

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

and wherein either

(a) X is $-\text{C}(\text{O})\text{NHCH}(\text{CH}_2\text{R}^3)-$;

R² is selected from: aryl and aryl-C₁-C₆ alkyl, each substituted with one or more substituents selected from: amino, amino-C₁-C₆ alkyl and amino-C₃-C₇ cycloalkyl. and

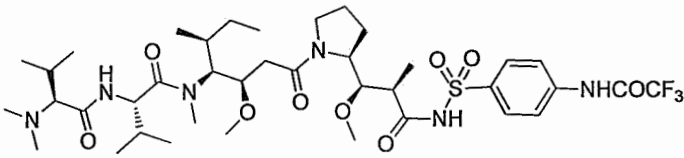
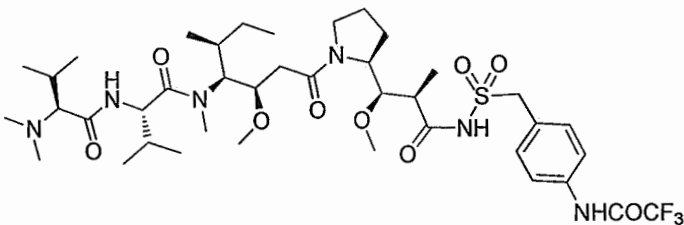
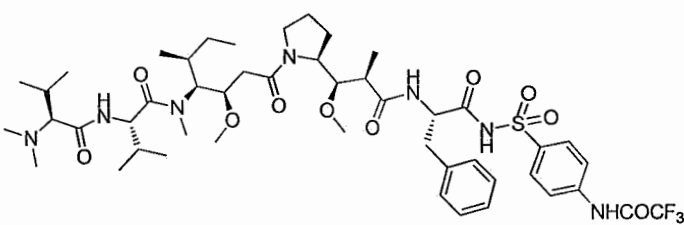
R³ is selected from: aryl, heteroaryl and C₃-C₇ cycloalkyl, each optionally substituted with one substituent selected from amino and hydroxyl; or

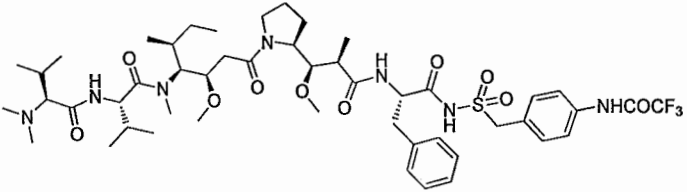
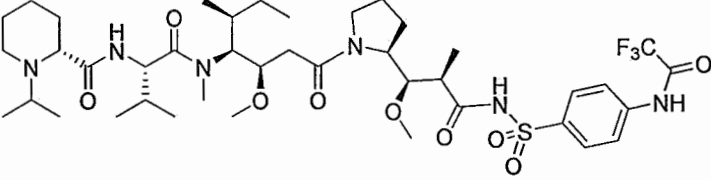
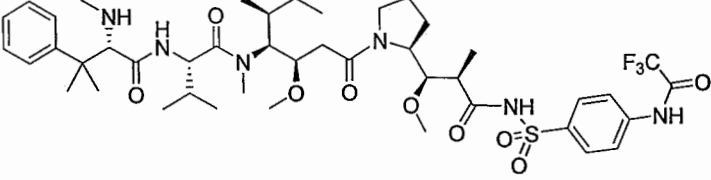
(b) X is absent, and

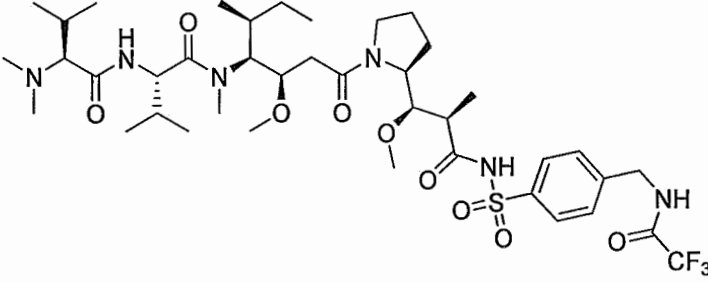
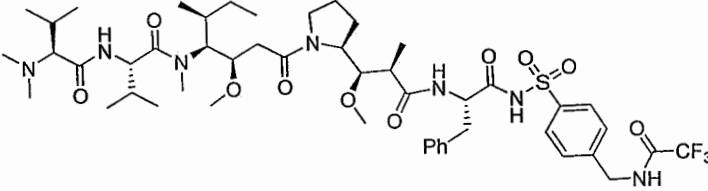
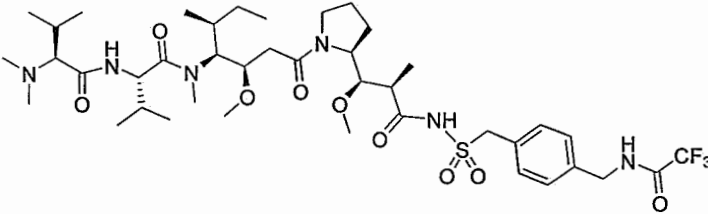
R² is selected from: C₂-C₆ alkyl, aryl, aryl-C₁-C₆ alkyl, C₄-C₇ cycloalkyl, C₃-C₇ cycloalkyl-C₁-C₆ alkyl, heteroaryl, heteroaryl-C₁-C₆ alkyl, and heterocyclyl, each optionally substituted with one or more substituents selected from: C₁-C₆ alkoxy, C₁-C₆ alkoxycarbonyl,

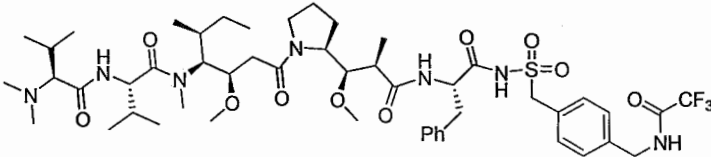
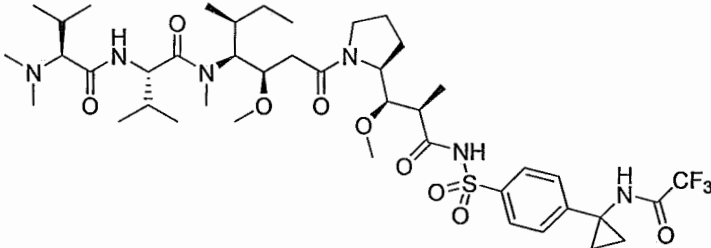
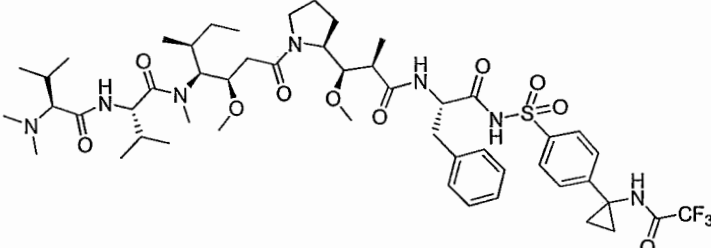
C₁-C₆ alkyl, C₁-C₆ alkylamino, amino, amino-C₁-C₆ alkyl, amino-aryl, amino-C₃-C₇ cycloalkyl, aryl, carboxamide, carboxyl, cyano, C₁-C₆ haloacyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio-C₁-C₆ alkyl;

In one embodiment, the invention provides a compound selected from the following, or a pharmaceutically acceptable salt thereof:

	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-1-methoxy-2-methyl-3-oxo-3-(4-(2,2,2-trifluoroacetamido)phenyl)sulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-N,3-dimethylbutanamide (Compound 4)</p>
	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-1-methoxy-2-methyl-3-oxo-3-((4-(2,2,2-trifluoroacetamido)phenyl)methylsulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-N,3-dimethylbutanamide (Compound 7)</p>
	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-1-methoxy-2-methyl-3-oxo-3-((S)-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)-N,3-dimethylbutanamide (Compound 10)</p>

	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-1-methoxy-2-methyl-3-oxo-3-((S)-1-oxo-3-phenyl-1-(4-(2,2,2-trifluoroacetamido)phenylmethylsulfonamido)propan-2-ylamino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-N,3-dimethylbutanamide (Compound 13)</p>
	<p>(R)-1-Isopropyl-N-((S)-1-(((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-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)piperidine-2-carboxamide (Compound 15)</p>
	<p>tert-Butyl (1-(((S)-1-(((3R,4S,5S)-3-Methoxy-1-((S)-2-((1R,2R)-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>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-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)-N,3-dimethylbutanamide (Compound 21)</p>
	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-1-methoxy-2-methyl-3-oxo-3-(((S)-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)-N,3-dimethylbutanamide (Compound 23)</p>
	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-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)-N,3-dimethylbutanamide (Compound 25)</p>

	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-1-methoxy-2-methyl-3-oxo-3-(((S)-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)-N,3-dimethylbutanamide (Compound 27)</p>
	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-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)-N,3-dimethylbutanamide (Compound 29)</p>
	<p>(S)-2-((S)-2-(Dimethylamino)-3-methylbutanamido)-N-((3R,4S,5S)-3-methoxy-1-((S)-2-((1R,2R)-1-methoxy-2-methyl-3-oxo-3-((S)-1-oxo-3-phenyl-1-(4-(1-(2,2,2-trifluoroacetamido)cyclopropyl)phenyl)sulfonamido)propan-2-ylamino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-N,3-dimethylbutanamide (Compound 31)</p>

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.

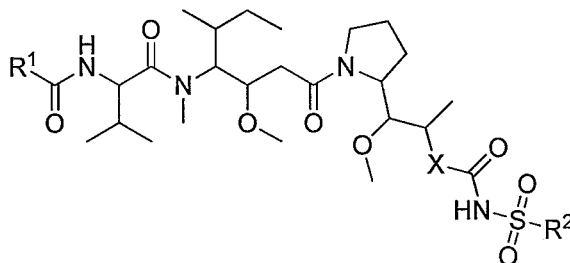
In another embodiment, the present disclosure provides a use of a compound described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a mammal.

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.

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;

and wherein either

(a) X is $-C(O)NHCH(CH_2R^3)-$;

R^2 is selected from: aryl and aryl- C_1-C_6 alkyl, each substituted with one or more substituents selected from: amino, amino- C_1-C_6 alkyl and amino- C_3-C_7 cycloalkyl. and

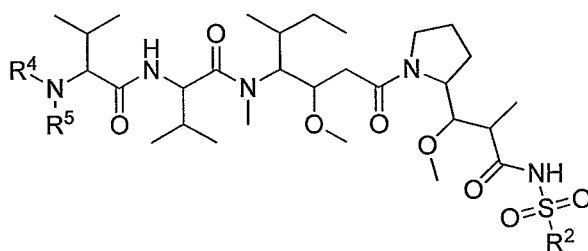
R^3 is selected from: aryl, heteroaryl and C_3-C_7 cycloalkyl, each optionally substituted with one substituent selected from amino and hydroxyl; or

(b) X is absent, and

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, 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 haloacyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, halo, hydroxyl, nitro, thio, and thio- C_1-C_6 alkyl.

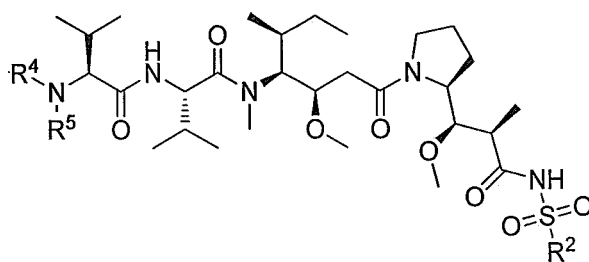
2. The compound of claim 1, wherein R^1 is selected from: amino- C_1-C_6 alkyl, amino-aryl, amino- C_3-C_7 cycloalkyl, amino-heterocyclyl, and heterocyclyl, each optionally substituted with one or more substituents selected from C_1-C_6 alkyl and halo.
3. The compound of claim 1, wherein R^1 is $R^aR^bNCH(R^c)-$.
4. The compound of claim 1, wherein R^1 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 $-C(O)NHCH(CH_2R^3)-$.
6. The compound of any one of claims 1 to 4, wherein X is absent.

7. The compound of claim 6, wherein R^2 is selected from: aryl, aryl- C_1 - C_6 alkyl, heteroaryl and heteroaryl- C_1 - C_6 alkyl, 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 haloacyl, C_1 - C_6 haloalkyl, C_1 - C_6 haloalkoxy, halo, hydroxyl, nitro, thio, and thio- C_1 - C_6 alkyl.
8. The compound of claim 6, wherein R^2 is selected from: aryl and aryl- C_1 - C_6 alkyl, each optionally substituted with one or more substituents selected from: amino, amino- C_1 - C_6 alkyl and amino- C_3 - C_7 cycloalkyl.
9. The compound of claim 1 having Formula Ia:



Ia

or Formula Id:



Id

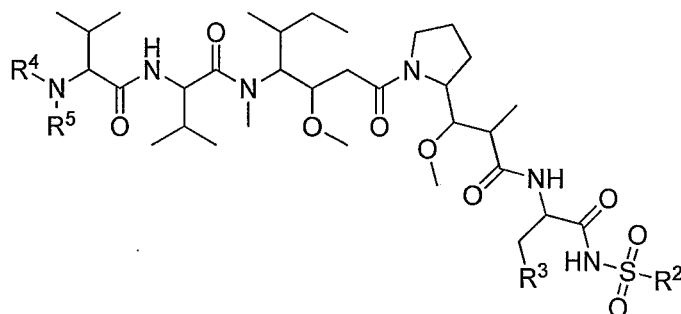
or a pharmaceutically acceptable salt thereof,
wherein:

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, 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

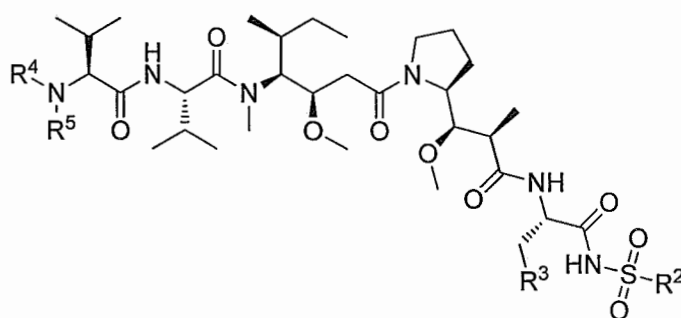
R⁴ and R⁵ are each independently selected from: H and C₁-C₆ alkyl.

10. The compound of claim 9, wherein R² is selected from: aryl, aryl-C₁-C₆ alkyl, heteroaryl and heteroaryl-C₁-C₆ alkyl, 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 haloacyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, halo, hydroxyl, nitro, thio, and thio-C₁-C₆ alkyl.
11. The compound of claim 9, 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.
12. The compound of claim 1 having Formula Ib:



Ib

or Formula Ie:



1e

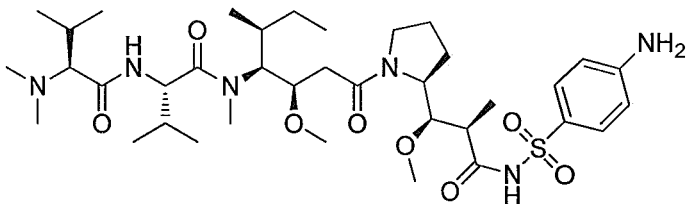
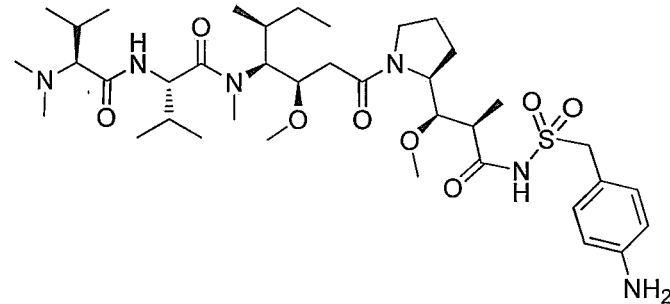
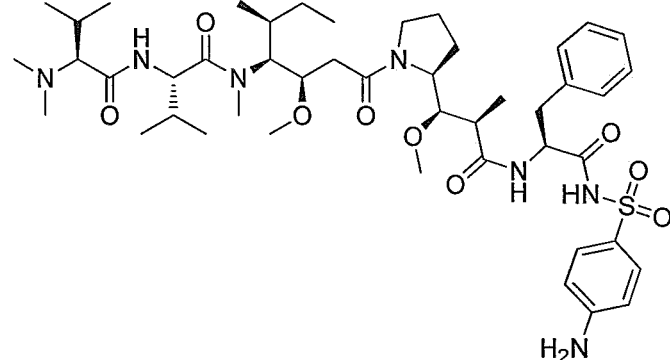
or a pharmaceutically acceptable salt thereof,
wherein:

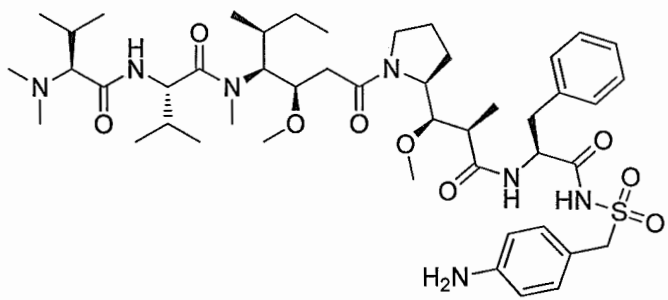
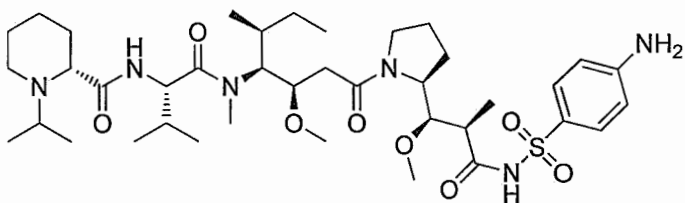
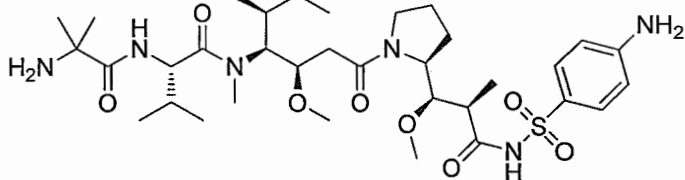
R^2 is selected from: aryl and aryl- C_1 - C_6 alkyl, each substituted with one or more substituents selected from: amino, amino- C_1 - C_6 alkyl and amino- C_3 - C_7 cycloalkyl;

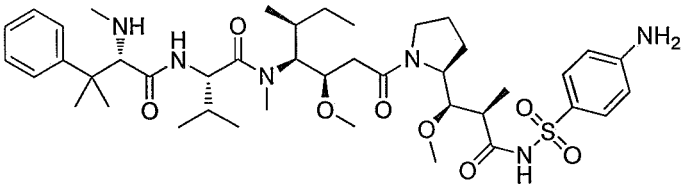
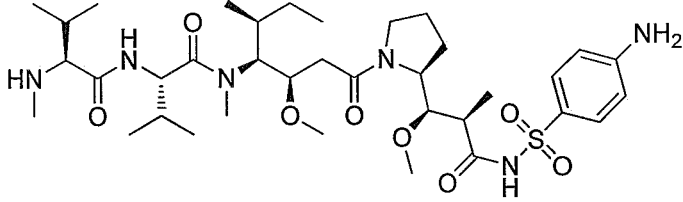
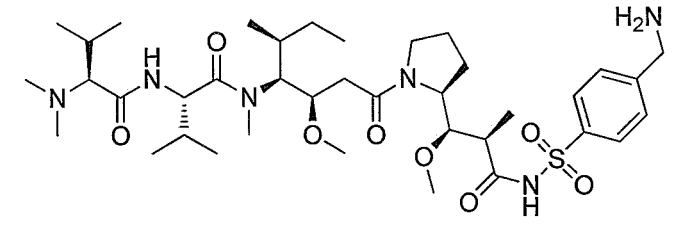
R^3 is selected from: aryl, heteroaryl, and C_3 - C_7 cycloalkyl, each optionally substituted with one substituent selected from amino and hydroxyl; and

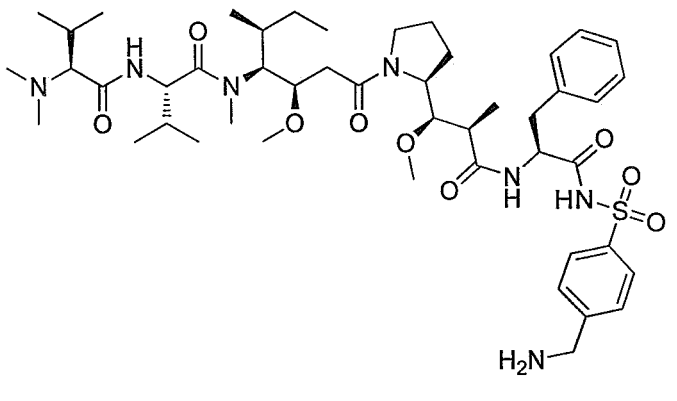
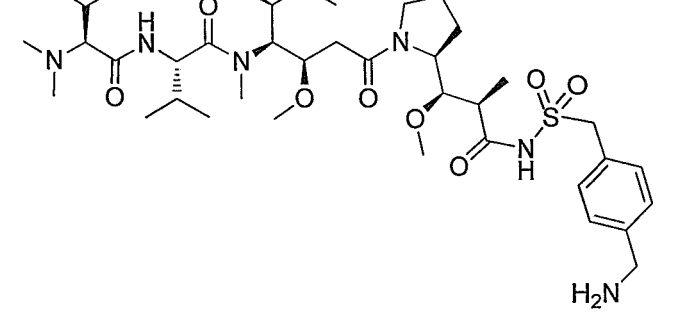
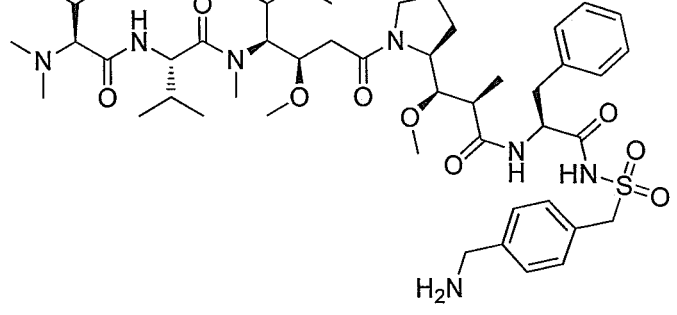
R^4 and R^5 are each independently selected from: H and C_1 - C_6 alkyl.

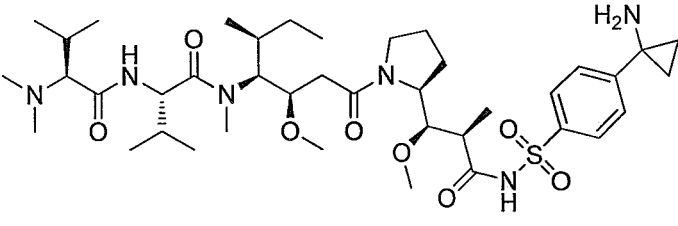
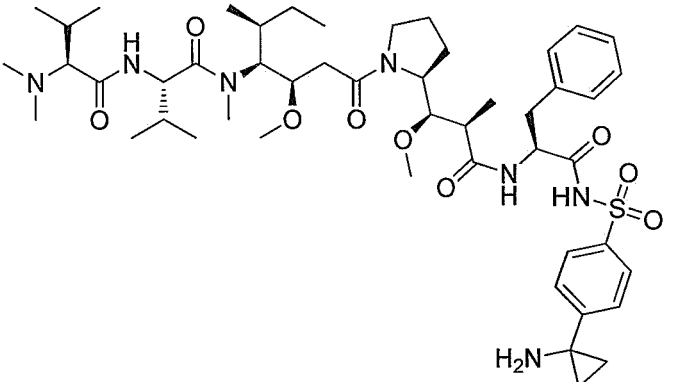
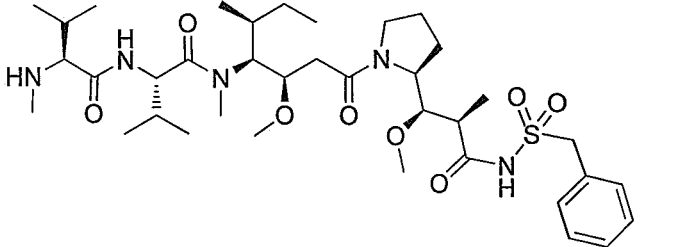
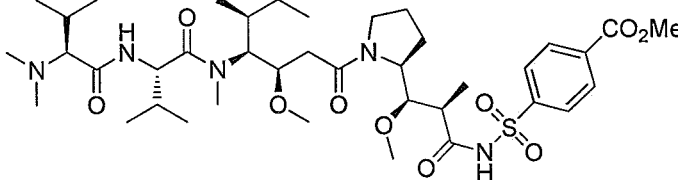
13. The compound of claim 12, wherein R^3 is aryl optionally substituted with one substituent selected from amino and hydroxyl.
14. The compound of any one of claims 9 to 13, wherein R^4 and R^5 are each C_1 - C_6 alkyl.
15. The compound of any one of claims 9 to 13, wherein R^4 is H and R^5 is C_1 - C_6 alkyl.
16. The compound of any one of claims 9 to 13, wherein R^4 and R^5 are each methyl.
17. The compound of any one of claims 9 to 13, wherein R^4 is H and R^5 is methyl.
18. The compound of any one of claims 1 to 17, wherein R^2 is selected from: 4-aminobenzyl, 4-(aminomethyl)benzyl, 4-(aminomethyl)phenyl, 4-aminophenyl, and benzyl.
19. 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>

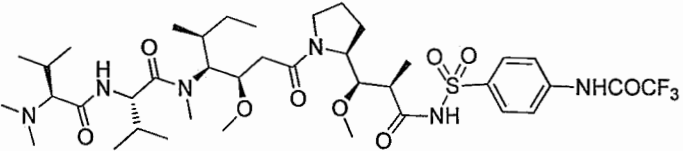
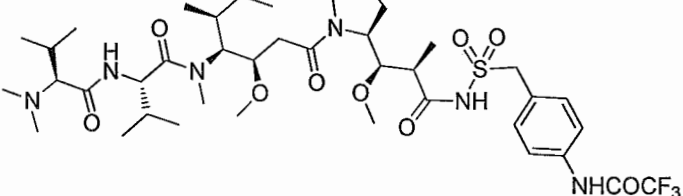
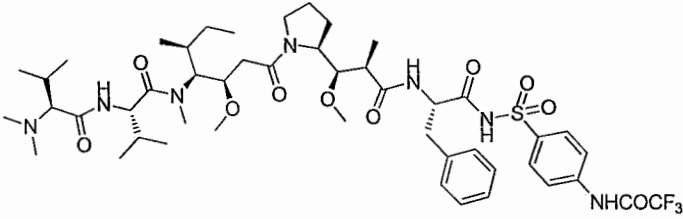
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((<i>S</i>)-1-(4-aminophenylmethylsulfonamido)-1-oxo-3-phenylpropan-2-ylamino)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-<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>

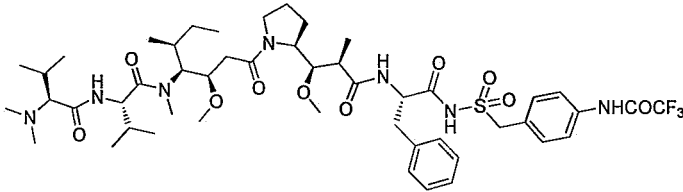
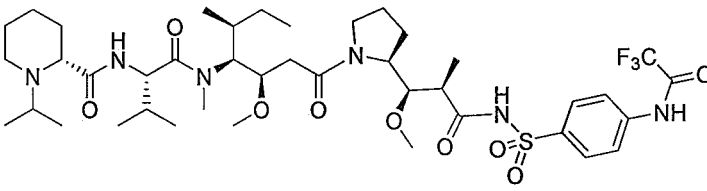
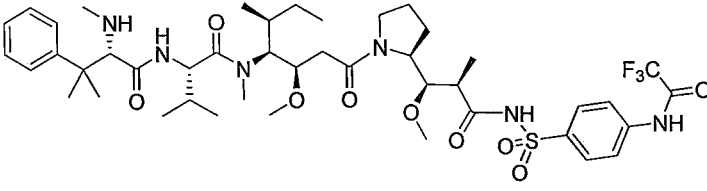
	<p><i>(S)</i>-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-((4-aminophenyl)sulfonamido)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethyl-2-((<i>S</i>)-3-methyl-2-(methylamino)-3-phenylbutanamido)butanamide (Compound 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 (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 (Compound 22)</p>

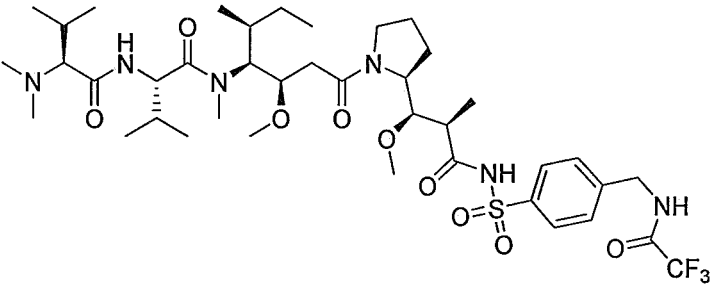
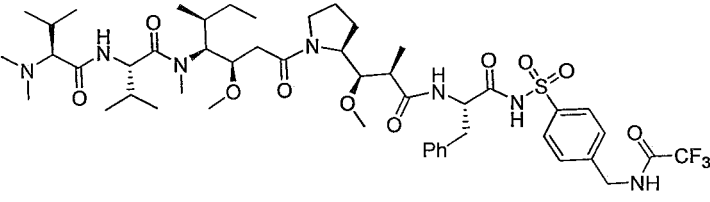
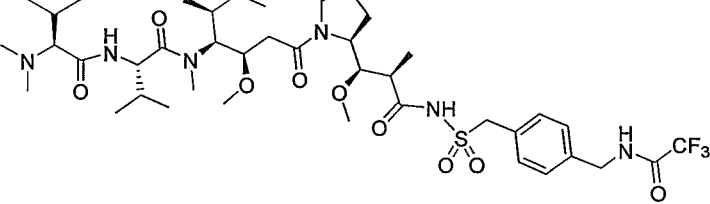
	<p>(<i>S</i>)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-3-(((<i>S</i>)-1-((4-(aminomethyl)phenyl)sulfonamido)-1-oxo-3-phenylpropan-2-yl)amino)-1-methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-2-((<i>S</i>)-2-(dimethylamino)-3-methylbutanamido)-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

20. A compound selected from the following, or a pharmaceutically acceptable salt thereof:

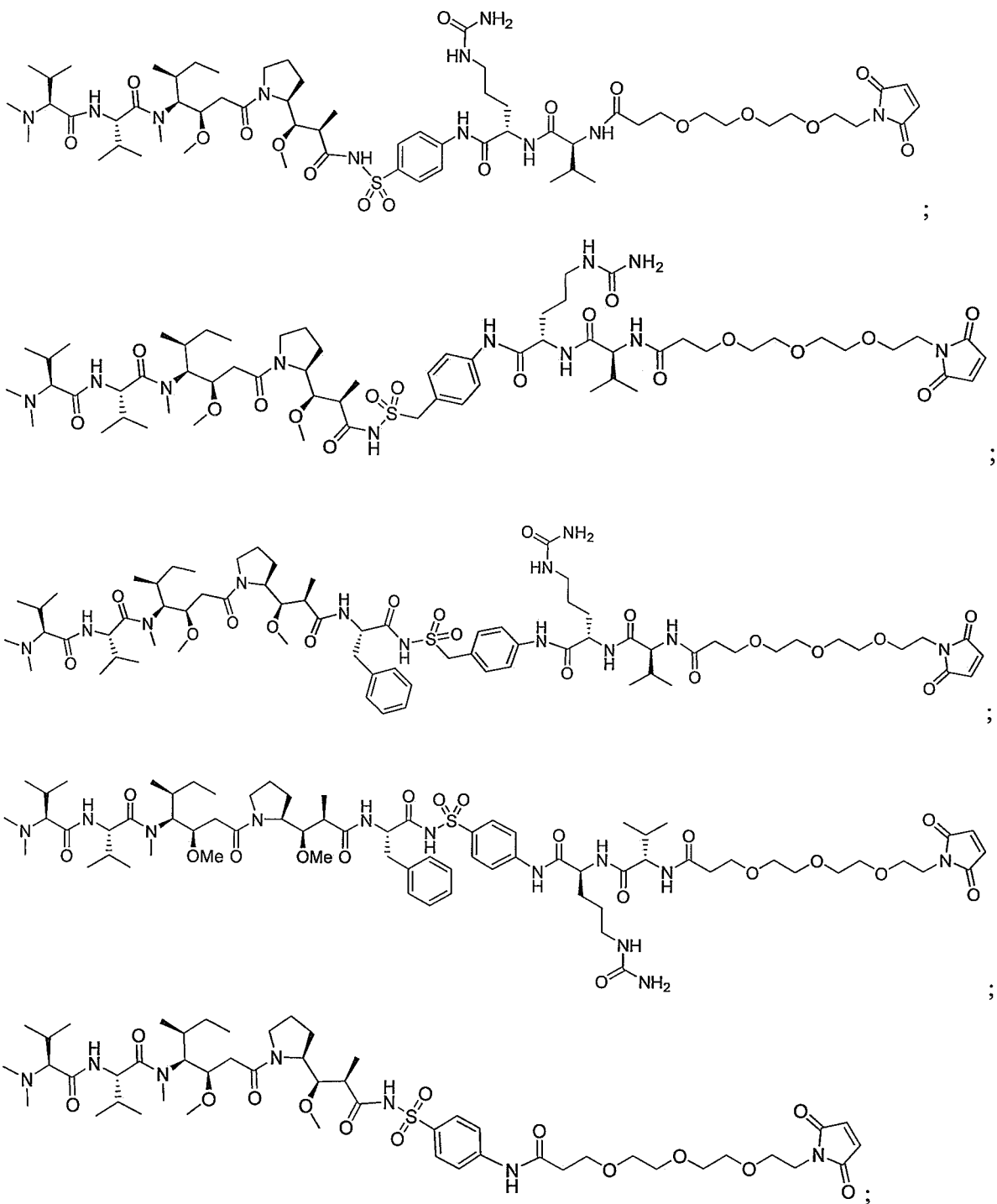
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-(4-(2,2,2-trifluoroacetamido)phenylsulfonamido)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (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)methylsulfonamido)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)phenylsulfonamido)propan-2-ylamino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<i>N</i>,3-dimethylbutanamide (Compound 10)</p>

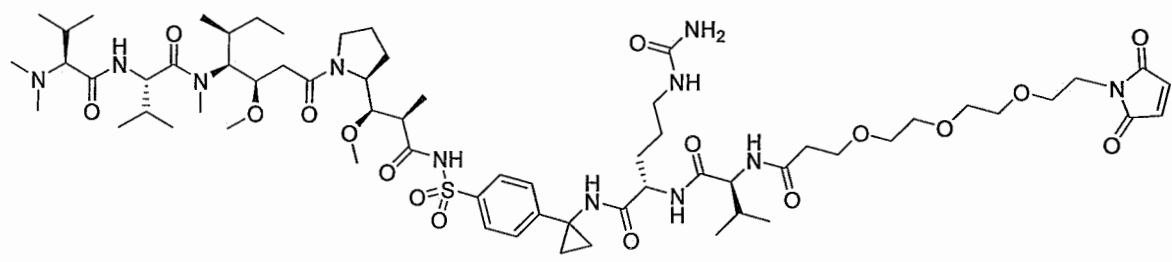
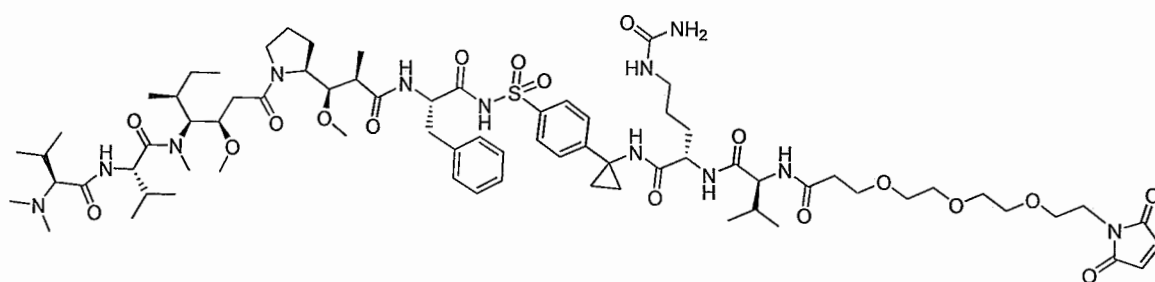
	<p>(<i>S</i>)-2-((<i>S</i>)-2-(Dimethylamino)-3-methylbutanamido)-<i>N</i>-((3<i>R</i>,4<i>S</i>,5<i>S</i>)-3-methoxy-1-((<i>S</i>)-2-((1<i>R</i>,2<i>R</i>)-1-methoxy-2-methyl-3-oxo-3-((<i>S</i>)-1-oxo-3-phenyl-1-(4-(2,2,2-trifluoroacetamido)phenylmethylsulfonamido)propan-2-ylamino)propyl)pyrrolidin-1-yl)-5-methyl-1-oxoheptan-4-yl)-<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)(methyl)amino)-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>

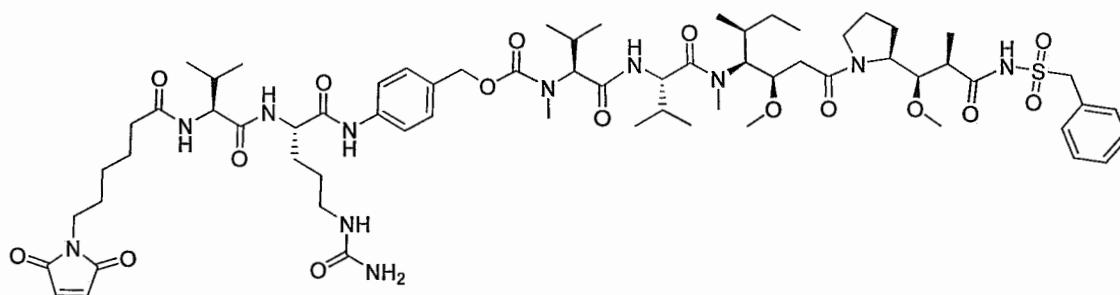
wherein (T) is a targeting moiety, (L) is a linker, and (D) is the compound according to any one of claims 1 to 19.

22. The composition of claim 21, wherein (L)-(D) has one of the following structures:





or



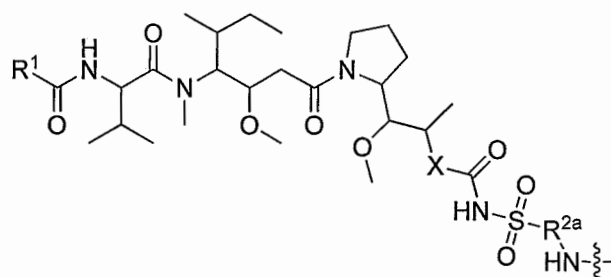
23. A composition of Formula III:

(T)-(L¹)-(D¹)

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

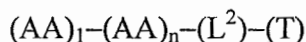
R^b and R^c taken together with the atoms to which they are each bonded form a heterocyclidiyl;

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 heterocyclidiyl, 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 $(\text{AA})_1$ in Formula V;

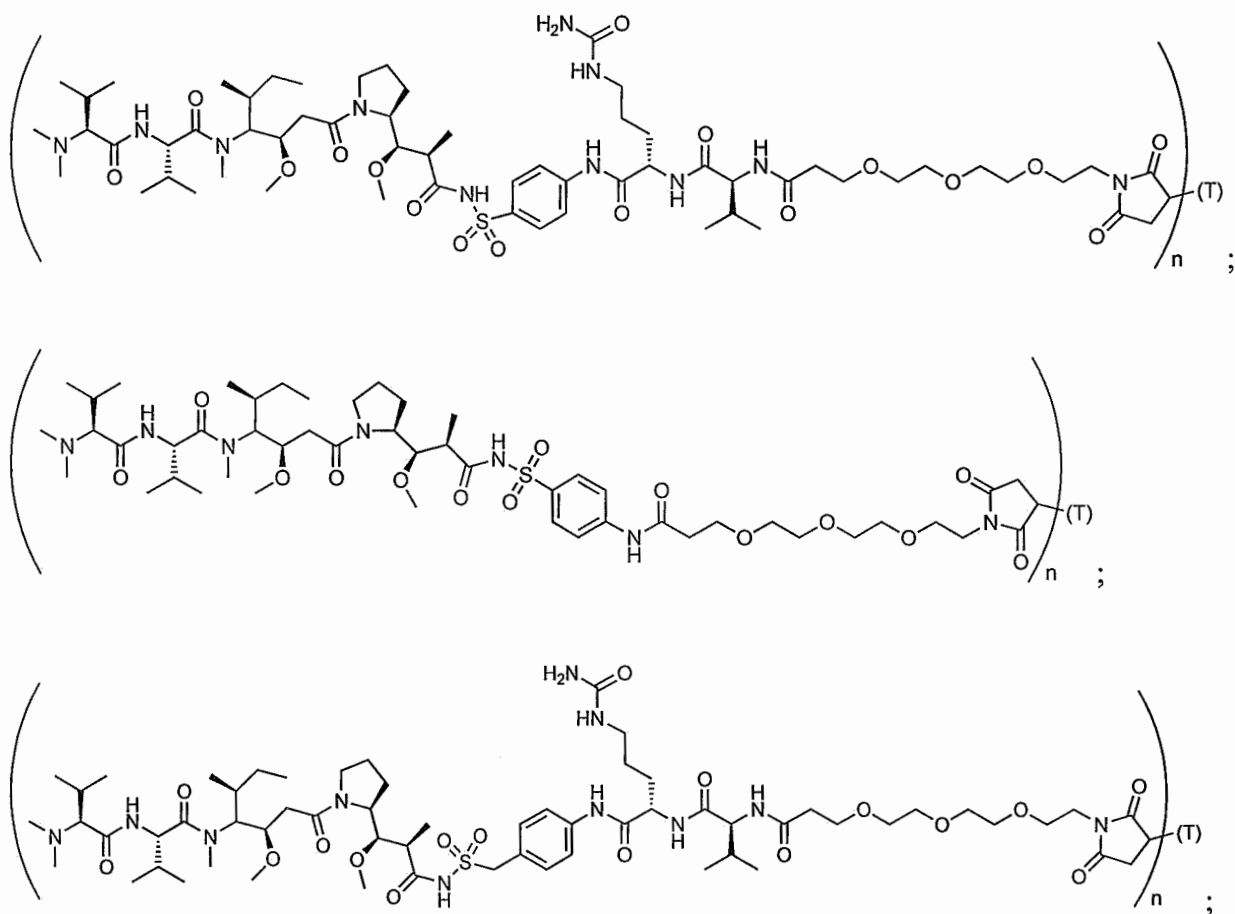
each AA is independently an amino acid;

n is an integer from 0 to 25, and

(L^2) is optionally the remaining portion of linker (L^1) ,

and wherein $(\text{AA})_1\text{-(AA)}_n$, taken together comprises an amino acid sequence capable of facilitating enzymatic cleavage of the JPB.

24. The composition of claim 23, wherein the composition is selected from:



n is 0, 1, 2, 3, 4, 5, 6, 7 or 8, and

(T) is a monoclonal antibody or antibody fragment.

25. The composition of any one of claims 21 to 23, wherein (T) is a monoclonal antibody or antibody fragment.
26. The composition of claim 24 or 25, wherein the antibody or antibody fragment is a bispecific antibody or antibody fragment.
27. The composition of any one of claims 24 to 26, wherein the antibody or antibody fragment specifically binds a cancer cell antigen.
28. The composition of claim 27, wherein the cancer cell antigen is HER2.
29. A pharmaceutical composition comprising the compound of any one of claims 1 to 20 or a pharmaceutically acceptable salt thereof, or the composition of any one of claims 21 to 28, and a pharmaceutically acceptable carrier, diluent or excipient.
30. Use of the compound of any one of claims 1 to 20 or a pharmaceutically acceptable salt thereof, or the composition of any one of claims 21 to 28, in the manufacture of a medicament for treating cancer in a mammal.