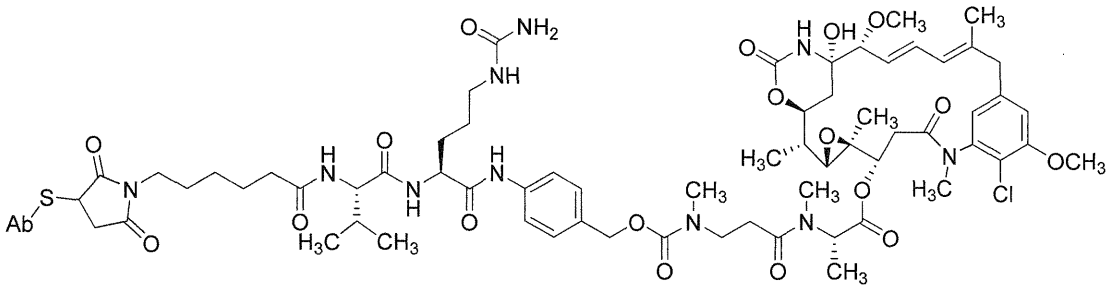
q is 4;

R_1 is –O-, -S-, NR_4, or -CR_5R_6-;

R_4, R_5, R_6, R_9, R_{10}, R_{11}, and R_{12} are each independently H or alkyl; and

A_3 is an alkyl.

15. The compound of claim 13, represented by the following structure:



wherein Ab is an antibody or a fragment thereof.

16. The compound of claim 1, wherein A is a peptide cleavable by a protease.

17. The compound of claim 1, wherein A is a peptide cleavable by a protease expressed in tumor tissue.

18. The compound of claim 17, wherein the protease is a cathepsin or a plasmin.

19. The pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers, diluents, or excipients.

20. An *ex vivo* method of reducing, retarding or stopping an abnormal cell growth comprising contacting the abnormal cell with a compound of claim 1, in an amount sufficient to retard, reduce or stop the abnormal cell growth, and wherein the abnormal cell growth is retarded, reduced or stopped.

21. An *ex vivo* method of killing a cell, comprising contacting the cell with a compound of claim 1, in an amount sufficient to kill the cell, and wherein the cell is killed.

22. The method of claim 21, wherein the cell is a tumor cell.

23. Use of a composition comprising a compound of claim 1 in the manufacture of a medicament for treating a medical disorder in an individual suffering from the medical disorder; wherein the medical disorder is selected from the group consisting of tumors, cancers, infectious diseases, neurodegenerative diseases, bone disorders, and cardiovascular diseases.

24. The use of claim 23, wherein the individual is a mammal.

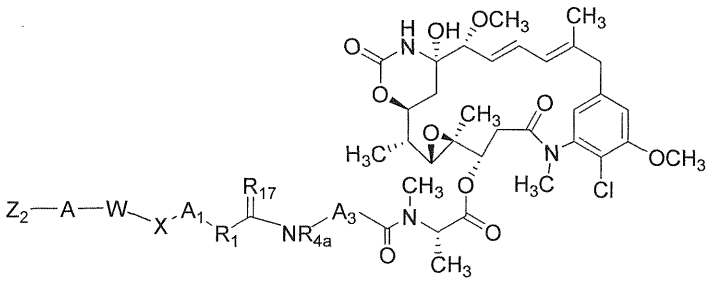
25. The use of claim 23, further comprising administering sequentially or consecutively an additional therapy.

26. The use of claim 25, wherein additional therapy is radiation therapy, chemotherapy, or a combination of both.

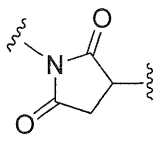
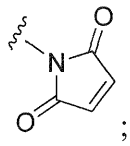
27. The use of claim 23, further comprising administering at least one additional therapeutic agent.

28. Use of a composition comprising a compound of claim 1 in the manufacture of a medicament for reducing tumor size, stopping tumor size increase, reducing tumor proliferation, or preventing tumor proliferation in an individual in need thereof comprising administering to the individual an effective amount of a composition to reduce tumor size, stop tumor size increase, reduce tumor proliferation, or prevent tumor proliferation.

29. A compound of the following formula



wherein:

Z_2 is represented by the following structural formula: $-Z_{2A}$-Z_{2B}-Z_{2C}-Z_{2D}, wherein Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$, -C(=O)-O-$(CH_x)_{p1}$, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-$)_{p3}$-, -($(CH_2)_{p2}$-O-$)_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -$N(R_4)$-C(=O)-$N(R_8)$-, -$N(R_4)$-C(=O)O-, -$N(R_4)$-C(=O)-, -C(=O)-$N(R_4)$-, -C(=O)-$N(R_4)$-C(=O)-, -O-C(=O)-$N(R_4)$, -O-C(=S)-$N(R_4)$-, -C(=S)-$N(R_4)$-, -N=C=S, -N=C=O,  or ;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is -O-, -S-, -CR_5R_6-, or -NR_4-;

X is a substituted or unsubstituted: aryl, heteroaryl, cycloalkyl, or heterocyclyl;

wherein A_1 and R_1 are each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$-, -C(=O)-O-$(CH_x)_{p1}$-, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-)$_{p3}$-, -($(CH_2)_{p2}$-O-)$_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-N(R_4)-C(=O)-, or -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl is optionally substituted;

A_3 is methyl, ethyl, 1-propyl, 2-propyl, or 1-butyl;

R_{17} is selected from the group consisting of O, S, NR_{18}, or CR_5R_6;

R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

R_{4a} is methyl;

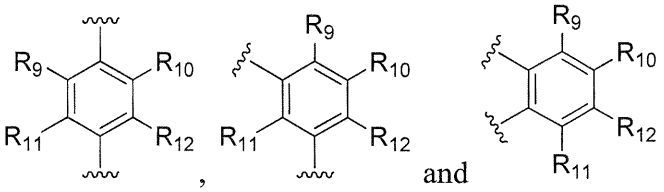
p1, p2 and p3 are each independently 0, or an integer from 1 to 100; and

x is 0, 1 or 2.

30. The compound of claim 29, wherein:

A is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine;

X is an aryl selected from the group consisting of



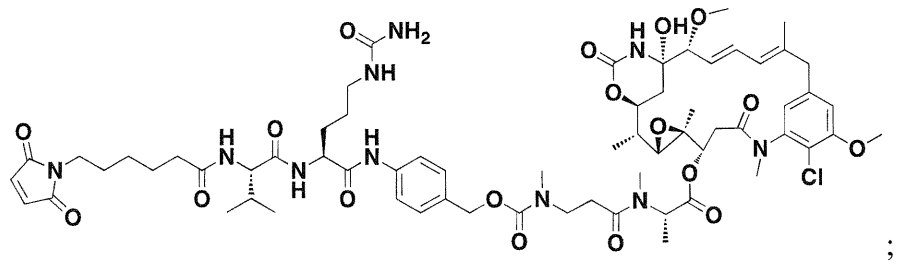
, and

wherein R_9, R_{10}, R_{11}, and R_{12} are each independently H, an alkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, -O-C(=O)-R_{15}, -C(=O)-R_{15}, -C(=O)-O-R_{15}, or -C(=O)-$NR_{13}R_{14}$,

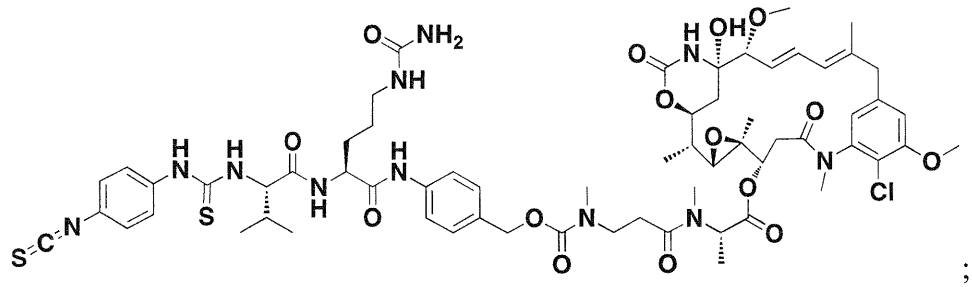
further wherein, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl; and

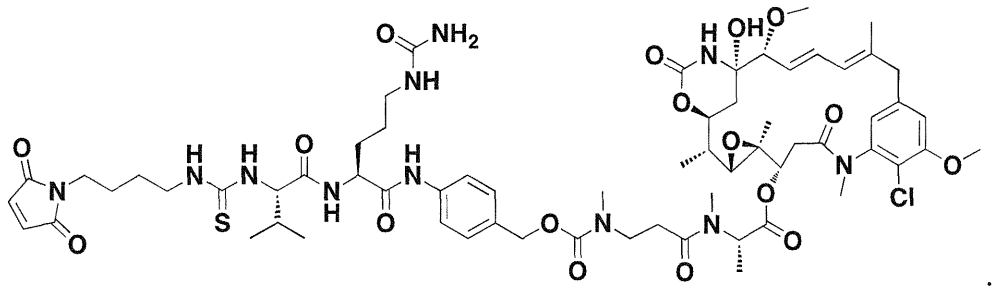
31. The compound of claim 29, having a structure selected from one member of the group consisting of:



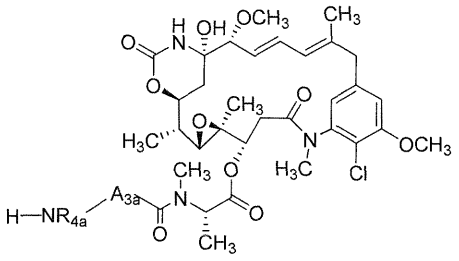
;



; and



32. A compound of the following formula :



wherein:

A_{3a} is methyl, ethyl, 1-propyl, 2-propyl, or 1-butyl, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-,

$-C(=O)-(CH_x)_{p1}-$,$-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$,$-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or $-O-C(=O)-NR_4-$, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted; and

p1, p2 and p3 are each independently 0, or an integer from 1 to 100;

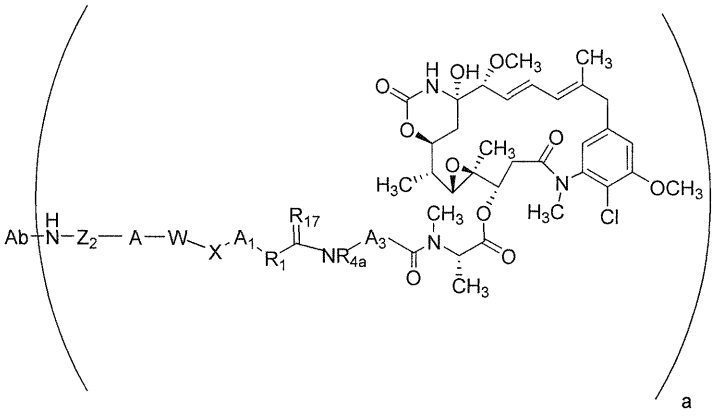
x is 0, 1 or 2;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl; and

R_{4a} is methyl.

33. The compound of claim 32 wherein the compound is about 10 fold less cytotoxic than the corresponding compound of claim 1.

34. A compound of formula (X):



wherein:

Ab is an antibody or a fragment thereof;

a is an integer from 1 to 10;

A is a natural or non-natural amino acid, or a peptide comprising 2-20 amino acids;

W is, -O-, -S-, $-CR_5R_6-$,or $-NR_4-$;

X is aryl, heteroaryl, cycloalkyl, or heterocyclyl, wherein aryl, heteroaryl, cycloalkyl, and heterocyclyl are optionally substituted;

A_1, and R_1 are each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, $--CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, $-C(=O)-(CH_x)_{p1}-$, $-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$, $-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or -O-C(=O)-NR_4-, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

A_{3a} is methyl, ethyl, 1-propyl, 2-propyl, or 1-butyl;

R_{17} is selected from the group consisting of O, S, NR_{18}, or CR_5R_6;

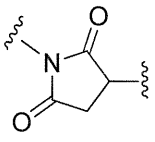
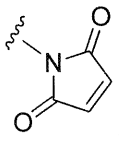
R_{18} is selected from the group consisting of H, alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, and acyl are optionally substituted;

R_4, R_5, R_6 and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, or heterocyclyl;

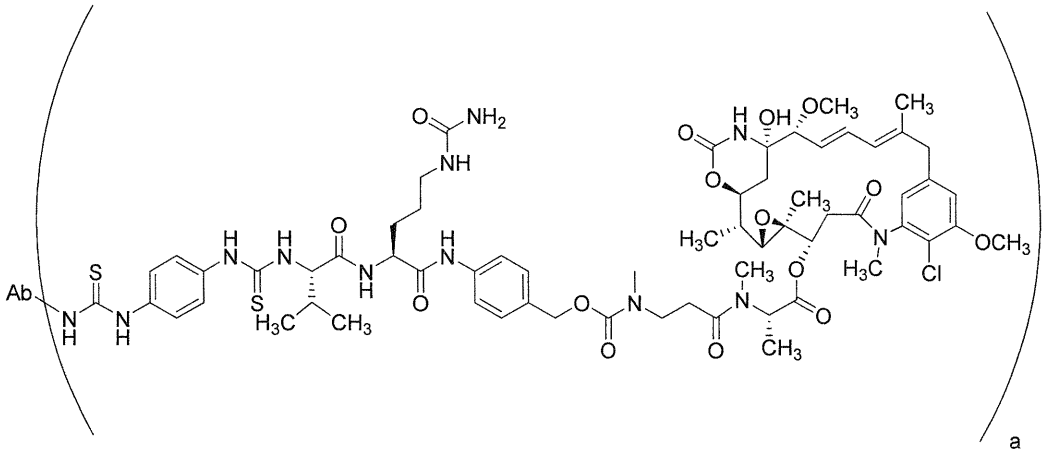
R_{4a} is methyl;

p1, p2 and p3 are each independently 0, or an integer from 1 to 100;

x is 0, 1 or 2; and

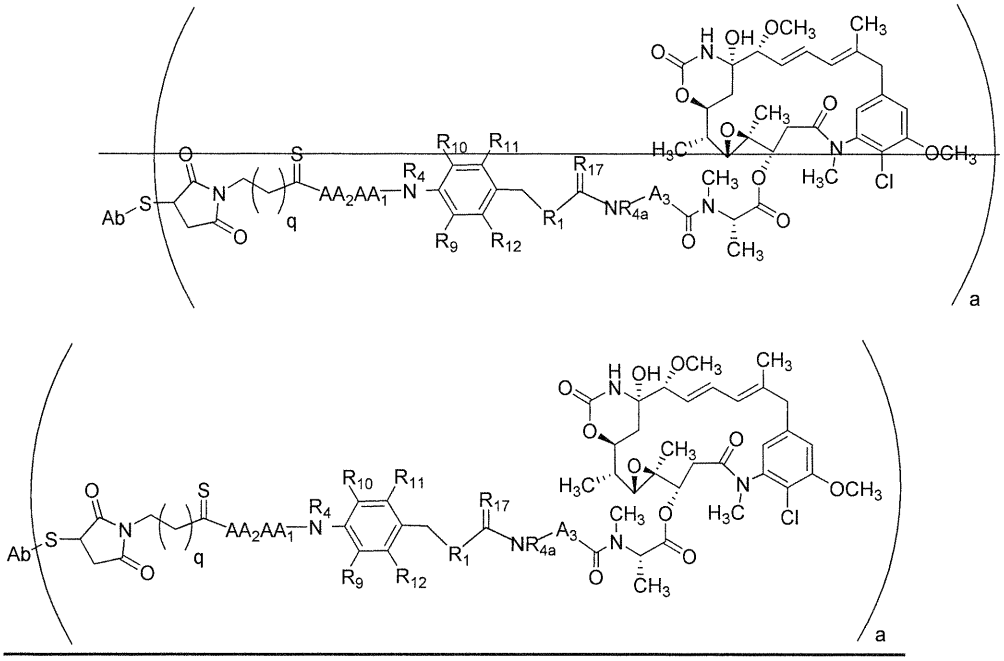
Z_2 is represented by the following structural formula: $-Z_{2A}$-Z_{2B}-Z_{2C}-Z_{2D}, wherein Z_{2A}, Z_{2B}, Z_{2C} and Z_{2D} are each independently absent, an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl, -CR_5R_6-, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-, -C(=O)-$(CH_x)_{p1}$, -C(=O)-O-$(CH_x)_{p1}$, -$(CH_x)_{p1}$-C(=O)-, -$(CH_x)_{p1}$-C(=O)-O-, -(O-$(CH_2)_{p2}$-)$_{p3}$-, -(($(CH_2)_{p2}$-O-)$_{p3}$-, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, -SO_2-, -NR_4-, -N(R_4)-C(=O)-N(R_8)-, -N(R_4)-C(=O)O-, -N(R_4)-C(=O)-, -C(=O)-N(R_4)-, -C(=O)-N(R_4)-C(=O)-, -O-C(=O)-N(R_4), -O-C(=S)-N(R_4)-, -C(=S)-N(R_4)-, -N=C=S, -N=C=O,  or .

35. The compound of claim 34 represented by the following structure:



wherein a is an integer from 1 to 10.

36. The compound of claim 8 having the following formula :



wherein:

Ab is an antibody or a fragment thereof;

AA_1-AA_2 is a peptide selected from the group consisting of valine-citrulline, citrulline-valine, lysine-phenylalanine, phenylalanine-lysine, valine-asparagine, asparagine-valine, threonine-asparagine, serine-asparagine, asparagine-serine, phenylalanine-asparagine, asparagine-phenylalanine, leucine-asparagine, asparagine-leucine, isoleucine-asparagine, asparagine-isoleucine, glycine-asparagine, asparagine-glycine, glutamic acid- asparagine, asparagine-glutamic acid, citrulline-asparagine, asparagine-citrulline, alanine-asparagine, and asparagine-alanine;

a is an integer from 1 to 10;

q is 0 or an integer from 1 to 5;

A_3, and R_1 are each independently an amino acid, a peptide having 2-20 amino acids, an alkyl, an alkynyl, an alkenyl, a cycloalkyl, an aryl, a heteroaryl, a heterocyclyl_, $-CR_5R_6-$, -O-, -C(=O)-, -O-C(=O)-, -C(=O)-O-, -O-C(=O)-O-,

$-C(=O)-(CH_x)_{p1}-$, $-C(=O)-O-(CH_x)_{p1}-$, $-(CH_x)_{p1}-C(=O)-$, $-(CH_x)_{p1}-C(=O)-O-$, $-(O-(CH_2)_{p2}-)_{p3}-$, $-((CH_2)_{p2}-O-)_{p3}-$, -C(=S)-, -C(=S)-S-, -C(=S)-NH-, -S-C(=S)-, -S-C(=S)-S-, -S-, -SO-, $-SO_2-$,

$-NR_4-$, $-N(R_4)-C(=O)-N(R_8)-$, $-N(R_4)-C(=O)O-$, $-N(R_4)-C(=O)-$, $-C(=O)-N(R_4)-$, $-C(=O)-N(R_4)-C(=O)-$, or $-O-C(=O)-NR_4-$, wherein alkyl, alkynyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally substituted;

R_{17} is selected from the group consisting of O, S, NR_{18}, or CR_5R_6;

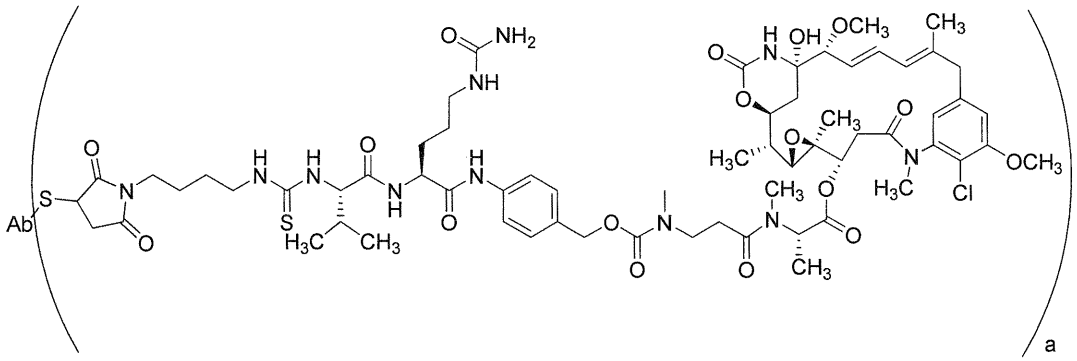
R_4, R_5, R_6, and R_8 are each independently H, or a substituted or unsubstituted: alkyl, alkenyl, alkynyl, aryl, heteroaryl, and heterocyclyl;

R_{4a} is methyl;

R_9, R_{10}, R_{11}, and R_{12} are each independently H, halogen, $NR_{13}R_{14}$, nitro, cyano, -OH, $-O-C(=O)-R_{15}$, $-C(=O)-R_{15}$, $-C(=O)-O-R_{15}$, $-C(=O)-NR_{13}\ R_{14}$, or substituted or unsubstituted: alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl;

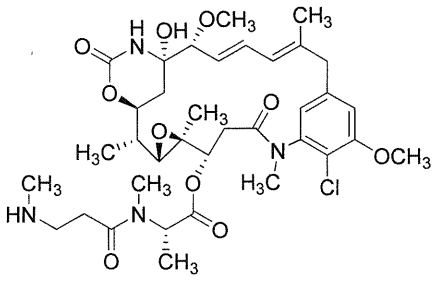
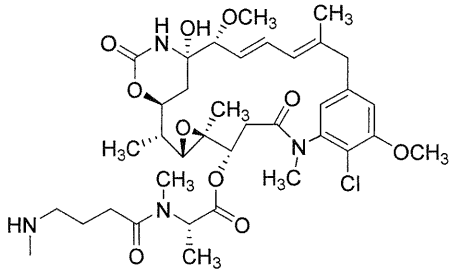
R_{13} and R_{14} are each independently H or an optionally substituted alkyl; and R_{15} is an optionally substituted alkyl.

37. The compound of claim 36 represented by the following structure:

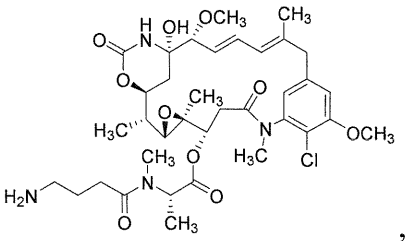
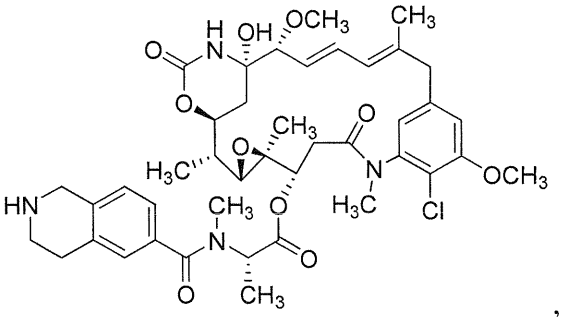
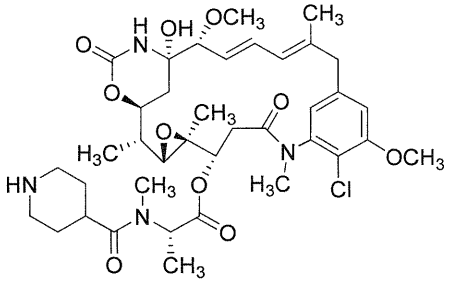


wherein a is an integer from 1 to 10.

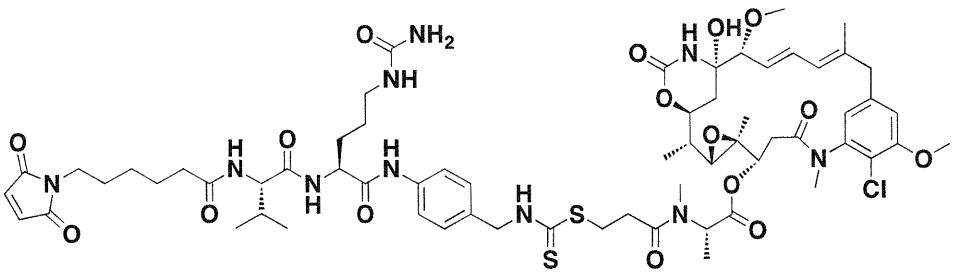
38. The compound of claim 32, having a structure selected from one member of the group consisting of


, and

.

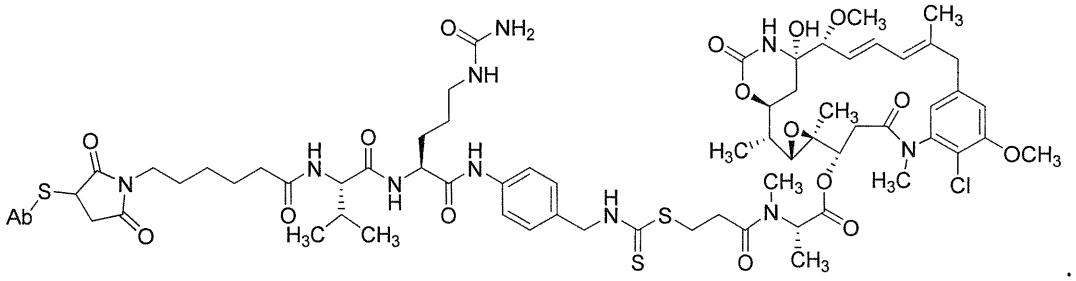
39. A compound having a structure selected from one member of the group consisting of


,

, and

.

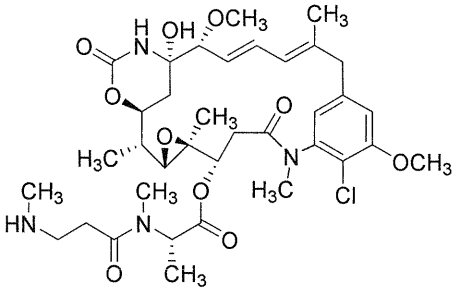
40. A compound having the following structure:


.

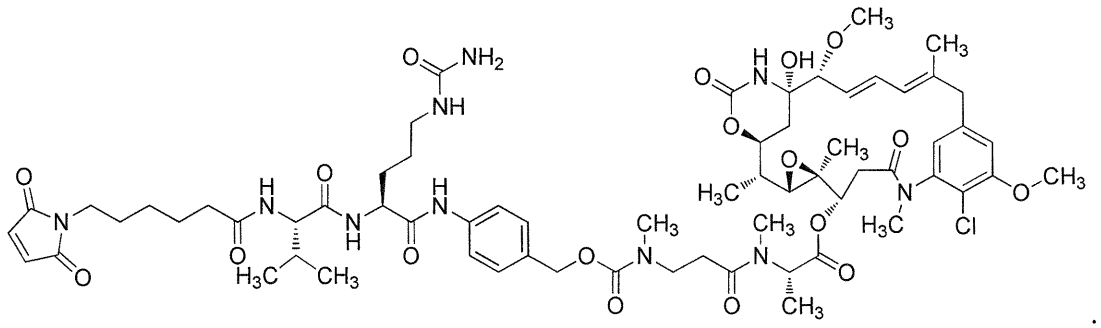
41. A compound having the following structure:



42. A compound having the following structure:



43. A compound having the following structure:



44. An antibody-drug conjugate comprising an antibody or antigen-binding fragment thereof conjugated to a payload of the following formula:

