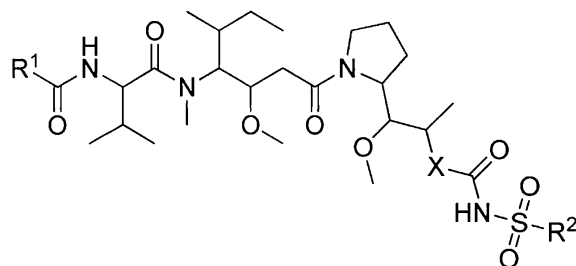


C₁-C₆ haloacyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio- C₁-C₆ alkyl;
and

X is -C(=O)NHCH(CH₂R³)-, or X is absent; and

R³ is selected from: aryl, heteroaryl, and C₃-C₇ cycloalkyl, each optionally substituted with one substituent selected from amino and hydroxyl.

In one embodiment, the invention provides a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof,

wherein:

R¹ is selected from: amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, amino-heterocyclyl, and heterocyclyl, each optionally substituted with one or more substituents selected from aryl, aryl-C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkylthio, carboxyl, carboxamide, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkyl-C₁-C₆ alkyl, guanidino, halo, C₁-C₆ haloalkyl, heterocyclyl, heterocyclyl-C₁-C₆ alkyl, hydroxyl, and thio; or

R¹ is R^aR^bNCH(R^c)-;

R^a is selected from: H and C₁-C₆ alkyl;

R^b is C₁-C₆ alkyl; and

R^c is R^d-C(CH₃)₂-; and

R^d is selected from: H, aryl, C₃-C₇ cycloalkyl, and heteroaryl, each of which is optionally substituted with one or more substituents selected from: C₁-C₄ acylthio, C₂-C₄ alkenyl, C₁-C₄ alkyl, C₁-C₄ alkylamino, C₁-C₄ alkyloxy, amino, amino-C₁-C₄ alkyl, halo, C₁-C₄ haloalkyl, hydroxyl, hydroxy-C₁-C₄ alkyl, and thio, wherein C₂-C₄ alkenyl, C₁-C₄ alkylamino and C₁-C₄ alkyloxy are further optionally substituted with one substituent selected from C₁-C₄ alkylaryl, hydroxyl, and thio; or

R^b and R^c taken together with the atoms to which they are each bonded form a heterocyclydiyl;

R² is selected from: C₂-C₆ alkyl, aryl, aryl-C₁-C₆ alkyl, C₄-C₇ cycloalkyl, C₃-C₇ cycloalkyl-C₁-C₆ alkyl, heteroaryl, heteroaryl-C₁-C₆ alkyl, and heterocyclyl, each optionally substituted with one or more substituents selected from: C₁-C₆ alkoxy, C₁-C₆ alkoxy carbonyl,

C₁-C₆ alkyl, C₁-C₆ alkylamino, amino, amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, aryl, carboxamide, carboxyl, cyano, C₁-C₆ haloacyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio-C₁-C₆ alkyl;

X is -C(O)NHCH(CH₂R³)-, or X is absent; and

R³ is selected from: aryl, heteroaryl, and C₃-C₇ cycloalkyl, each optionally substituted with one substituent selected from amino and hydroxyl;

provided that when R¹ is 2-methyl-1-(methylamino)propyl, and X is -C(O)NHCH(CH₂Ph)-, R² is other than ethyl, isopropyl, n-butyl or phenyl. In one embodiment, the invention provides a method of making a compound described herein or pharmaceutically acceptable salt thereof.

In another embodiment, a pharmaceutical composition is provided comprising a compound described herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

In another embodiment, a method of using a compound described herein or a pharmaceutically acceptable salt thereof, in therapy is provided. In particular, the present disclosure provides a method of treating cancer in a mammal comprising administering to a mammal in need thereof an effective amount of a compound described herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound described herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier diluent or excipient.

In another embodiment, the present disclosure provides a method of inhibiting tumor growth in a mammal comprising administering to a mammal in need thereof an effective amount of a compound described herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound described herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

In another embodiment, the present disclosure provides a method of killing cancer cells *in vitro* using a compound described herein or a pharmaceutically acceptable salt thereof. In another embodiment, the present disclosure provides a method of killing cancer cells *in vivo* in a mammal, comprising administering to a mammal in need thereof an effective amount of a compound described

herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound described herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

In another embodiment, the present disclosure provides a method of increasing the survival time of a mammal having cancer, comprising administering to such mammal an effective amount of a compound described herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound described herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

In another embodiment, the present disclosure provides a use of a compound described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a mammal.

In another embodiment, the present disclosure provides a use of the compound as described herein or a pharmaceutically acceptable salt thereof, or the composition as described herein, in the manufacture of a medicament for treating cancer in a mammal.

In another embodiment, the present disclosure provides a use of a compound described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for inhibiting tumor growth in a mammal.

In another embodiment, the present disclosure provides a use of a compound described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for increasing survival of a mammal having cancer.

In another embodiment, the present disclosure provides a compound or a pharmaceutical composition described herein, for use in a method of treatment of the human or animal body by therapy.

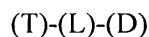
In another embodiment, the present disclosure provides a compound or a pharmaceutical composition described herein, for use in treating cancer in a mammal.

In another embodiment, the present disclosure provides a compound or a pharmaceutical composition described herein, for use in inhibiting tumor growth in a mammal.

In another embodiment, the present disclosure provides a compound or a pharmaceutical composition described herein, for use in increasing survival of a mammal having cancer.

In one embodiment, compositions comprising a biologically active compound as described herein or a pharmaceutically acceptable salt thereof, linked directly or indirectly to a targeting moiety are provided.

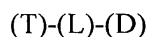
In one embodiment, the invention provides compositions of Formula II:



II

wherein (T) is a targeting moiety, (L) is an optional linker, and (D) is a compound of Formula I, Ia, Ib, Ic, Id, Ie, If, Ig, Ih, Ii, Ij, or Ik, or a pharmaceutically acceptable salt thereof. (D) is covalently attached to (L), if (L) is present, or (T), if (L) is not present.

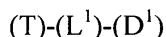
In one embodiment, the invention provides a composition of Formula II:



II

wherein (T) is a targeting moiety, (L) is a linker, and (D) is the compound as described herein.

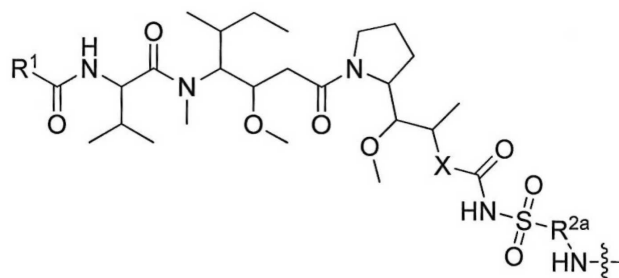
In one embodiment, the invention provides a composition of Formula III:



III

wherein:

(D¹) has structure (IV):



IV

wherein:

R^1 is selected from: amino- C_1 - C_6 alkyl, amino-aryl, amino- C_3 - C_7 cycloalkyl, amino-heterocyclyl, and heterocyclyl, each optionally substituted with one or more substituents selected from aryl, aryl- C_1 - C_6 alkyl, C_1 - C_6 alkyl, C_1 - C_6 alkylthio, carboxyl, carboxamide, C_3 - C_7 cycloalkyl, C_3 - C_7 cycloalkyl- C_1 - C_6 alkyl, guanidino, halo, C_1 - C_6 haloalkyl, heterocyclyl, heterocyclyl- C_1 - C_6 alkyl, hydroxyl, and thio; or

R^1 is $R^a R^b NCH(R^c)-$;

R^a is selected from: H and C_1 - C_6 alkyl;

R^b is C_1 - C_6 alkyl; and

R^c is $R^d-C(CH_3)_2-$; and

R^d is selected from: H, aryl, C_3 - C_7 cycloalkyl, and heteroaryl, each of which is optionally substituted with one or more substituents selected from: C_1 - C_4 acylthio, C_2 - C_4 alkenyl, C_1 - C_4 alkyl, C_1 - C_4 alkylamino, C_1 - C_4 alkyloxy, amino, amino- C_1 - C_4 alkyl, halo, C_1 - C_4 haloalkyl, hydroxyl, hydroxy- C_1 - C_4 alkyl, and thio, wherein C_2 - C_4 alkenyl, C_1 - C_4 alkylamino and C_1 - C_4 alkyloxy are further optionally substituted with one substituent selected from C_1 - C_4 alkylaryl, hydroxyl, and thio; or

R^b and R^c taken together with the atoms to which they are each bonded form a heterocyclyldiyl;

X is $-C(O)NHCH(CH_2R^3)-$, or X is absent;

R^{2a} is selected from: C_2 - C_6 alkylidiyl, arylidiyl, C_4 - C_7 cycloalkylidiyl, heteroarylidiyl, and heterocyclyldiyl, each optionally substituted with one or more substituents selected from: C_1 - C_6 alkoxy, C_1 - C_6 alkoxycarbonyl, C_1 - C_6 alkyl, C_1 - C_6 alkylamino, amino, amino- C_1 - C_6 alkyl, amino-aryl, amino- C_3 - C_7 cycloalkyl, aryl, carboxamide, carboxyl, cyano, C_1 - C_6 haloalkyl, C_1 - C_6 haloalkoxy, halo, hydroxyl, nitro, thio, and thio- C_1 - C_6 alkyl;

R^3 is selected from: aryl, heteroaryl, and C_3 - C_7 cycloalkyl, each optionally substituted with one substituent selected from amino and hydroxyl, and

(L^1) -(T) has structure (V):



V

wherein:

the -NH- group bonded to R^{2a} in Formula IV forms an enzymatically cleavable peptide bond (JPB) with (AA)₁ in Formula V;

each AA is independently an amino acid;

n is an integer from 0 to 25, and

(L²) is optionally the remaining portion of linker (L¹),

and wherein (AA)₁-(AA)_n, taken together comprises an amino acid sequence capable of facilitating enzymatic cleavage of the JPB.

In one embodiment, the targeting moiety is an antibody. Accordingly, in one embodiment, antibody-drug conjugates (ADCs) comprising a compound described herein, or a pharmaceutically acceptable salt or prodrug thereof, are provided.

In one embodiment, the invention provides a method of making a composition of Formula II.

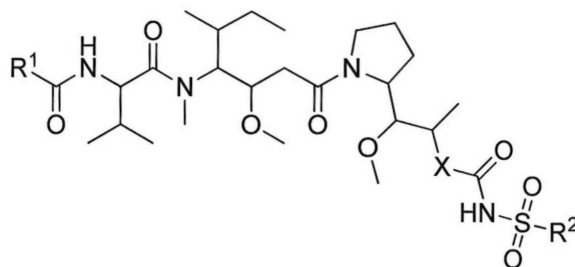
In another embodiment, a pharmaceutical composition is provided comprising a composition of Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

In another embodiment, a method of using a composition of Formula II in therapy is provided. In particular, the present disclosure provides a method of treating cancer in a mammal comprising administering to a mammal in need thereof an effective amount of a composition of Formula II or a pharmaceutical composition comprising a composition of Formula II and a pharmaceutically acceptable carrier diluent or excipient.

CLAIMS

What is claimed is:

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is selected from: amino- C_1 - C_6 alkyl, amino-aryl, amino- C_3 - C_7 cycloalkyl, amino-heterocyclyl, and heterocyclyl, each optionally substituted with one or more substituents selected from aryl, aryl- C_1 - C_6 alkyl, C_1 - C_6 alkyl, C_1 - C_6 alkylthio, carboxyl, carboxamide, C_3 - C_7 cycloalkyl, C_3 - C_7 cycloalkyl- C_1 - C_6 alkyl, guanidino, halo, C_1 - C_6 haloalkyl, heterocyclyl, heterocyclyl- C_1 - C_6 alkyl, hydroxyl, and thio; or

R^1 is $R^a R^b NCH(R^c)-$;

R^a is selected from: H and C_1 - C_6 alkyl;

R^b is C_1 - C_6 alkyl; and

R^c is $R^d-C(CH_3)_2-$; and

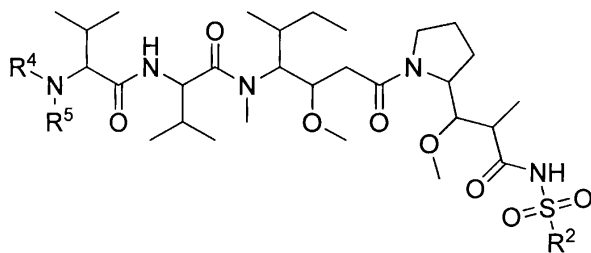
R^d is selected from: H, aryl, C_3 - C_7 cycloalkyl, and heteroaryl, each of which is optionally substituted with one or more substituents selected from: C_1 - C_4 acylthio, C_2 - C_4 alkenyl, C_1 - C_4 alkyl, C_1 - C_4 alkylamino, C_1 - C_4 alkyloxy, amino, amino- C_1 - C_4 alkyl, halo, C_1 - C_4 haloalkyl, hydroxyl, hydroxy- C_1 - C_4 alkyl, and thio, wherein C_2 - C_4 alkenyl, C_1 - C_4 alkylamino and C_1 - C_4 alkyloxy are further optionally substituted with one substituent selected from C_1 - C_4 alkylaryl, hydroxyl, and thio; or

R^b and R^c taken together with the atoms to which they are each bonded form a heterocyclyldiyl;

R^2 is selected from: C_2 - C_6 alkyl, aryl, aryl- C_1 - C_6 alkyl, C_4 - C_7 cycloalkyl, C_3 - C_7 cycloalkyl- C_1 - C_6 alkyl, heteroaryl, heteroaryl- C_1 - C_6 alkyl, and heterocyclyl, each optionally substituted with one or more substituents selected from: C_1 - C_6 alkoxy, C_1 - C_6 alkoxycarbonyl,

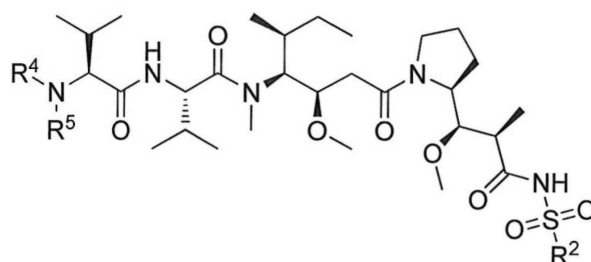
provided that when R¹ is 2-methyl-1-(methylamino)propyl, and X is -C(O)NHCH(CH₂Ph)-, R² is other than ethyl, isopropyl, n-butyl or phenyl.

2. The compound of claim 1, wherein R¹ is selected from: amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, amino-heterocyclyl, and heterocyclyl, each optionally substituted with one or more substituents selected from C₁-C₆ alkyl and halo.
3. The compound of claim 1, wherein R¹ is R^aR^bNCH(R^c)—.
4. The compound of claim 1, wherein R¹ is selected from: 1-(dimethylamino)-2-methylpropyl, 2-methyl-1-(methylamino)propyl, 1-aminocyclopentyl, 1-aminocyclopropyl, 4-aminophenyl, 2-aminopropan-2-yl, 1-aminocyclohexyl, 3-aminooxetan-3-yl, 2-(methylamino)propan-2-yl, 1-amino-2-methylpropan-2-yl, 2-methylpyrrolidin-2-yl, 2-amino-3-methylbutan-2-yl, 2-aminobutan-2-yl, 2-methyl-1-(methylamino)propan-2-yl, 1-methylpiperidin-2-yl, 3-fluoropyrrolidin-3-yl, 1,2-dimethylpyrrolidin-2-yl, and 2-(dimethylamino)propan-2-yl).
5. The compound of any one of claims 1 to 4, wherein X is —C(O)NHCH(CH₂R³)—.
6. The compound of any one of claims 1 to 4, wherein X is absent.
7. The compound of claim 1 having Formula Ia:



Ia

or Formula Id:



Id

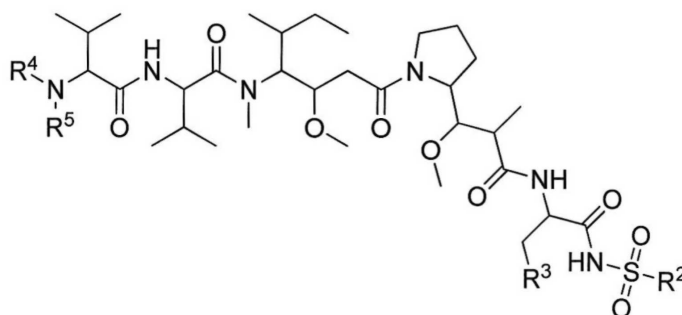
or a pharmaceutically acceptable salt thereof,

wherein:

R² is selected from: C₂-C₆ alkyl, aryl, aryl-C₁-C₆ alkyl, C₄-C₇ cycloalkyl, C₃-C₇ cycloalkyl-C₁-C₆ alkyl, heteroaryl, heteroaryl-C₁-C₆ alkyl, and heterocyclyl, each optionally substituted with one or more substituents selected from: C₁-C₆ alkoxy, C₁-C₆ alkoxycarbonyl, C₁-C₆ alkyl, C₁-C₆ alkylamino, amino, amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, aryl, carboxamide, carboxyl, cyano, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio-C₁-C₆ alkyl; and

R⁴ and R⁵ are each independently selected from: H and C₁-C₆ alkyl.

8. The compound of claim 1 having Formula Ib:



Ib

or Formula Ie:



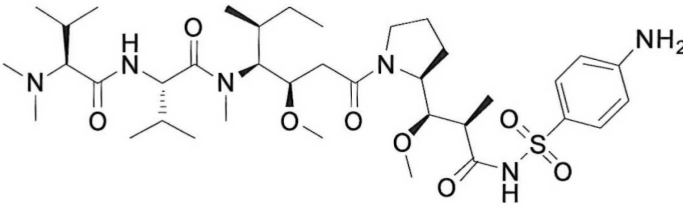
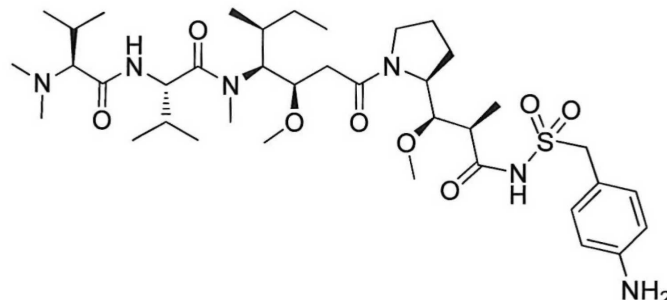
R² is selected from: C₂-C₆ alkyl, aryl, aryl-C₁-C₆ alkyl, C₄-C₇ cycloalkyl, C₃-C₇ cycloalkyl-C₁-C₆ alkyl, heteroaryl, heteroaryl-C₁-C₆ alkyl, and heterocyclyl, each optionally substituted with one or more substituents selected from: C₁-C₆ alkoxy, C₁-C₆ alkoxycarbonyl, C₁-C₆ alkyl, C₁-C₆ alkylamino, amino, amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, aryl, carboxamide, carboxyl, cyano, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio-C₁-C₆ alkyl;

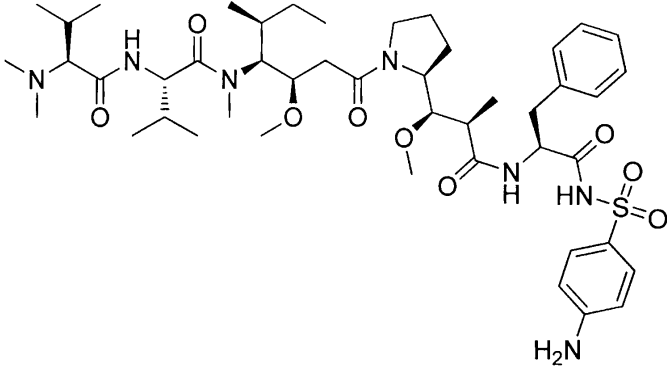
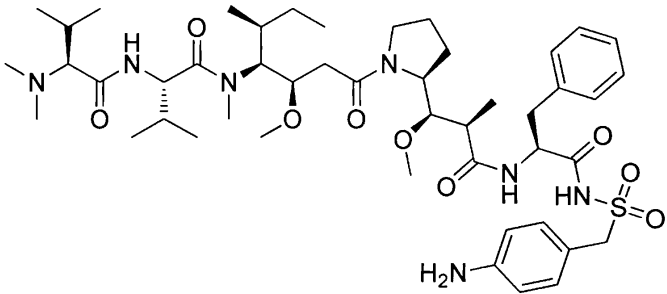
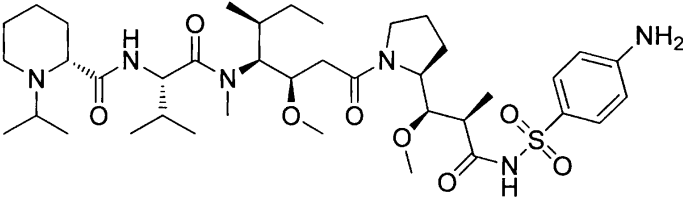
R⁴ and R⁵ are each independently selected from: H and C₁-C₆ alkyl.

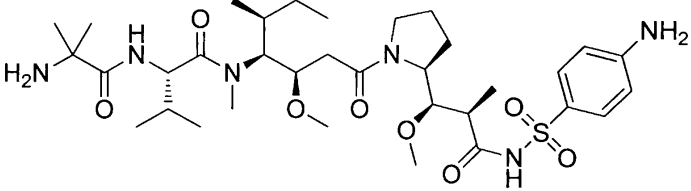
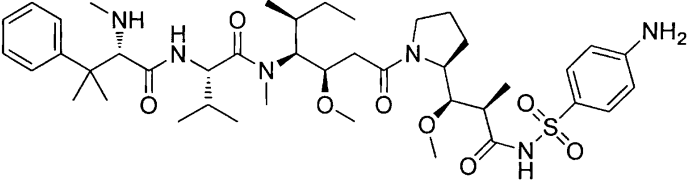
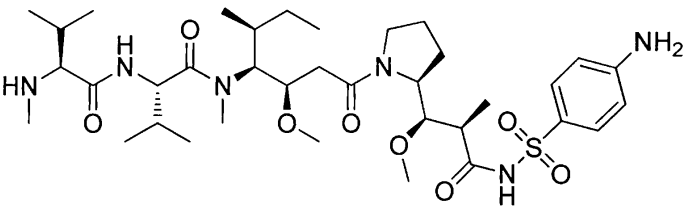
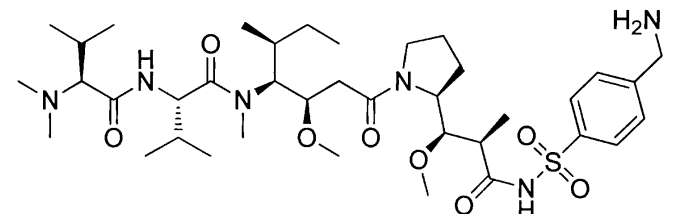
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amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, aryl, carboxamide, carboxyl, cyano, C₁-C₆ haloacyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio-C₁-C₆ alkyl.

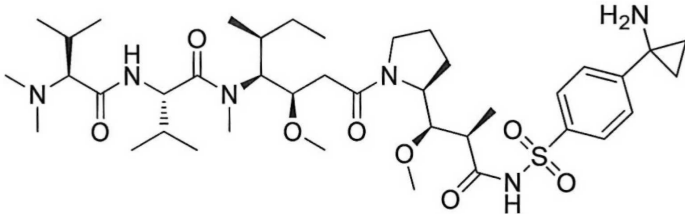
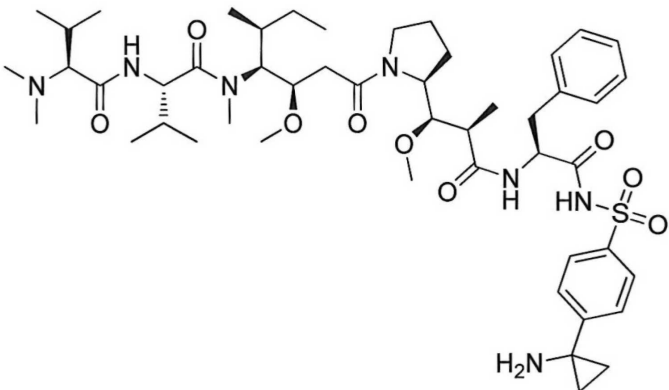
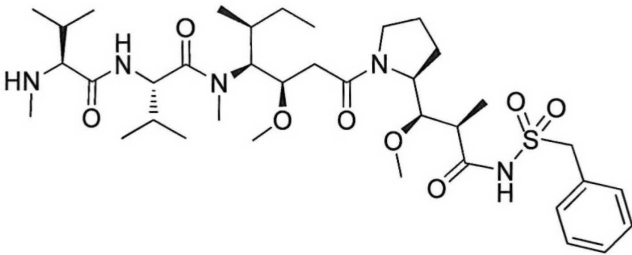
15. The compound of any one of claims 1 to 13, wherein R² is selected from: aryl and aryl-C₁-C₆ alkyl, each optionally substituted with one or more substituents selected from: amino, amino-C₁-C₆ alkyl and amino-C₃-C₇ cycloalkyl.
16. The compound of any one of claims 1 to 13, wherein R² is selected from: 4-aminobenzyl, 4-(aminomethyl)benzyl, 4-(aminomethyl)phenyl, 4-aminophenyl, and benzyl.
17. The compound of claim 1 selected from the following, or a pharmaceutically acceptable salt thereof:

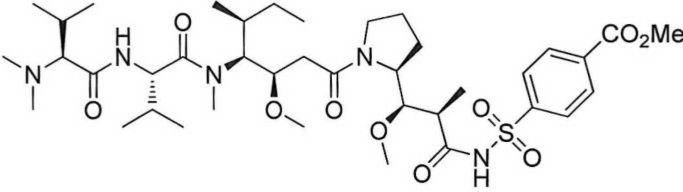
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-(4-aminophenylsulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 5)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((4-aminophenyl)methylsulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 8)</p>

	<p>(<i>S</i>)-<i>N</i>-(((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((<i>S</i>)-1-(4-aminophenylsulfonamido)-1-oxo-3-phenylpropan-2-ylamino)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 11)</p>
	<p>(<i>S</i>)-<i>N</i>-(((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((<i>S</i>)-1-(4-aminophenylmethylsulfonamido)-1-oxo-3-phenylpropan-2-ylamino)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 14)</p>
	<p>(<i>R</i>)-<i>N</i>-((<i>S</i>)-1-(((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((4-aminophenyl)sulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)(methylamino)-3-methyl-1-oxobutan-2-yl)-1-isopropylpiperidine-2-carboxamide</p> <p>(Compound 16)</p>

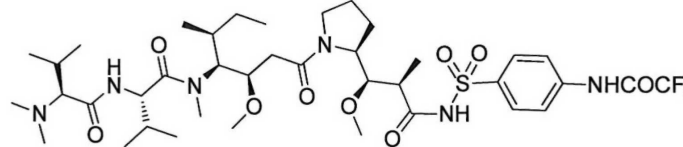
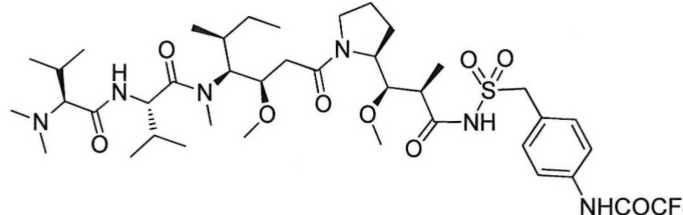
	<p>(<i>S</i>)-2-(2-amino-2-methylpropanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((4-aminophenyl)sulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 17)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((4-aminophenyl)sulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethyl-2-((<i>S</i>)-3-methyl-2-(methylamino)-3-phenylbutanamido)butanamide</p> <p>(Compound 19)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((4-aminophenyl)sulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethyl-2-((<i>S</i>)-3-methyl-2-(methylamino)butanamido)butanamide</p> <p>(Compound 20)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((4-(aminomethyl)phenyl)sulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 22)</p>

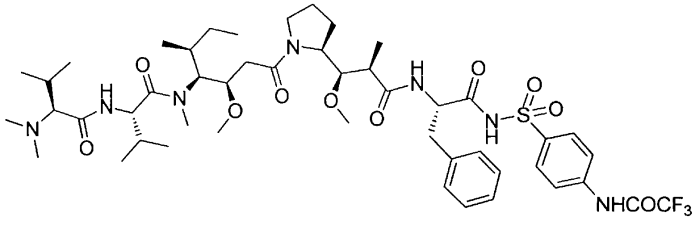
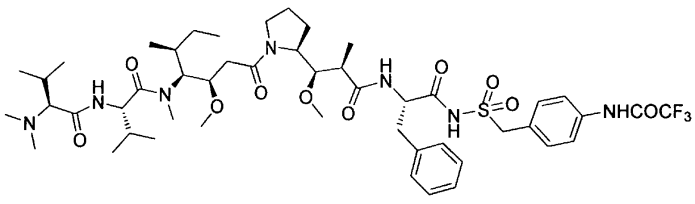
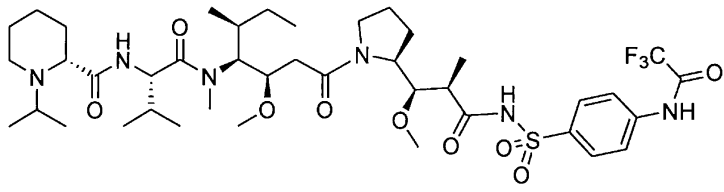
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-(((<i>S</i>)-1-((4-(aminomethyl)phenyl)sulfonamido)-1-oxo-3-phenylpropan-2-yl)amino)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 24)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-(((4-(aminomethyl)phenyl)methyl)sulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 26)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-(((<i>S</i>)-1-(((4-(aminomethyl)phenyl)methyl)sulfonamido)-1-oxo-3-phenylpropan-2-yl)amino)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 28)</p>

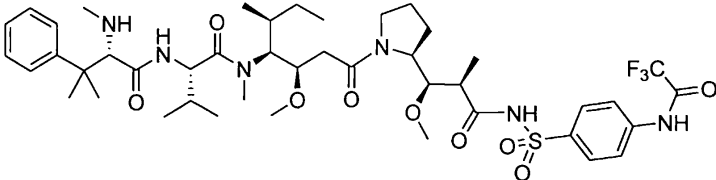
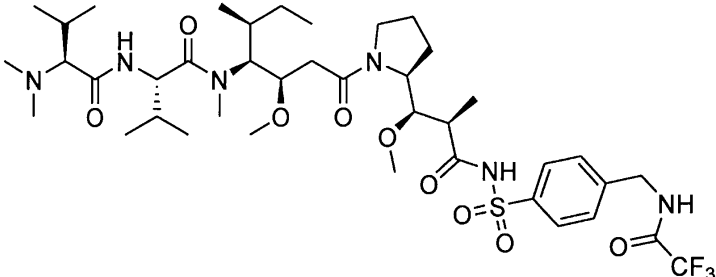
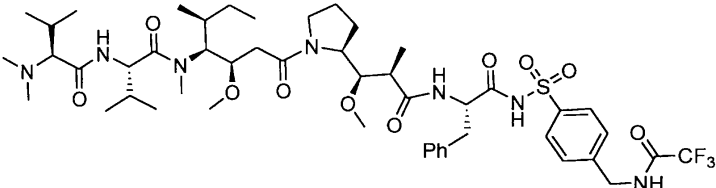
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-(4-(1-aminocyclopropyl)phenylsulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 30)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((<i>S</i>)-1-(4-(1-aminocyclopropyl)phenylsulfonamido)-1-oxo-3-phenylpropan-2-ylamino)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamide</p> <p>(Compound 32)</p>
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((phenylmethyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethyl-2-((<i>S</i>)-3-methyl-2-(methylamino)butanamido)butanamide</p> <p>(Compound 33)</p>

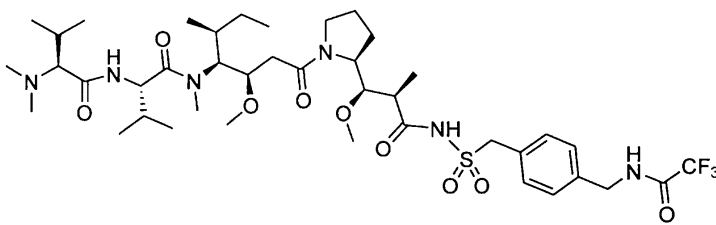
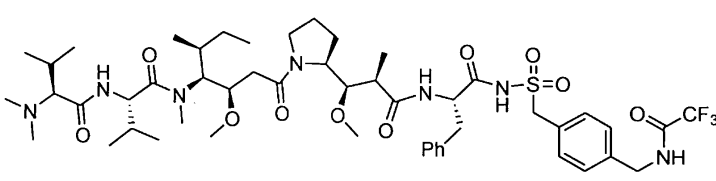
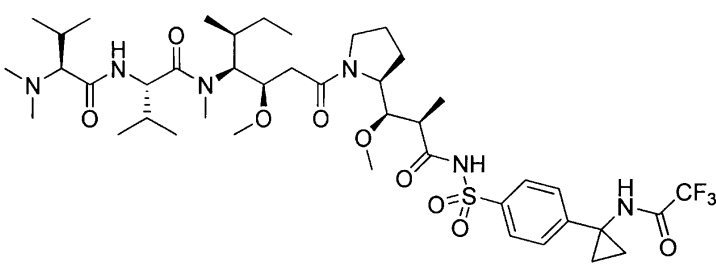
	<p>methyl 4-<i>N</i>-((2<i>R</i>,3<i>R</i>)-3-((<i>S</i>)-1-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-4-((<i>S</i>)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<i>N</i>,3-dimethylbutanamido)-3-methoxy-5-methylheptanoyl)pyrrolidin-2-yl)-3-methoxy-2-methylpropanoyl)sulfamoyl)benzoate (Compound 34).</p>
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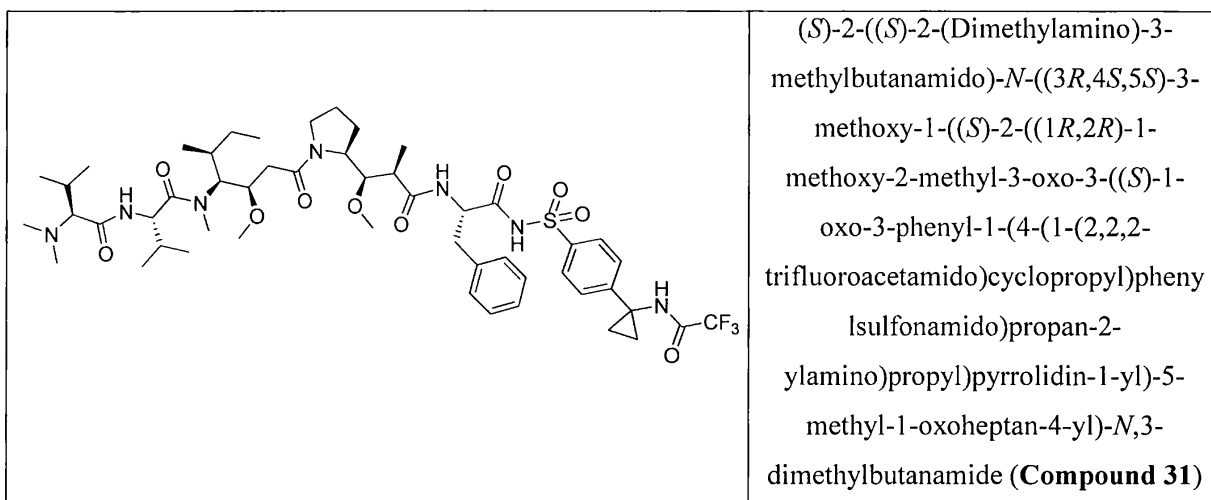
18. The compound of claim 1 selected from the following, or a pharmaceutically acceptable salt thereof:

	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-(4-(2,2,2-trifluoroacetamido)phenyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 4)</p>
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((4-(2,2,2-trifluoroacetamido)phenyl)methyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 7)</p>

	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((<i>S</i>)-1-oxo-3-phenyl-1-(4-(2,2,2-trifluoroacetamido)phenyl)sulfonamido)propan-2-ylamino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 10)</p>
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((<i>S</i>)-1-oxo-3-phenyl-1-(4-(2,2,2-trifluoroacetamido)phenylmethyl)sulfonamido)propan-2-ylamino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 13)</p>
	<p>(<i>R</i>)-1-Isopropyl-<i>N</i>-((<i>S</i>)-1-(((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((4-(2,2,2-trifluoroacetamido)phenyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)(methylamino)-3-methyl-1-oxobutan-2-yl)piperidine-2-carboxamide (Compound 15)</p>

	<p>tert-Butyl (1-(((<i>S</i>)-1-(((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-Methoxy-1-(((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((4-(2,2,2-trifluoroacetamido)phenyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)(methyl)amino)-3-methyl-1-oxobutan-2-yl)amino)-2-methyl-1-oxopropan-2-yl)carbamate (Compound 18)</p>
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-(((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((4-((2,2,2-trifluoroacetamido)methyl)phenyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 21)</p>
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-(((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-(((<i>S</i>)-1-oxo-3-phenyl-1-((4-(2,2,2-trifluoroacetamido)methyl)phenyl)sulfonamido)propan-2-yl)amino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 23)</p>

	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-(((4-(2,2,2-trifluoroacetamido)methyl)phenyl)methyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 25)</p>
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-(((<i>S</i>)-1-oxo-3-phenyl-1-(((4-((2,2,2-trifluoroacetamido)methyl)phenyl)methyl)sulfonamido)propan-2-yl)amino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 27)</p>
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-(4-(1-(2,2,2-trifluoroacetamido)cyclopropyl)phenyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 29)</p>



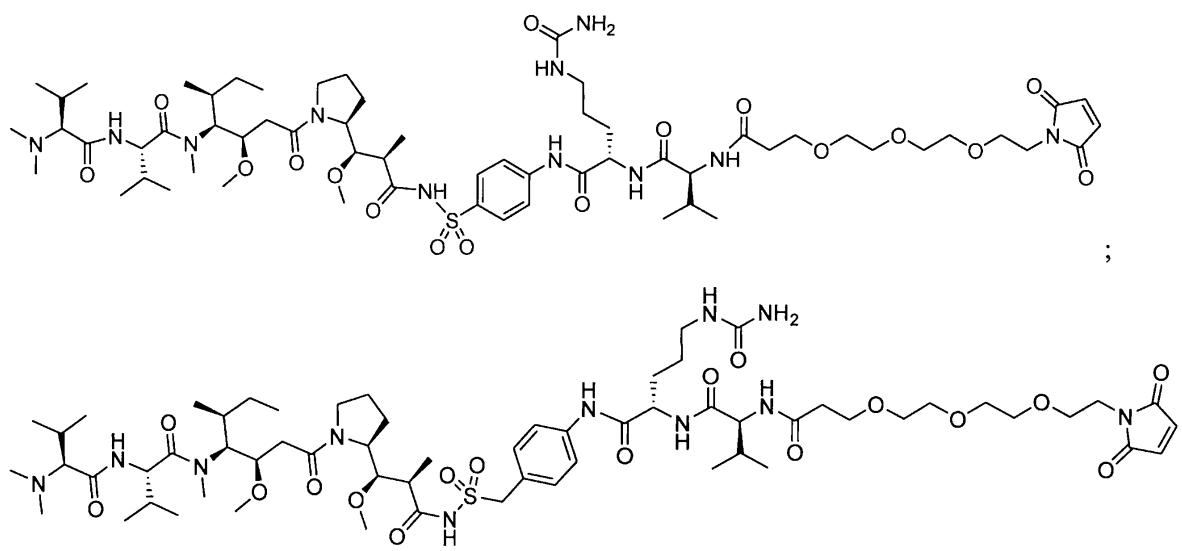
19. A composition of Formula II:

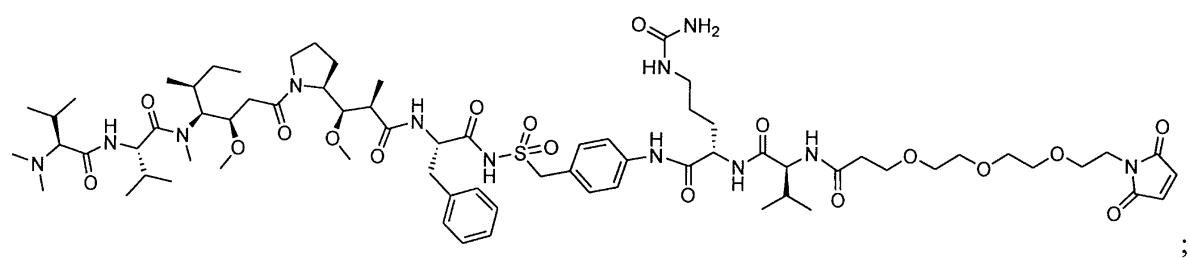
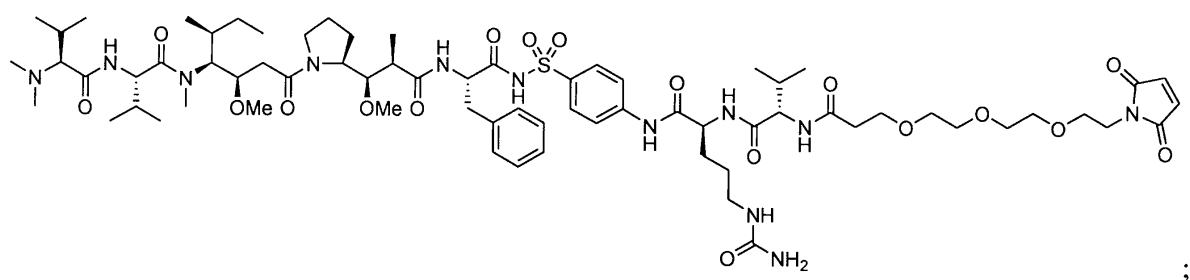
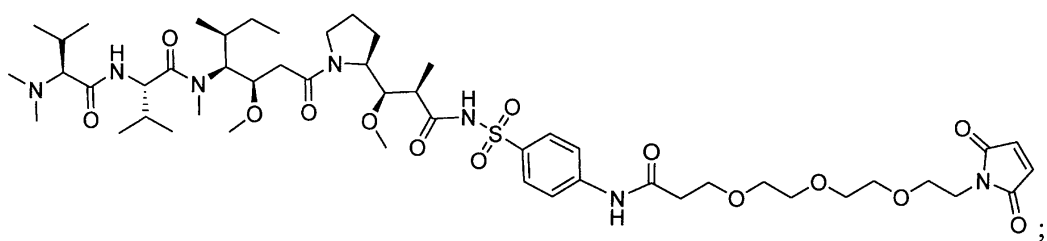
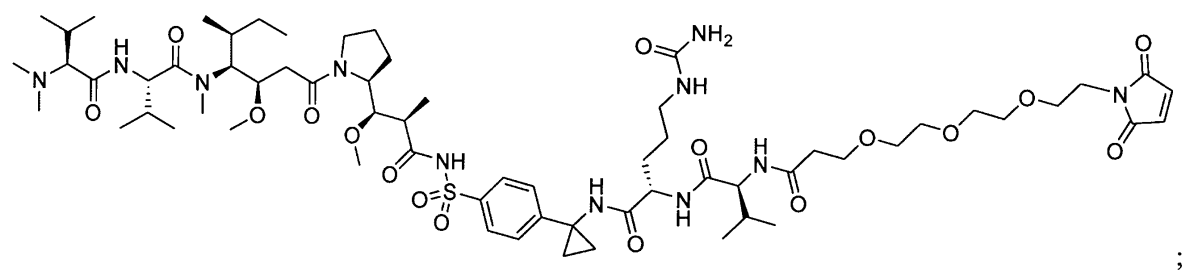
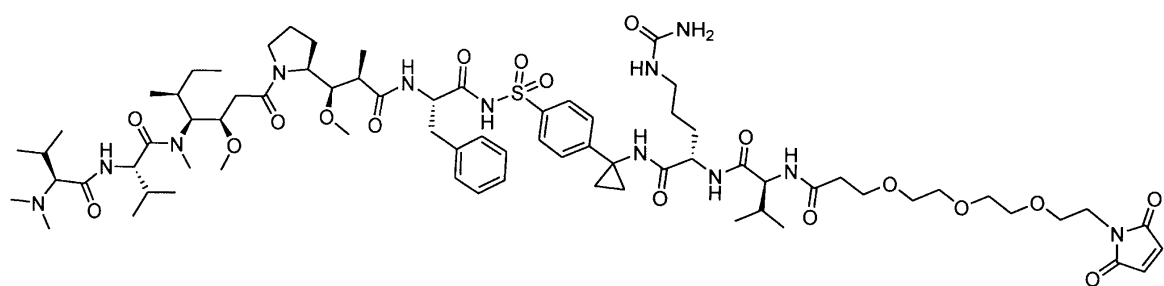
(T)-(L)-(D)

II

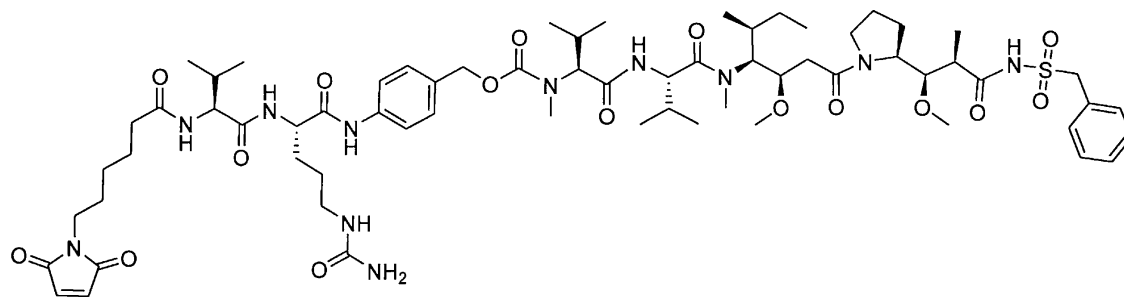
wherein (T) is a targeting moiety, (L) is a linker, and (D) is the compound according to any one of claims 1 to 17.

20. The composition of claim 19, wherein (L)-(D) has one of the following structures:





or



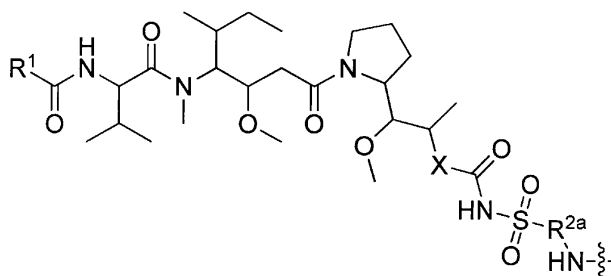
21. A composition of Formula III:

(T)-(L¹)-(D¹)

III

wherein:

(D¹) has structure (IV):



IV

wherein:

R¹ is selected from: amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, amino-heterocyclyl, and heterocyclyl, each optionally substituted with one or more substituents selected from aryl, aryl-C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkylthio, carboxyl, carboxamide, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkyl-C₁-C₆ alkyl, guanidino, halo, C₁-C₆ haloalkyl, heterocyclyl, heterocyclyl-C₁-C₆ alkyl, hydroxyl, and thio; or

R¹ is R^aR^bNCH(R^c)—;

R^a is selected from: H and C₁-C₆ alkyl;

R^b is C₁-C₆ alkyl; and

R^c is R^d-C(CH₃)₂—; and

R^d is selected from: H, aryl, C₃-C₇ cycloalkyl, and heteroaryl, each of which is optionally substituted with one or more substituents selected from: C₁-C₄ acylthio, C₂-C₄ alkenyl, C₁-C₄ alkyl, C₁-C₄ alkylamino, C₁-C₄ alkyloxy, amino, amino-C₁-C₄ alkyl, halo, C₁-C₄ haloalkyl, hydroxyl, hydroxy-C₁-C₄ alkyl, and thio, wherein C₂-C₄ alkenyl, C₁-C₄ alkylamino and C₁-C₄

alkyloxy are further optionally substituted with one substituent selected from C₁-C₄ alkylaryl, hydroxyl, and thio; or

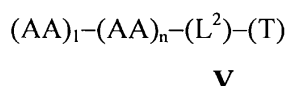
R^b and R^c taken together with the atoms to which they are each bonded form a heterocyclydiyl;

X is -C(O)NHCH(CH₂R³)-, or X is absent;

R^{2a} is selected from: C₂-C₆ alkylidiyl, arylidiyl, C₄-C₇ cycloalkylidiyl, heteroarylidiyl, and heterocyclydiyl, each optionally substituted with one or more substituents selected from: C₁-C₆ alkoxy, C₁-C₆ alkoxy carbonyl, C₁-C₆ alkyl, C₁-C₆ alkylamino, amino, amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, aryl, carboxamide, carboxyl, cyano, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio-C₁-C₆ alkyl;

R³ is selected from: aryl, heteroaryl, and C₃-C₇ cycloalkyl, each optionally substituted with one substituent selected from amino and hydroxyl, and

(L¹)-(T) has structure (V):



wherein:

the -NH- group bonded to R^{2a} in Formula IV forms an enzymatically cleavable peptide bond (JPB) with (AA)₁ in Formula V;

each AA is independently an amino acid;

n is an integer from 0 to 25, and

(L²) is optionally the remaining portion of linker (L¹),

and wherein (AA)₁-(AA)_n, taken together comprises an amino acid sequence capable of facilitating enzymatic cleavage of the JPB.

22. The composition of any one of claims 19 to 21, wherein (T) is a monoclonal antibody or antibody fragment.
23. The composition of claim 22, wherein the antibody or antibody fragment is a bispecific antibody or antibody fragment.
24. The composition of claim 22 or 23, wherein the antibody or antibody fragment specifically binds a cancer cell antigen.

25. The composition of claim 24, wherein the cancer cell antigen is HER2.
26. A pharmaceutical composition comprising the compound of any one of claims 1 to 18 or a pharmaceutically acceptable salt thereof, or the composition of any one of claims 19 to 25, and a pharmaceutically acceptable carrier, diluent or excipient.
27. Use of the compound of any one of claims 1 to 18 or a pharmaceutically acceptable salt thereof, or the composition of any one of claims 19 to 25, in the manufacture of a medicament for treating cancer in a mammal.