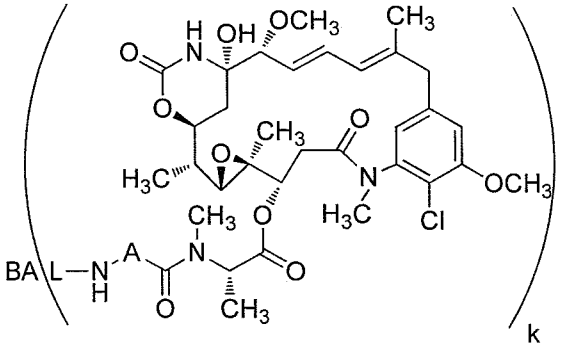
SUMMARY

[0004] Providd herein are compounds of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof,

wherein:

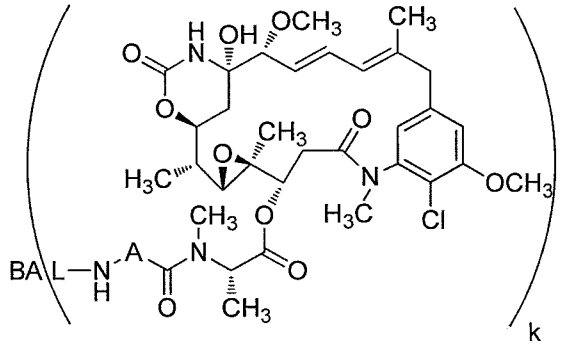
A is arylene or heteroarylene;

L is a linker;

BA is a binding agent; and

k is an integer from 1 to 30. Also provided herein are stereoisomers of compounds of Formula (I).

[0004a] One aspect provided herein are compounds of Formula (I)



(I)

or a pharmaceutically acceptable salt thereof,

wherein

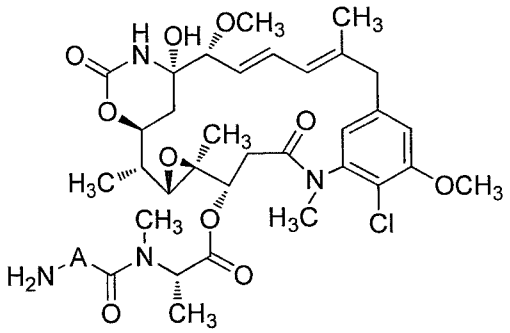
A is arylene or heteroarylene;

L is a linker;

BA is an antibody or an antigen binding fragment thereof; and

k is an integer from 1 to 30.

[0005] Another aspect provided herein are also compounds of Formula (II)



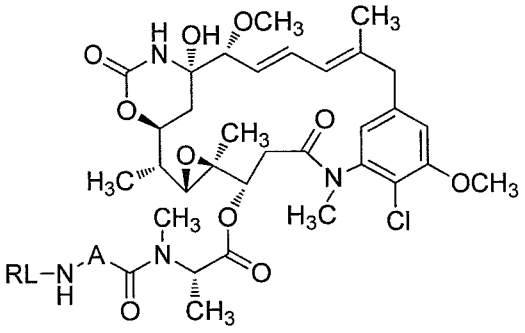
(II)

or a pharmaceutically acceptable salt thereof, wherein A is arylene or heteroarylene. Also provided herein are stereoisomers of compounds of Formula (II).

[0005a] Another aspect provided herein is a pharmaceutical composition comprising the compound as defined herein and a pharmaceutically acceptable excipient .

[0005b] Another aspect provided herein is use of a compound as defined herein or a composition as definded herein in the manufacture of a medicament for treating cancer.

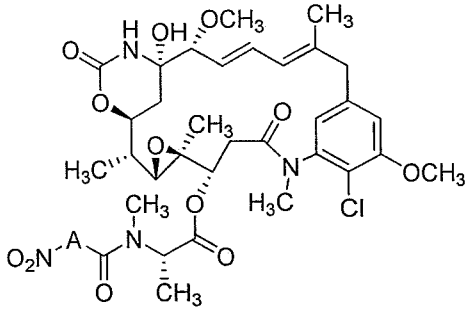
[0005c] Another aspect provided herein are also compounds of Formula P1



P1

wherein A is arylene or heteroarylene; and RL is a reactive linker.

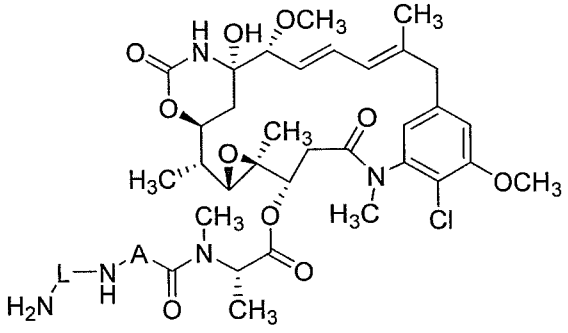
[0006] Another aspect provided herein are also compounds of Formula PP5:



PP5

or a salt thereof, wherein A is arylene or heteroarylene. Also provided herein are stereoisomers of compounds of Formula PP5.

[0007] Provided herein are also compounds of Formula PT1:

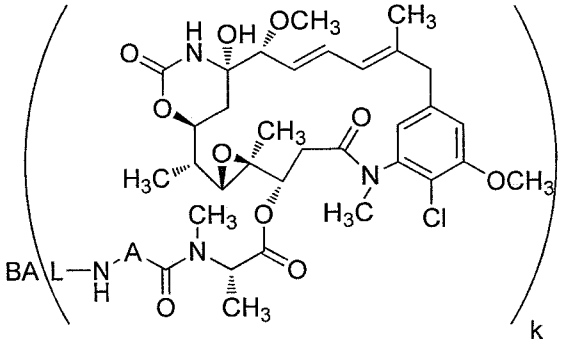


PT1

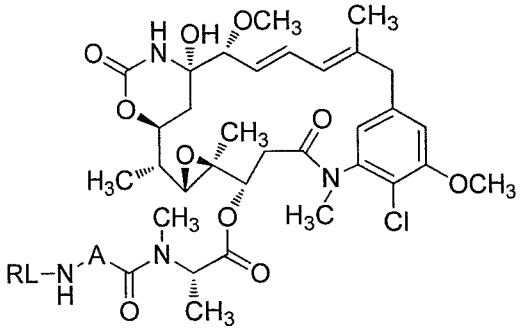
PT1

or a salt thereof, wherein A is arylene or heteroarylene and L is a linker. Also provided herein are stereoisomers of compounds of Formula PT1.

[0007a] Another aspect provided herein is a process of preparing a compound of Formula (I)



comprising contacting a compound of Formula P1



P1

with an antibody or antigen binding fragment thereof under conjugation conditions,

wherein A is arylene or heteroarylene;

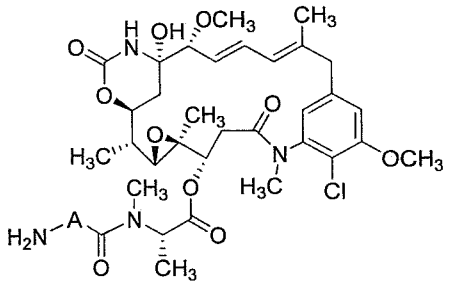
L is a linker;

BA is an antibody or antigen binding fragment thereof;

k is an integer from 1 to 10;

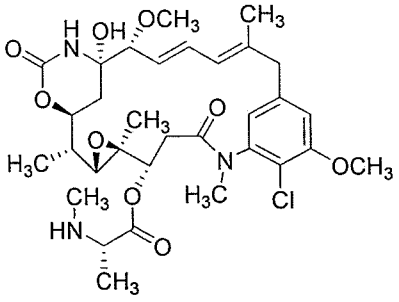
and RL is a reactive linker.

[0007b] Another aspect provided herein is a process of making a compound of formula PP3



PP3 , comprising

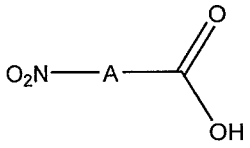
(a) contacting a compound of formula P2



P2

,

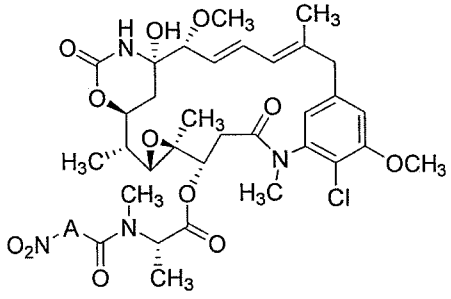
with a compound of formula PP6



PP6

,

under amide synthesis conditions to form a compound of formula PP5



PP5

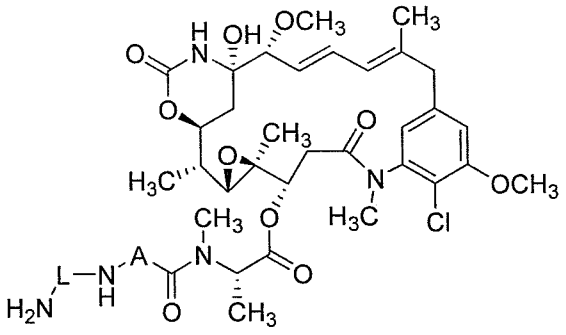
,

wherein A is arylene or heteroarylene; and

(b) reducing the compound of formula PP5 by contacting the compound of formula PP5 with a reducing agent to form a compound of formula PP3.

[0007c] Another aspect provided herein is a process of preparing an antibody-drug-conjugate compound of Formula (I) comprising

(a) reacting a deglycosylated antibody or aglycosylated antibody with a compound of Formula (PT1) in the presence of transglutaminase



PT1

wherein

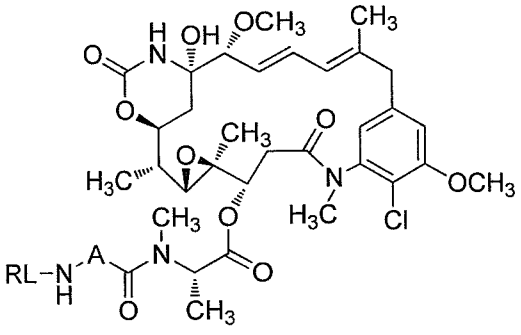
A is arylene or heteroarylene; and L is a linker.

[0007d] Another aspect provided herein is a glutaminyl-modified antibody produced by the process as defined herein.

[0007e] Another aspect provided herein is a pharmaceutical composition comprising the antibody as defined herein and one or more pharmaceutically acceptable diluents, excipients, or carriers.

[0007f] Another aspect provided herein is use of the antibody as defined herein in the manufacture of a medicament for treating a condition in a subject in need thereof, wherein the condition is selected from the group consisting of cancer, renal cell carcinoma, pancreatic carcinoma, head and neck cancer, prostate cancer, malignant gliomas, osteosarcoma, colorectal cancer, gastric cancer, gastric cancer with MET amplification, malignant mesothelioma, multiple myeloma, ovarian cancer, small cell lung cancer, non-small cell lung cancer, synovial sarcoma, thyroid cancer, breast cancer, and melanoma.

[0007g] Another aspect provided herein is a compound prepared by the process of contacting a compound of Formula P1 with an antibody or antigen binding fragment thereof under conjugation conditions,



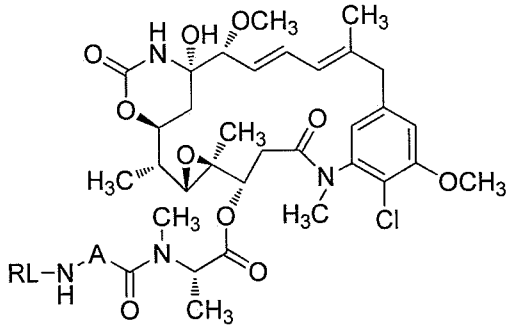
P1

wherein A is arylene or heteroarylene;

RL is a reactive linker; and

wherein Formula P1 is coupled to one or more cysteine or lysine residues of the antibody or antigen binding fragment thereof.

[0007h] Another aspect provided herein is a compound comprising an antibody or antigen binding fragment thereof conjugated to a compound of Formula P1

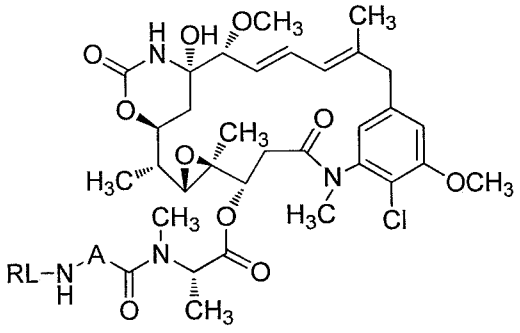


wherein

RL is a reactive linker; and

A is arylene or heteroarylene.

[0007i] Another aspect provided herein is a compound prepared by the process of contacting a compound of Formula P1 with an antibody or antigen binding fragment thereof under conjugation conditions,



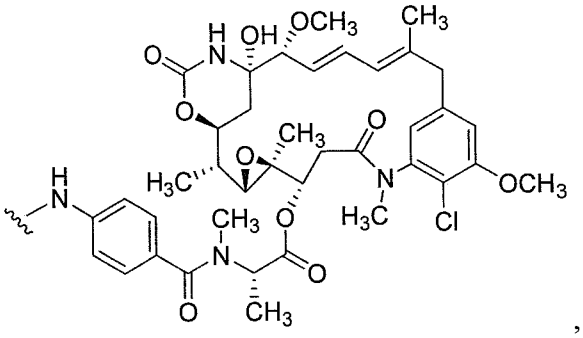
P1

wherein A is arylene or heteroarylene;

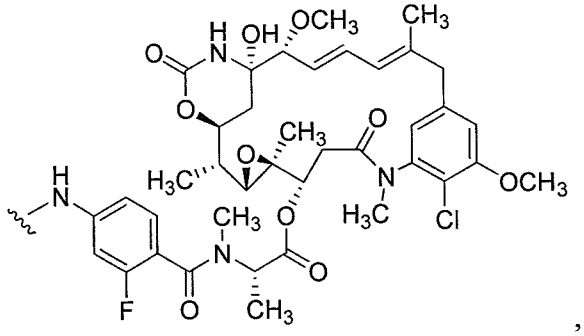
RL is a reactive linker; and

wherein Formula P1 is coupled to one or more cysteine or lysine residues of the antibody or antigen binding fragment thereof.

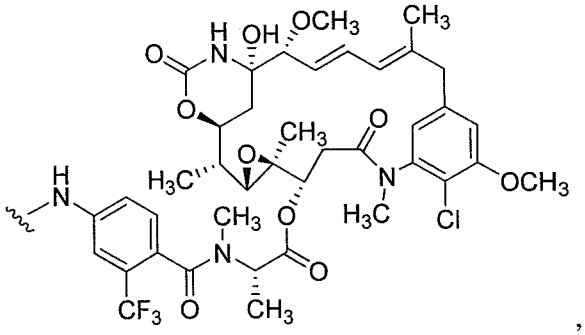
[0007j] Another aspect provided herein is an antibody-drug conjugate comprising an antibody or antigen-binding fragment thereof conjugated to a payload selected from the group consisting of



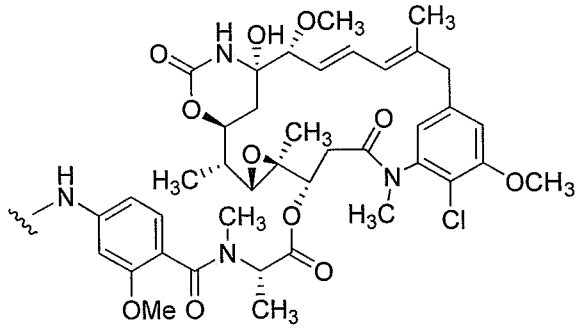
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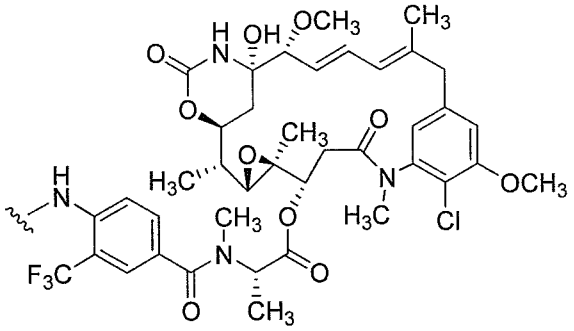
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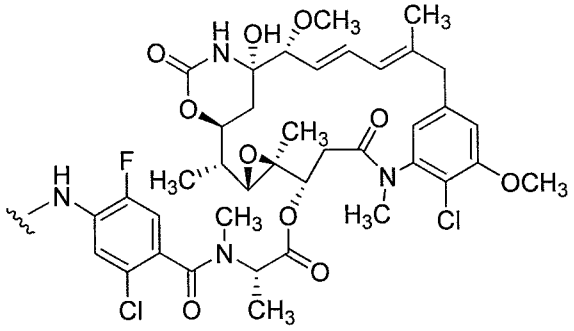


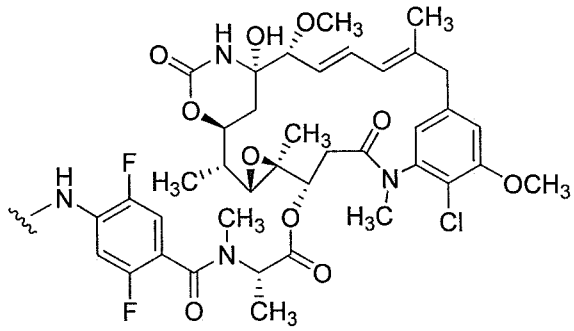
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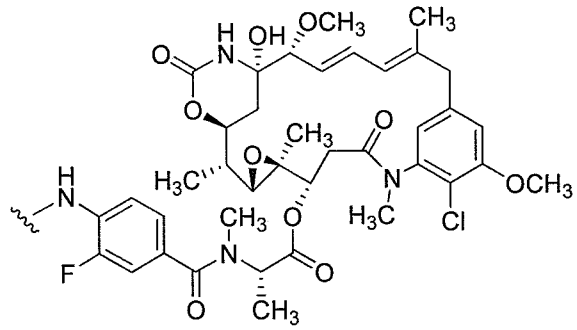


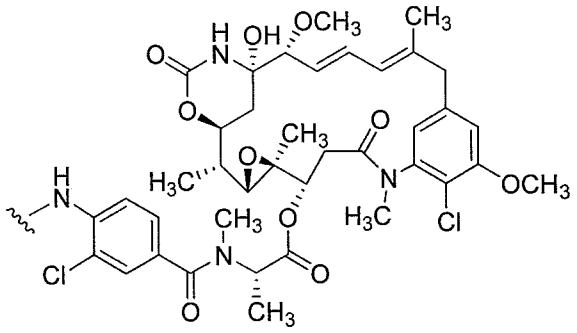
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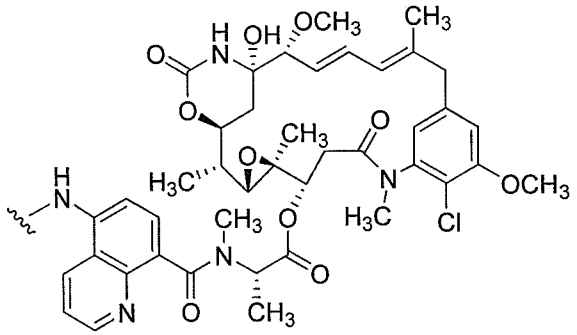

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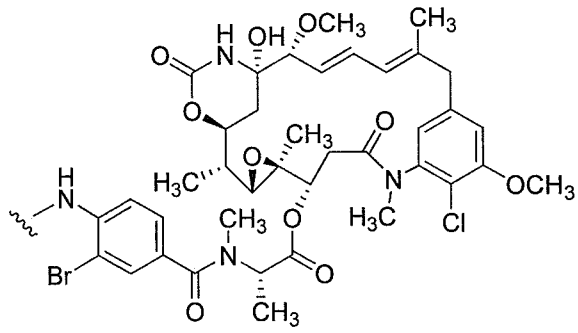

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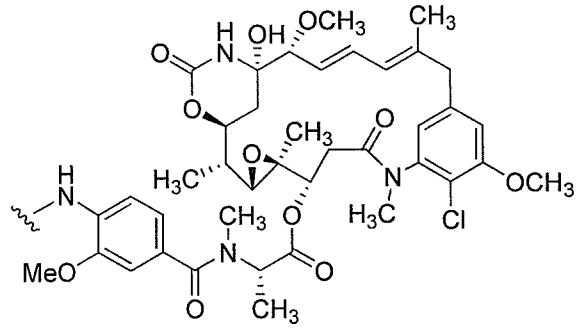

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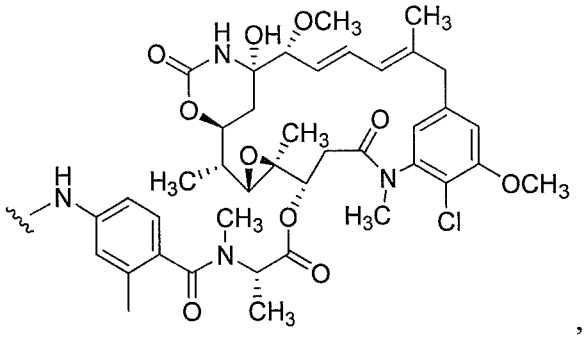

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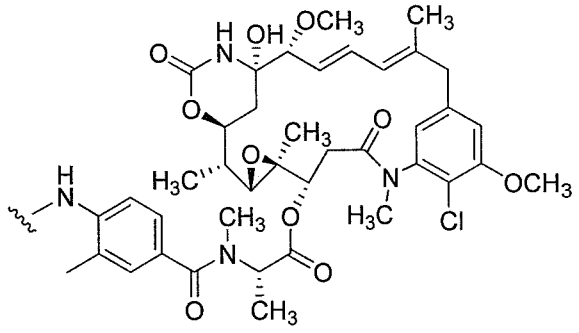

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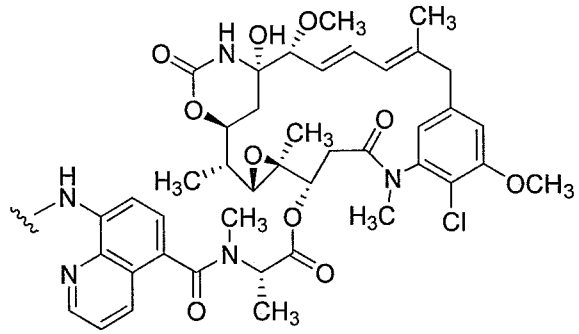

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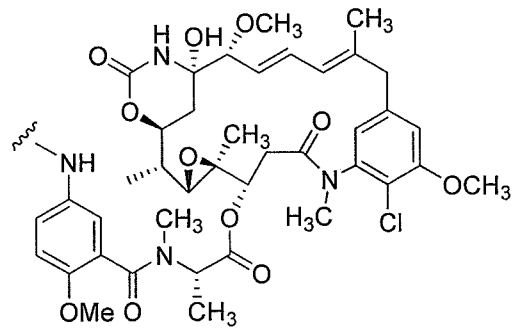

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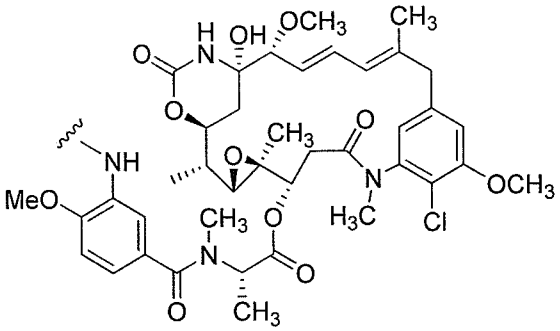

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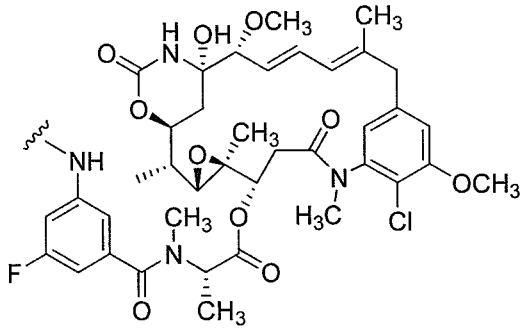

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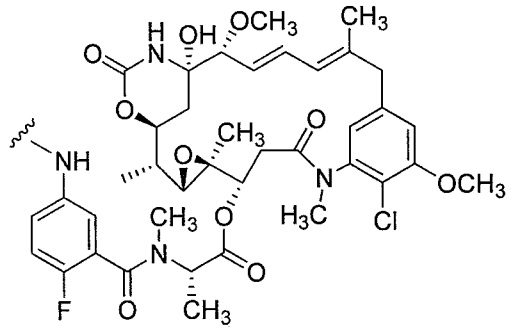

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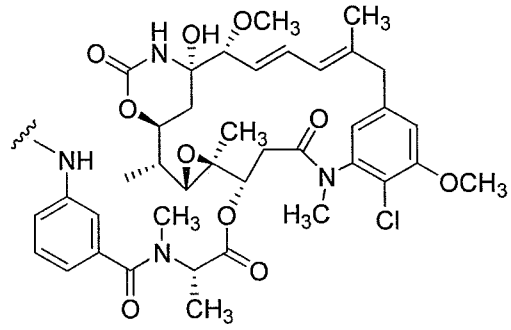

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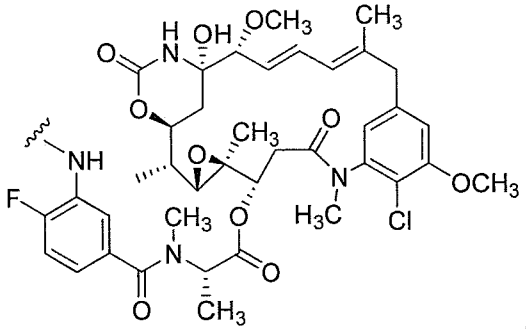

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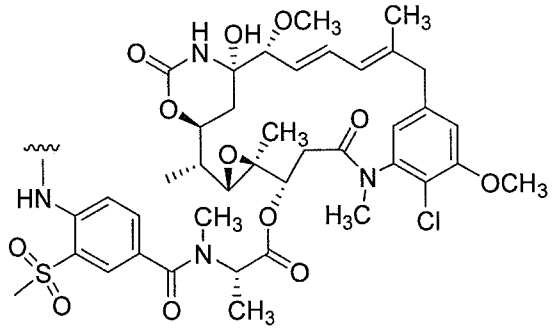

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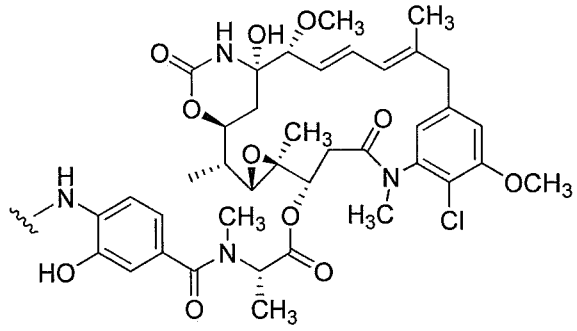

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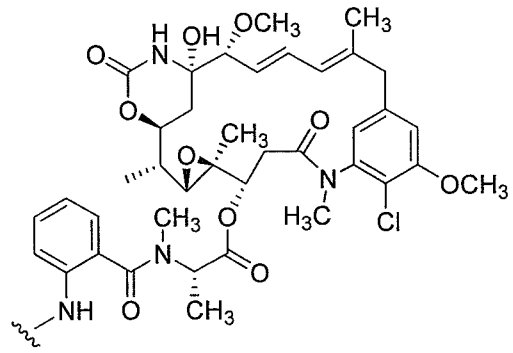

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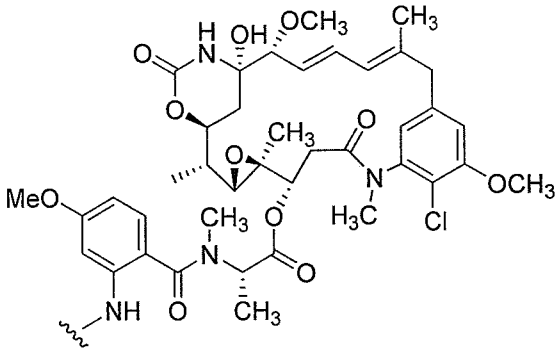

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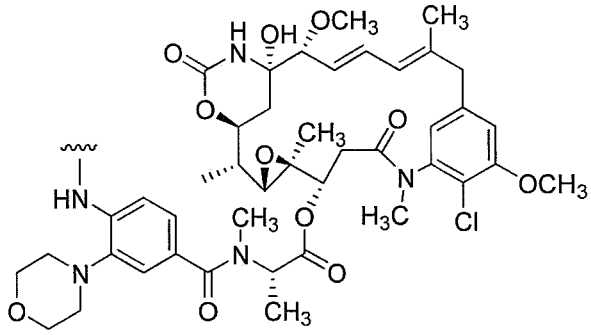

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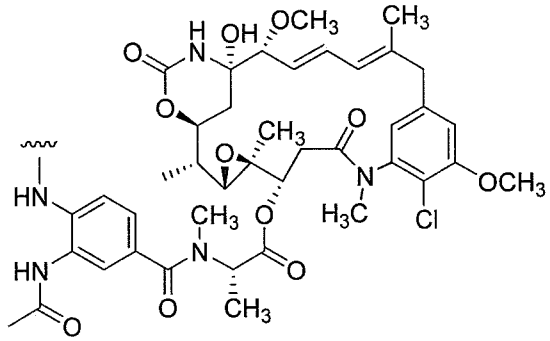

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, and



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[0008] Furthermore, provided herein are methods of treating proliferative diseases comprising administering the compounds described herein.

[0009] Furthermore, provided herein are methods of treating proliferative diseases comprising administering the conjugates described herein.

[0010] Furthermore, provided herein are of methods of preparing compounds of Formula (I) comprising reacting a deglycosylated antibody or aglycosylated antibody with a compound of Formula (PT1) in the presence of transglutaminase.

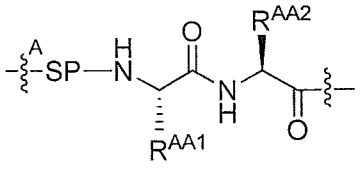
BRIEF DESCRIPTIONS OF THE DRAWINGS

m is an integer from 0 to 3;

p is an integer from 0 to 6; and

q is an integer from 0 to 5.

3. The compound of claim 1 or 2, wherein L is



wherein

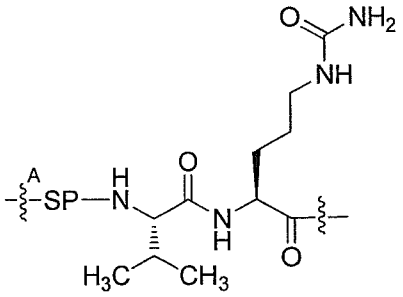
SP is a spacer;

 is one or more bonds to the antibody or antigen binding fragment thereof;

R^{AA1} is an amino acid side chain; and

R^{AA2} is an amino acid side chain.

4. The compound of claim 3, wherein L is

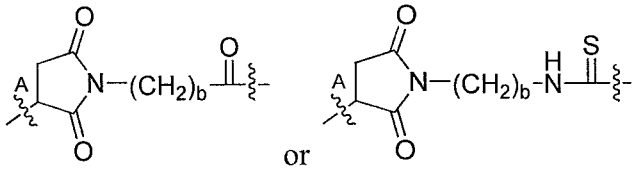


wherein

SP is a spacer; and

 is one or more bonds to the antibody or antigen binding fragment thereof.

5. The compound of claim 4, wherein SP is

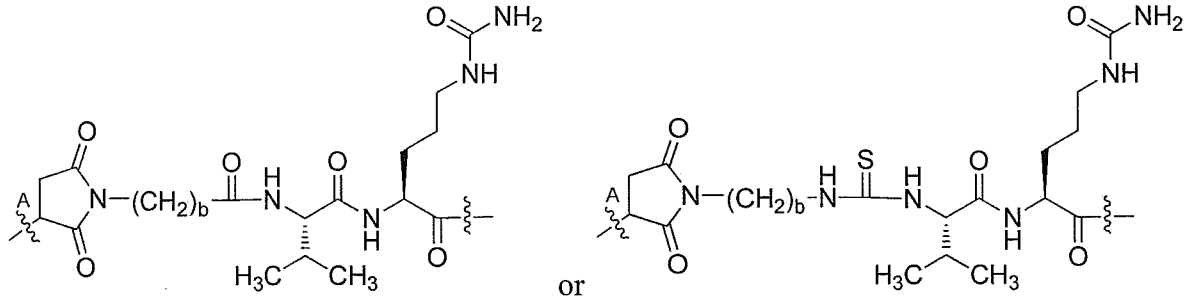


wherein

 is a bond to the antibody or antigen binding fragment thereof; and

b is an integer from 2 to 8.

6. The compound of claim 1 or 2, wherein L is

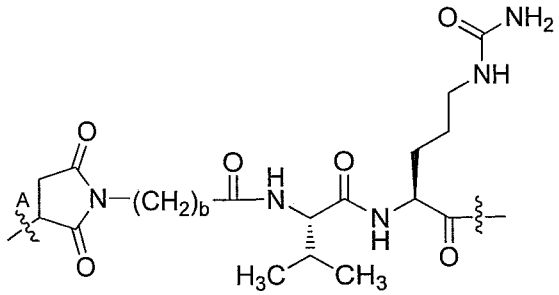


wherein

 is a bond to the antibody or antigen binding fragment thereof; and

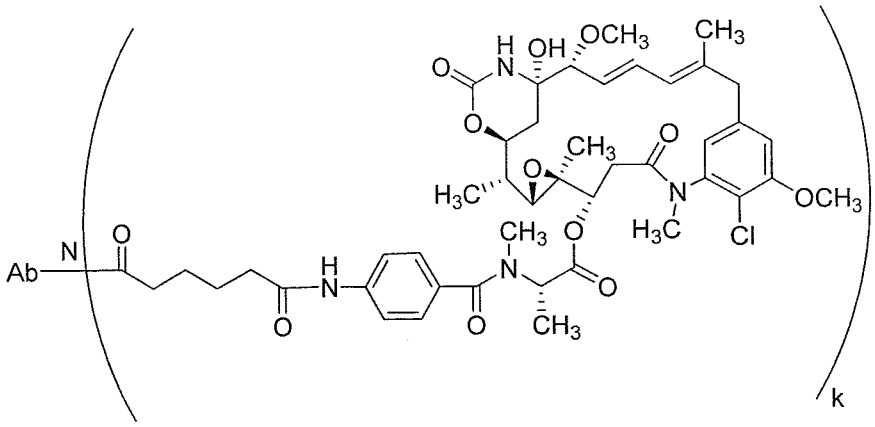
b is an integer from 2 to 8.

7. The compound of claim 6, wherein L is

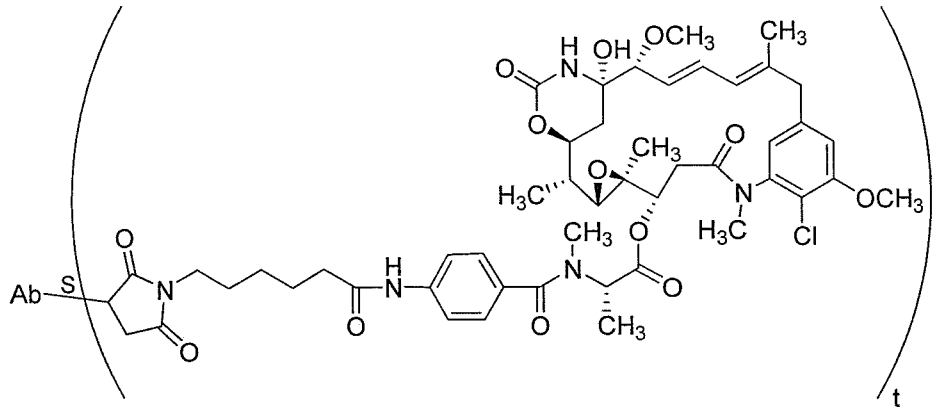


wherein  is a bond to the antibody or antigen binding fragment thereof.

8. The compound of claim 1 or 2, wherein L is



, or



;

wherein

Ab is an antibody or an antigen binding fragment thereof;

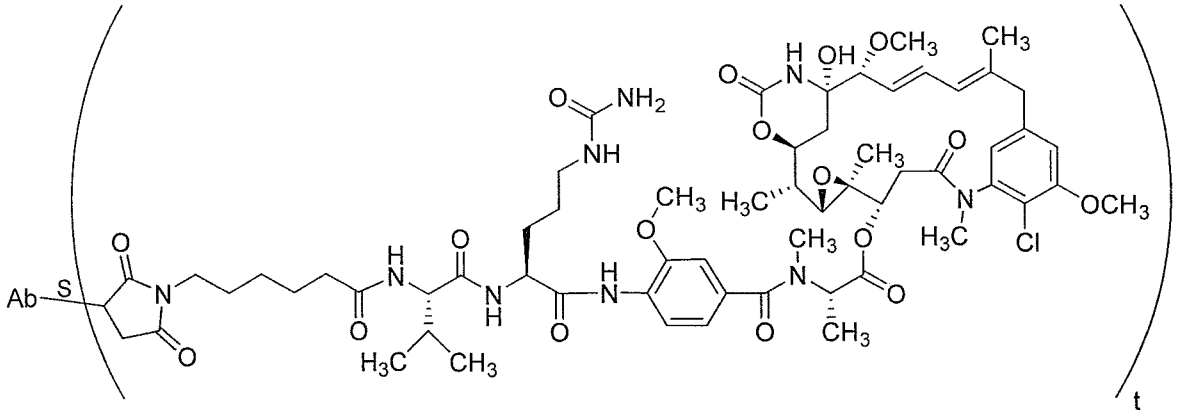
—S— is a bond to a cysteine residue of the antibody or an antigen binding fragment thereof;

—N— is a bond to a lysine residue of the antibody or an antigen binding fragment thereof;

k is an integer from 1 to 30; and

t is an integer from 1 to 8.

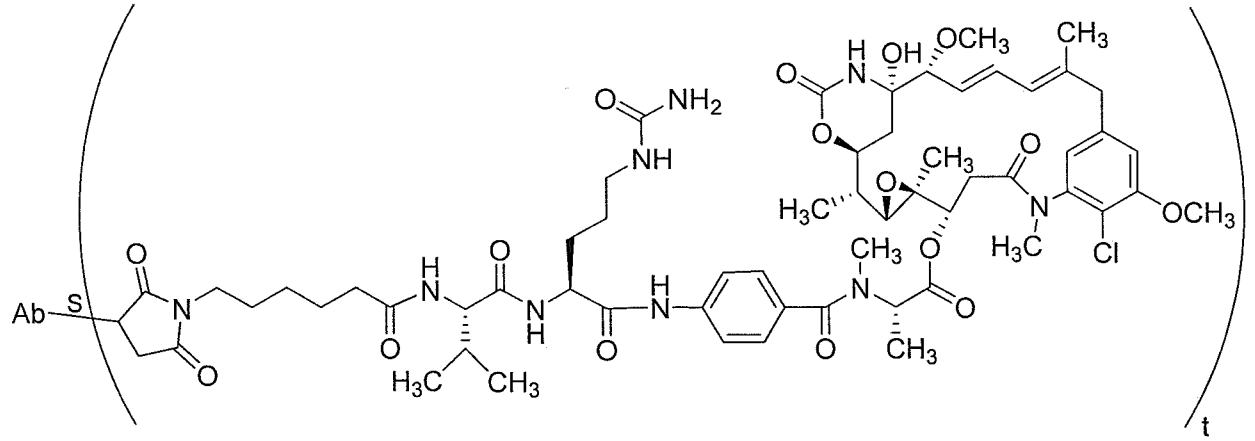
11. The compound of claim 10, wherein the compound is

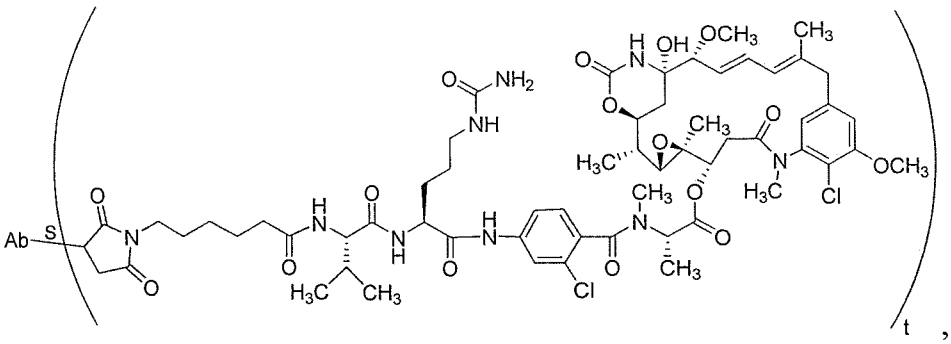


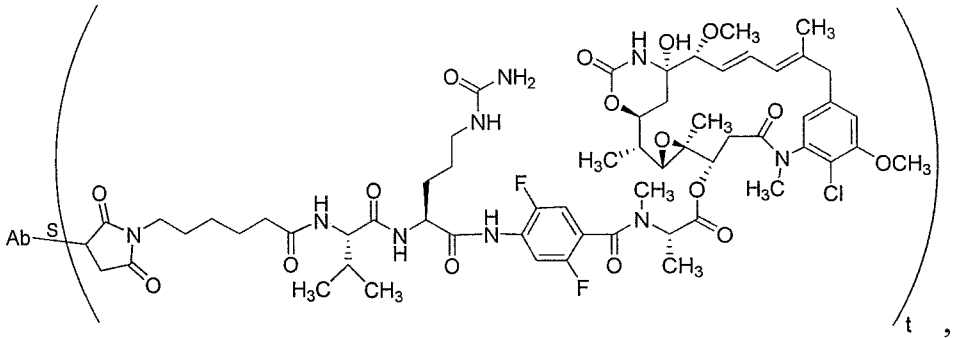
12. The compound of any one of claims 1-11, wherein t is 1.

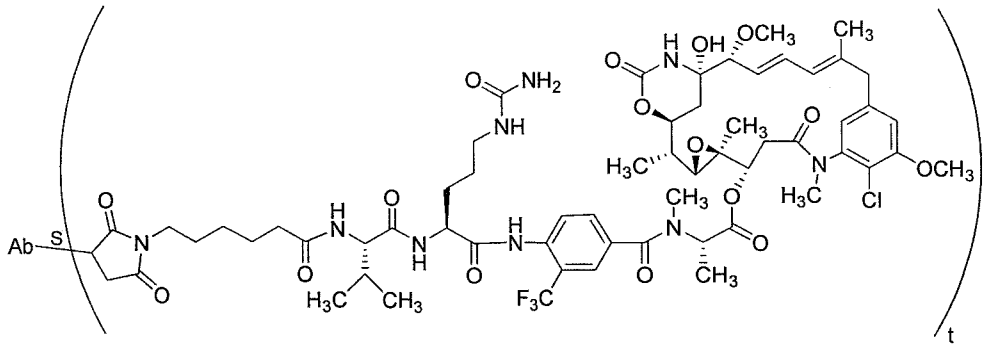
13. The compound of any of one claims 1-12, wherein the antibody or an antigen binding fragment thereof is an anti-MUC16 antibody, an anti-PRLR antibody, or an anti-PSMA antibody.

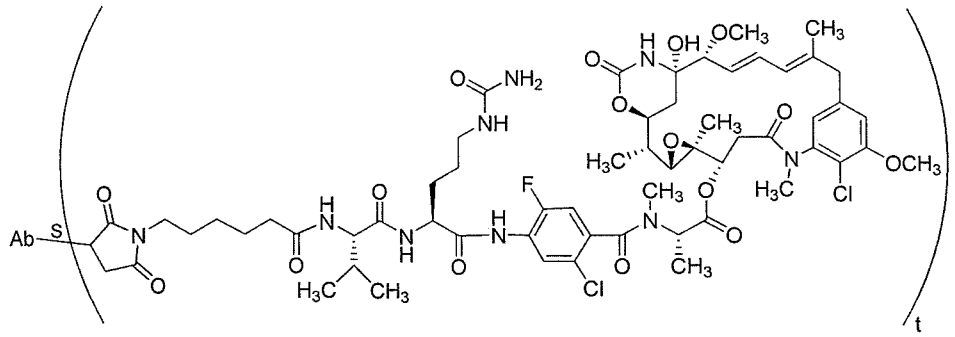
14. The compound of claim 1 selected from




t ,


t ,


t , or

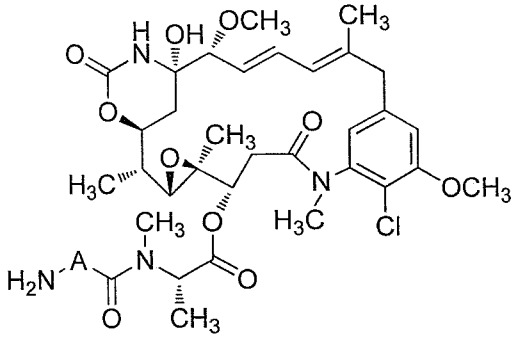

t ; and

t is an integer from 1 to 8.

15. The compound of any one of claims 1-10 or 14 wherein t is 1.

16. The compound of any one of claims 1-14 wherein the antibody or antigen binding fragment thereof is an anti-MUC16 antibody or an anti-PSMA antibody.

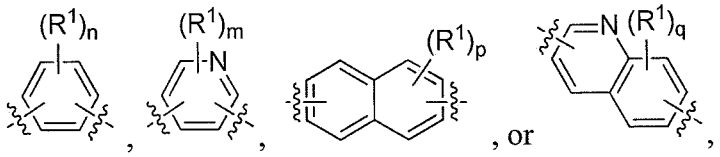
17. A compound of Formula II



(II)

or a pharmaceutically acceptable salt thereof, wherein A is arylene or heteroarylene.

18. The compound of claim 17, wherein A is



wherein

R^1 is, independently at each occurrence, alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkyl, haloalkoxy, heteroaryl, heterocycloalkyl, cyano, nitro, $-OR^A$, $-SO_2R^A$, $-C(=O)R^A$, or azido,

wherein

R^A is alkyl;

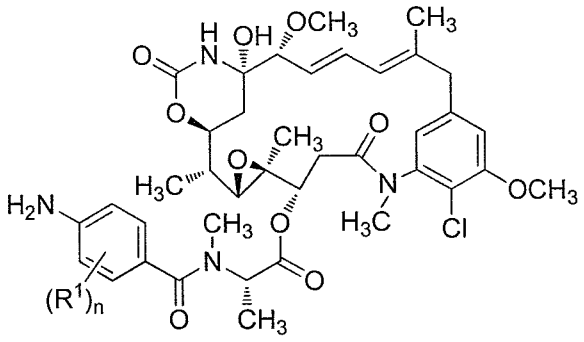
n is an integer from 0 to 4;

m is and integer from 0 to 3;

p is an integer from 0 to 6; and

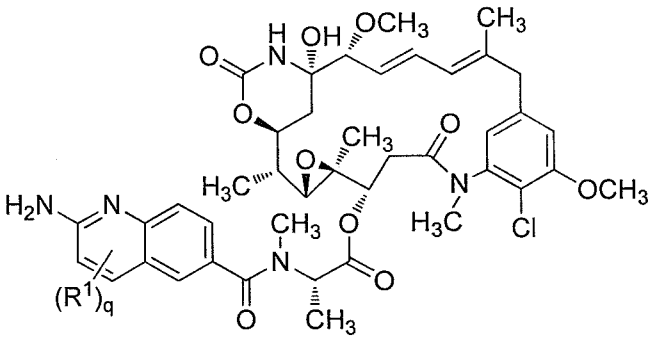
q is an integer from 0 to 5.

19. The compound of claim 17, wherein the compound is a compound of the Formula (IIA)



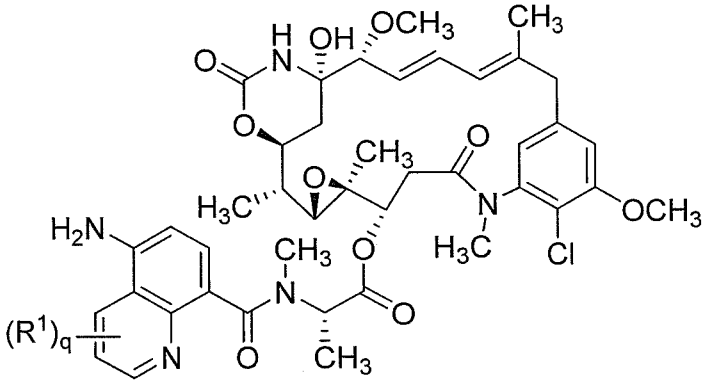
(IIA).

20. The compound of claim 17, wherein the compound is a compound of the Formula (IIB)



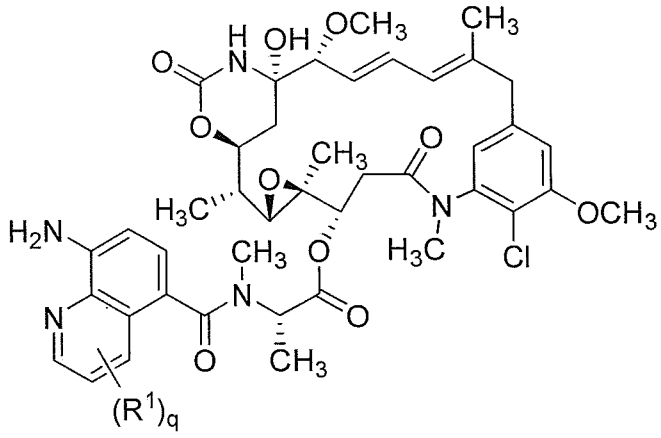
(IIB).

21. The compound of claim 17, wherein the compound is a compound of the Formula (IIB2)



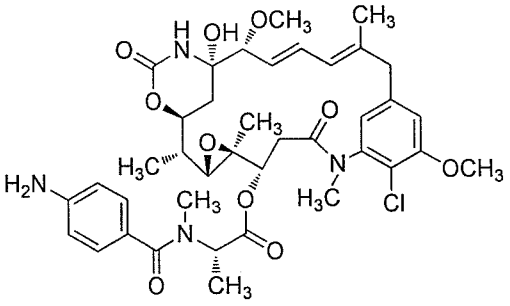
(IIB2).

22. The compound of claim 17, wherein the compound is a compound of the Formula (IIB3)

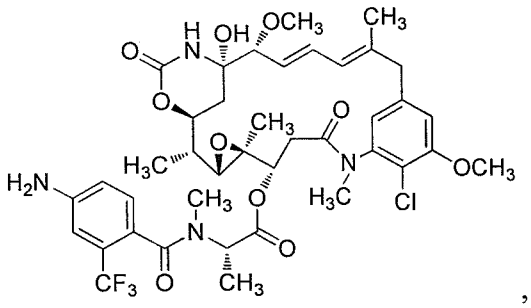


(IIB3).

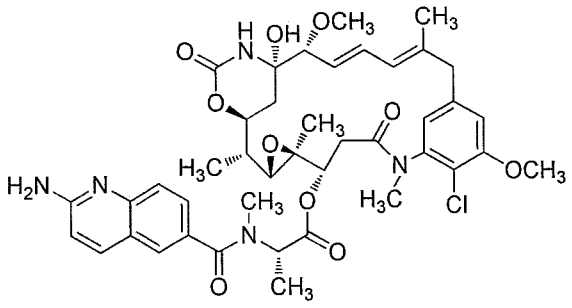
23. The compound of claim 17, wherein the compound is



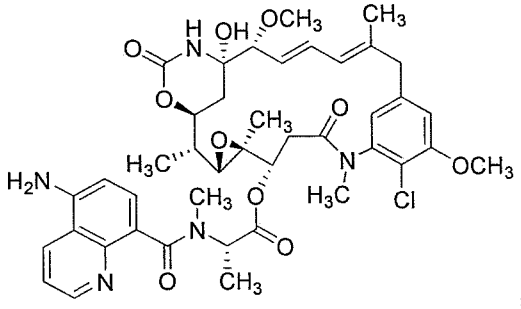
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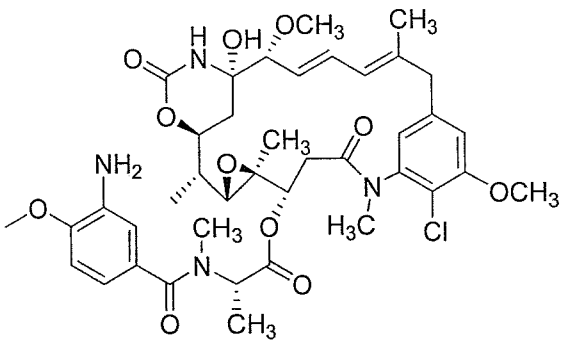
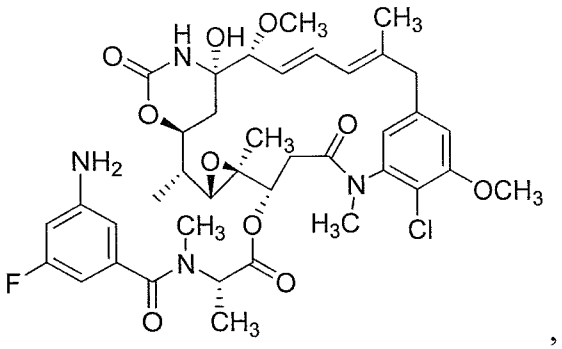
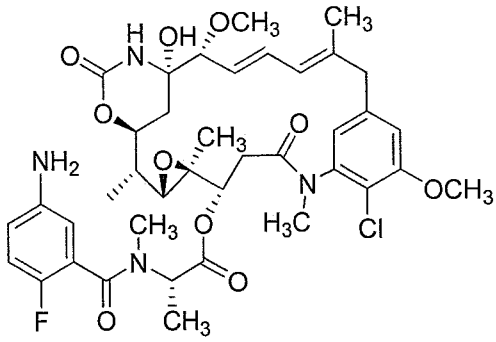
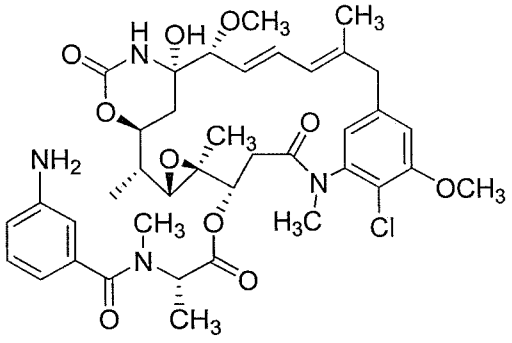
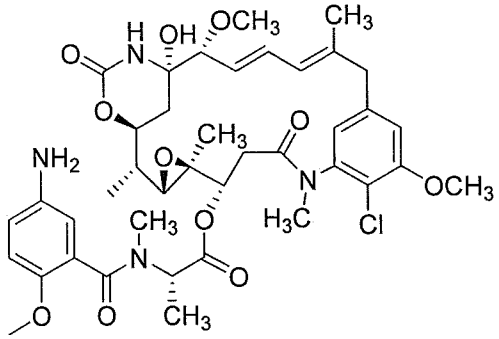
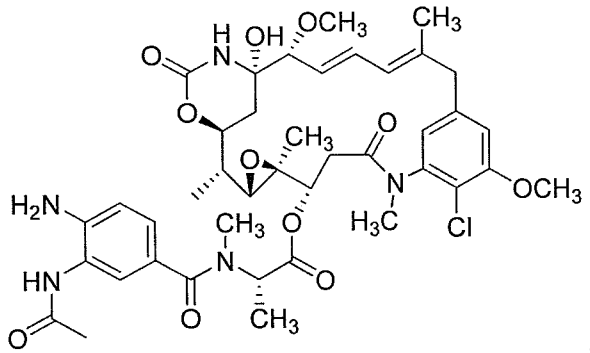
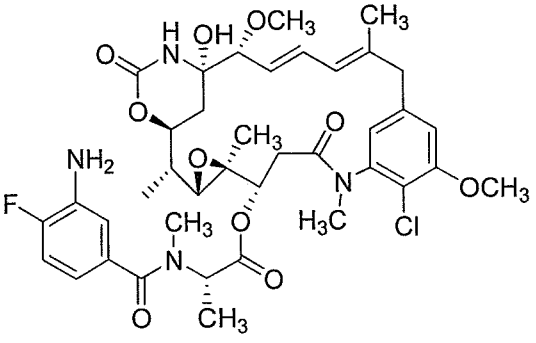
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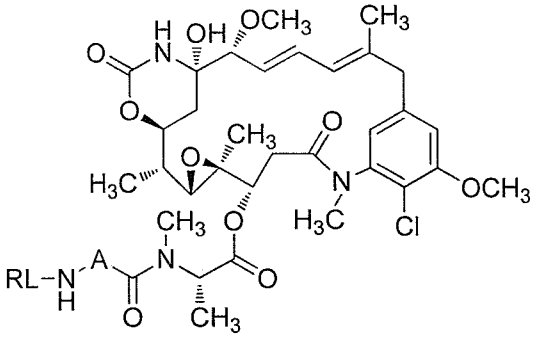
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, or

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24. A pharmaceutical composition comprising the compound of any one of claims 1-23 and a pharmaceutically acceptable excipient.

25. Use of a compound of any one of claims 1-23 or a composition of claim 24 in the manufacture of a medicament for treating cancer .

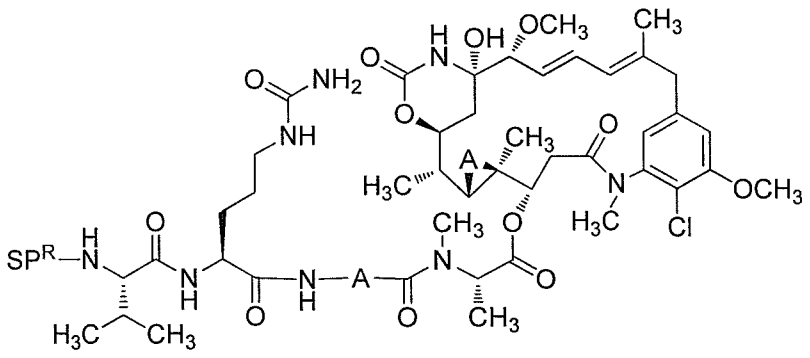
26. A compound of Formula P1



P1

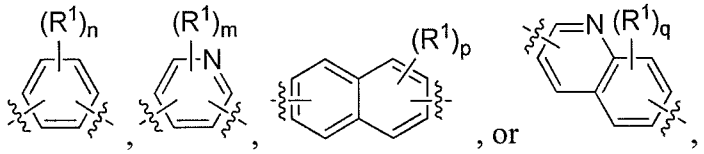
wherein A is arylene or heteroarylene; and RL is a reactive linker.

27. The compound of claim 26, wherein the compound is a compound of Formula P1B



P1B

wherein A is



wherein

R^1 is alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkyl, haloalkoxy, heteroaryl, heterocycloalkyl, cyano, nitro, , , , or azido,

wherein

R^A is alkyl;

n is an integer from 0 to 4;

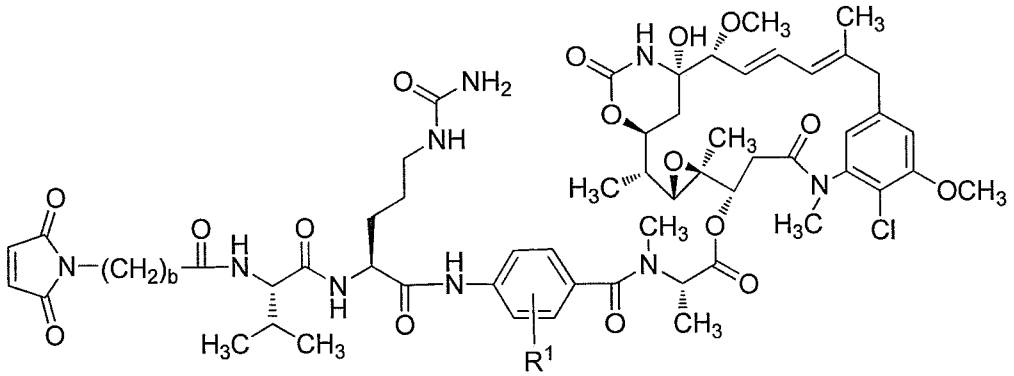
m is an integer from 0 to 3;

p is an integer from 0 to 6;

q is an integer from 0 to 5; and

SP^R is a reactive spacer.

28. The compound of claim 26, wherein the compound is a compound of Formula P1H



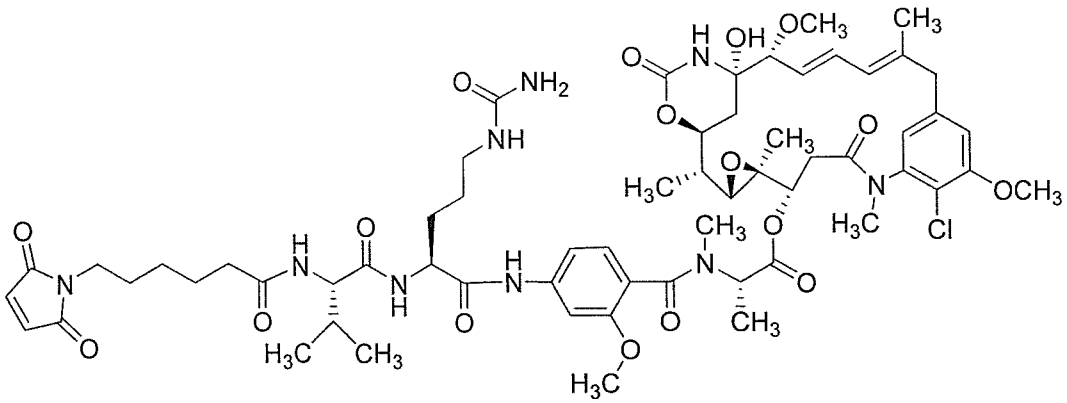
P1H

wherein

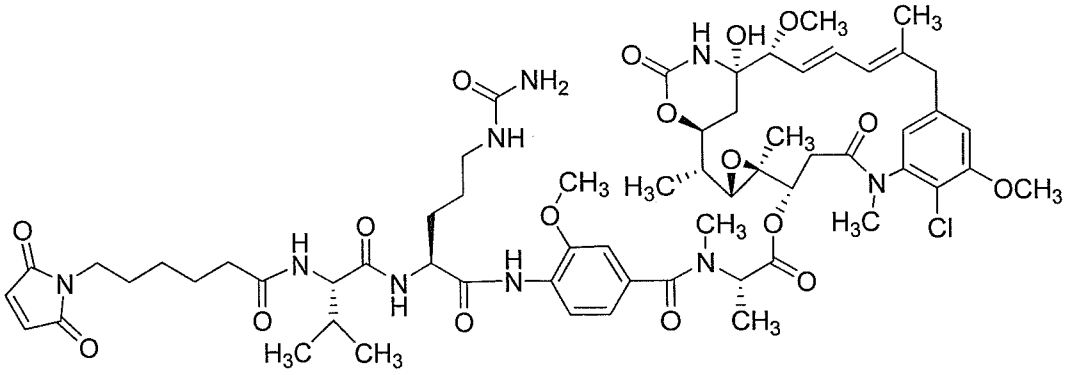
R^1 is hydrogen, alkoxy, halo, haloalkyl, or trifluoromethyl; and

b is an integer from 2 to 8.

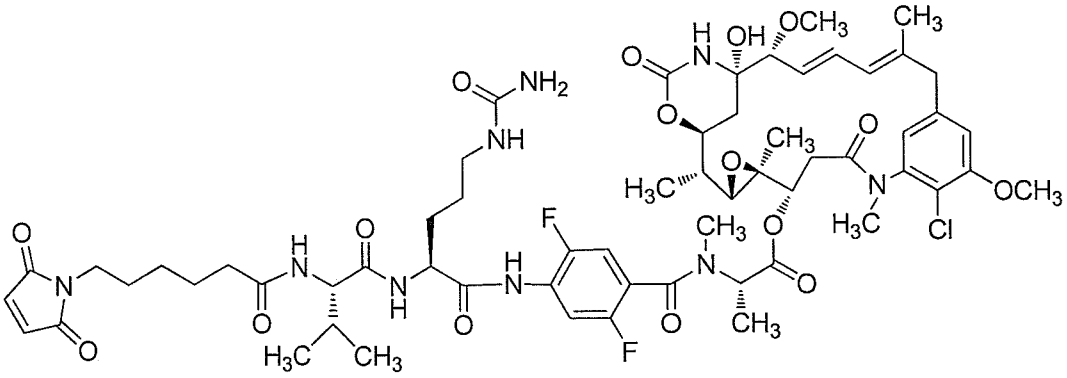
29. The compound of claim 26, wherein the compound is



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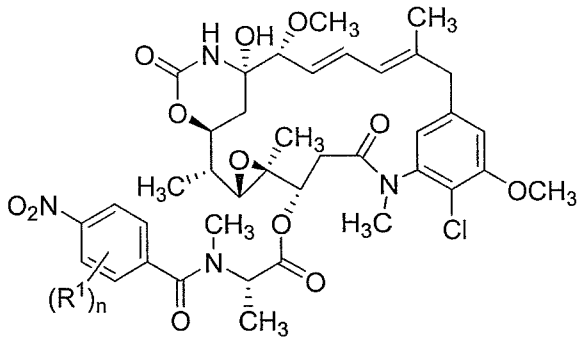


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32. The compound of claim 31, wherein the compound is a compound of Formula PP5A



PP5A

wherein

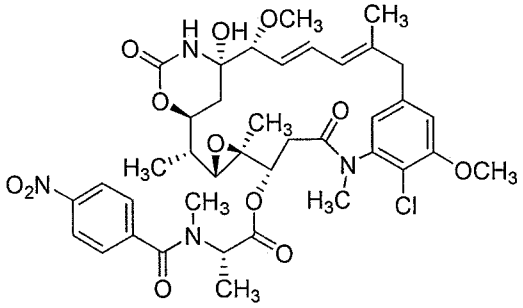
R^1, independently at each occurrence, is alkyl, alkenyl, alkynyl, alkoxy, haloalkyl, haloalkoxy, heteroalkyl, aryl, alkaryl, aralkyl, halo, heteroaryl, heterocycloalkyl, cyano, nitro, -§-OR^A, -§-SO_2R^A, -§-C(=O)-R^A, or azido,

wherein

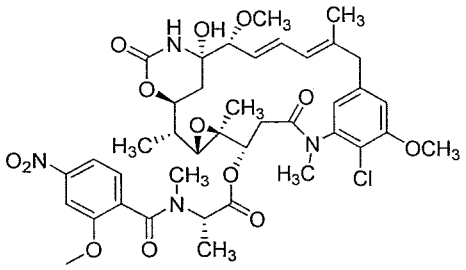
R^A is alkyl; and

n is an integer from 0 to 4.

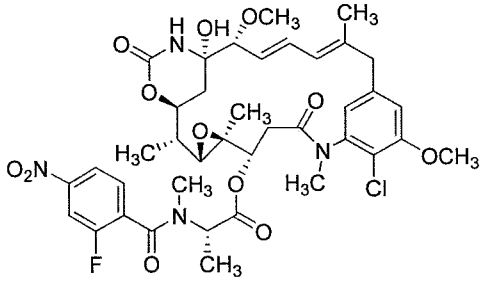
33. The compound of claim 31, wherein the compound is a compound selected from



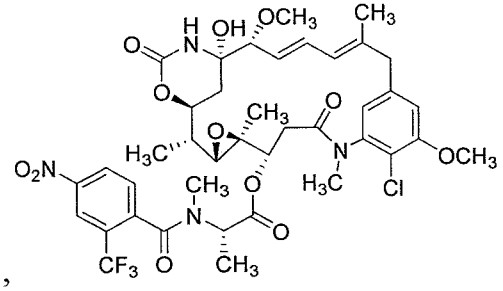
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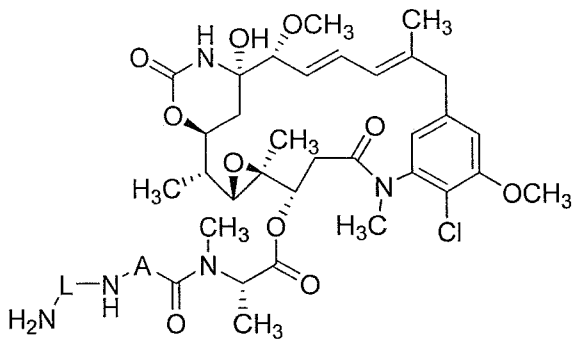
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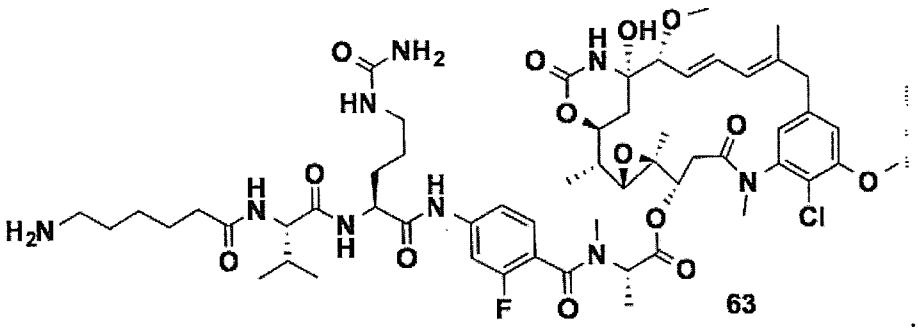
PT1

wherein

A is arylene or heteroarylene; and

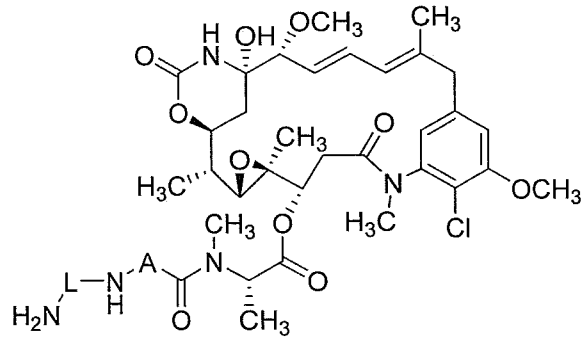
L is a linker.

38. The process of claim 37, wherein the compound of Formula (PT1) is



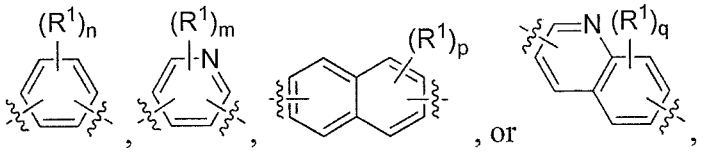
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39. The process of any one of claims 37 or 38, wherein the compound of Formula (PT1) of step (a) is



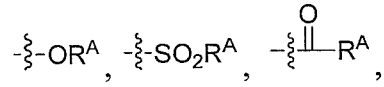
PT1

wherein A is



wherein

R^1, independently at each occurrence, is alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkyl, haloalkoxy, heteroaryl, heterocycloalkyl, hydroxyl, cyano, nitro,



wherein

R^A is alkyl or heteroalkyl;

n is an integer from 0 to 4;

m is an integer from 0 to 3;

p is an integer from 0 to 6; and

q is an integer from 0 to 5.

40. The process of any one of claims 37-39, further comprising

(b) reacting the glutaminyl-modified antibody with a reactive payload compound to form an antibody-payload conjugate.

41. The process of any one of claims 37-39, further comprising

(b) reacting the glutaminyl-modified antibody with a reactive linker-payload compound to form an antibody-linker-payload conjugate.

42. The process of any one of claims 37-39, further comprising

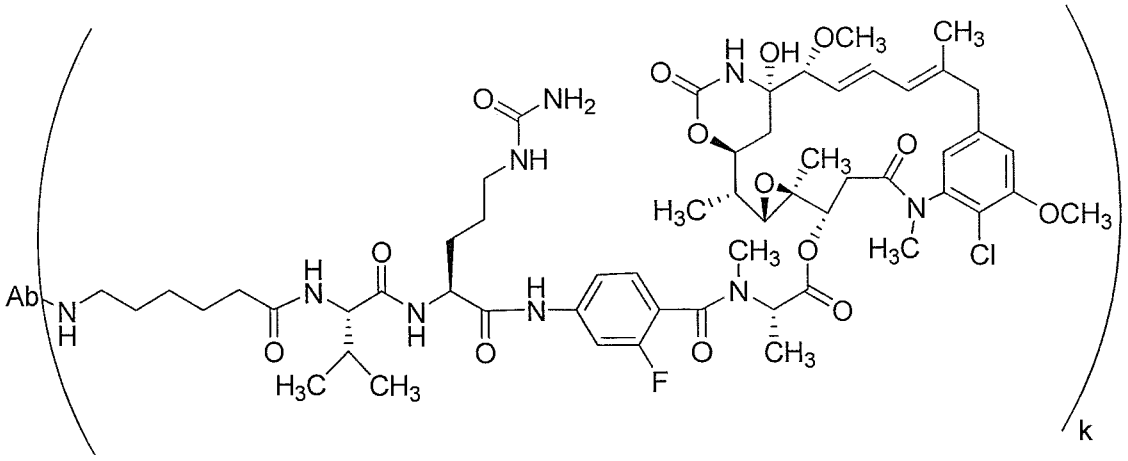
(b) reacting the glutaminyl-modified antibody with a reactive linker compound to form an antibody-linker conjugate; and

(c) reacting the antibody-linker conjugate with a reactive payload compound to form an antibody-linker-payload conjugate.

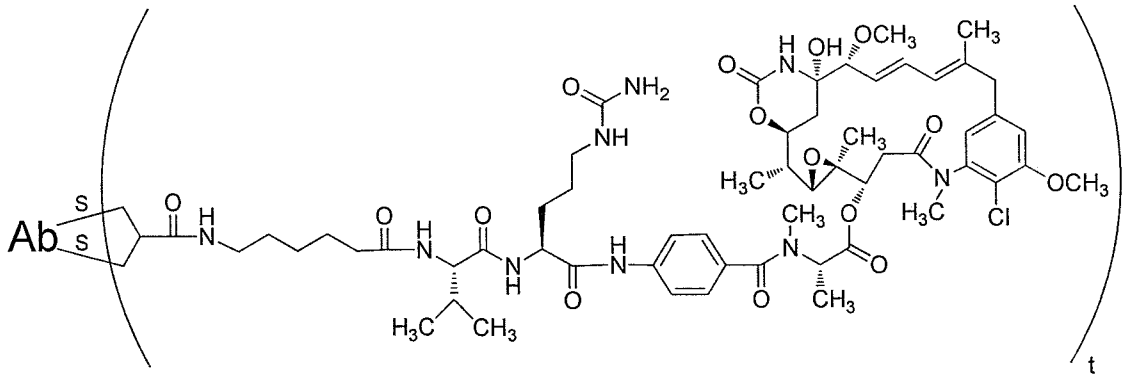
43. A glutaminyl-modified antibody produced by the process of any one of claims 37-39.

44. A pharmaceutical composition comprising the antibody of claim 43 and one or more pharmaceutically acceptable diluents, excipients, or carriers.

45. Use of the antibody of claim 43 in the manufacture of a medicament for treating a condition in a subject in need thereof, wherein the condition is selected from the group consisting of cancer, renal cell carcinoma, pancreatic carcinoma, head and neck cancer, prostate cancer, malignant gliomas, osteosarcoma, colorectal cancer, gastric cancer, gastric cancer with MET amplification, malignant mesothelioma, multiple myeloma, ovarian cancer, small cell lung cancer, non-small cell lung cancer, synovial sarcoma, thyroid cancer, breast cancer, and melanoma.



, and



,

wherein

Ab is an antibody or an antigen binding fragment thereof;

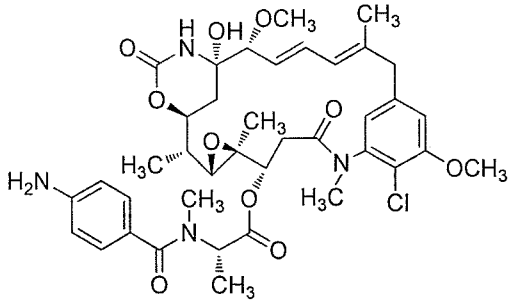
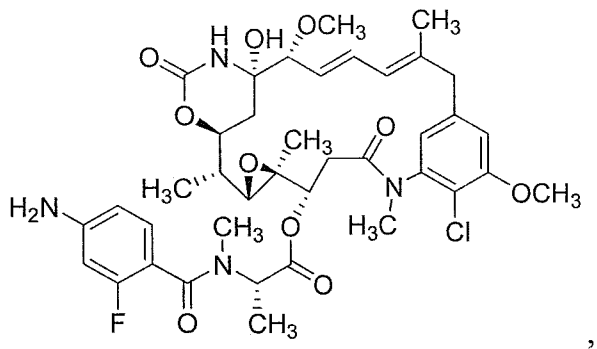
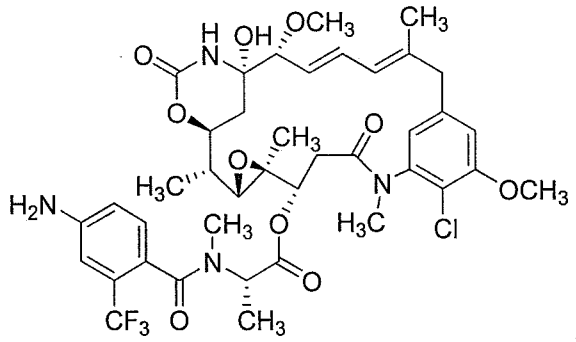
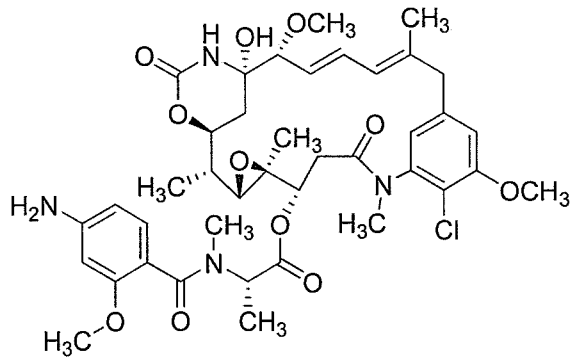
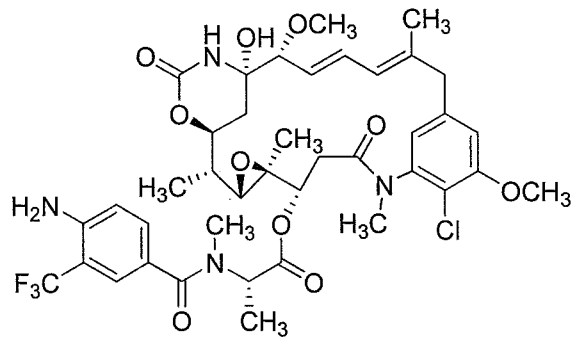
—S— is a bond to a cysteine residue of the antibody or an antigen binding fragment thereof;

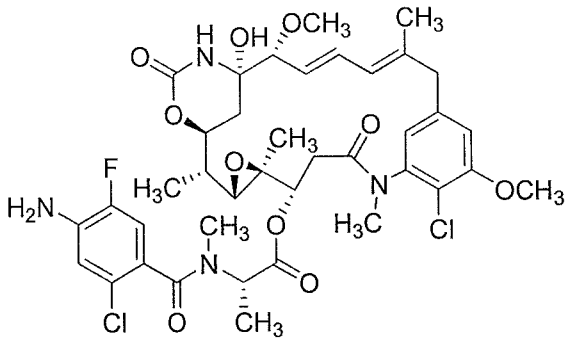
—N— is a bond to a lysine residue of the antibody or an antigen binding fragment thereof;

k is 1, 2, 3, or 4; and

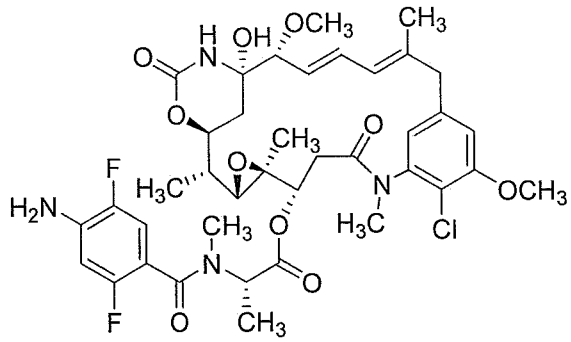
t is 1, 2, 3, or 4.

48. The compound of claim 17 selected from the group consisting of

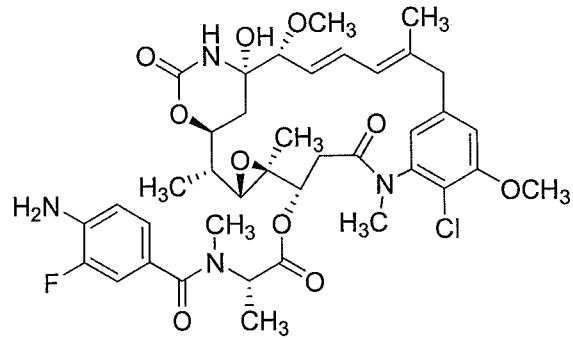

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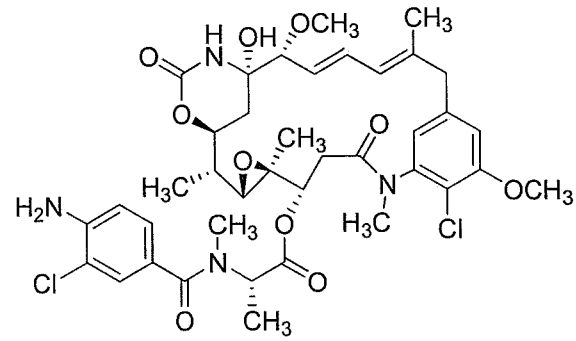
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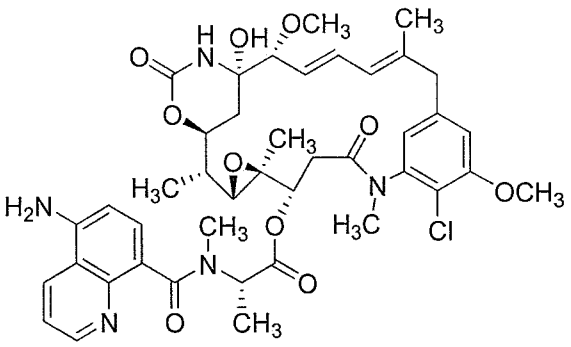
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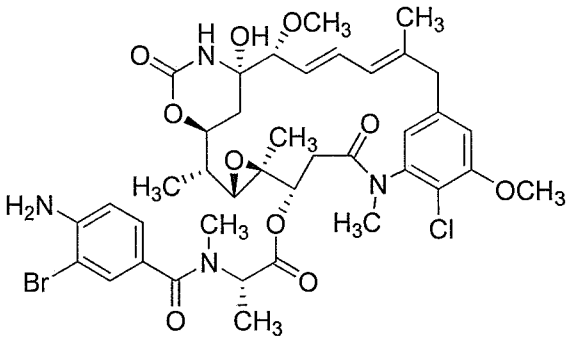
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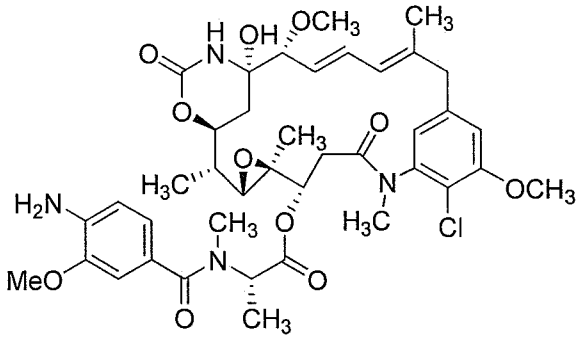
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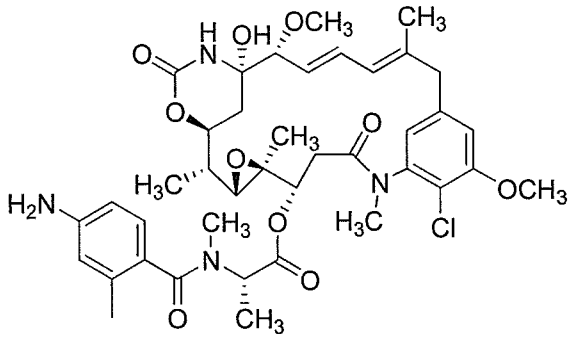
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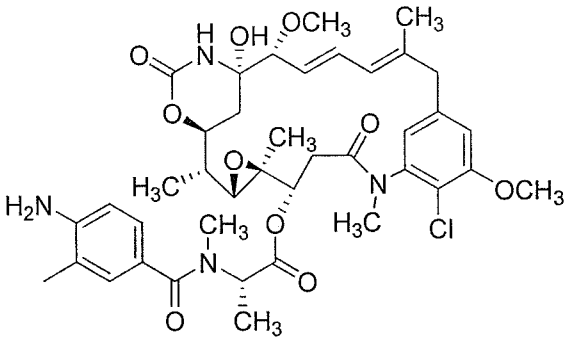
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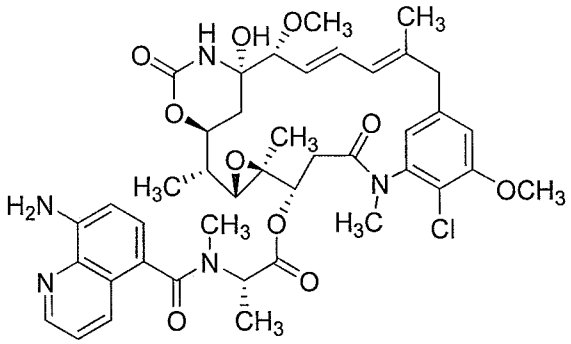
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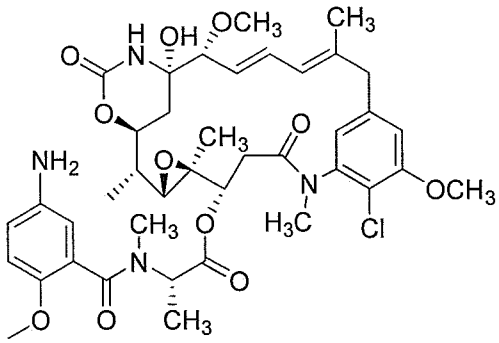
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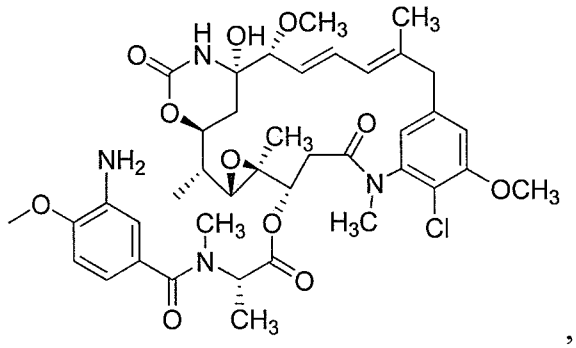
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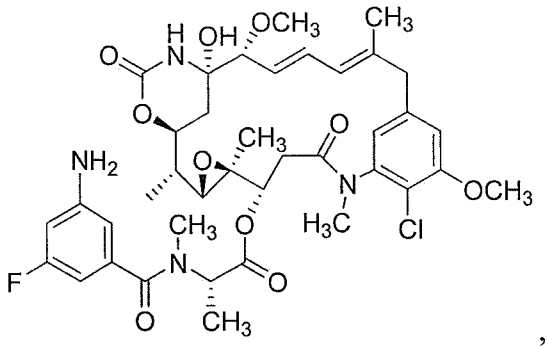
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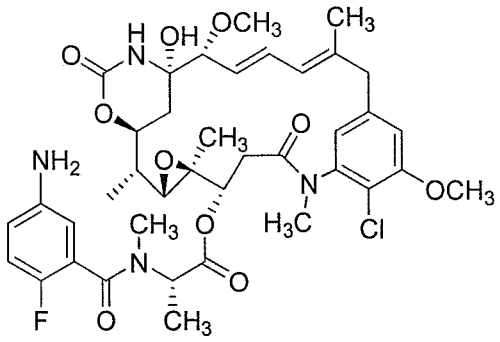
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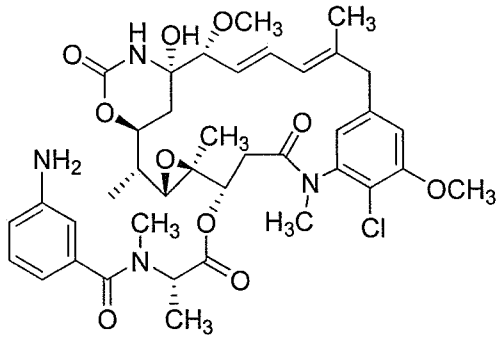
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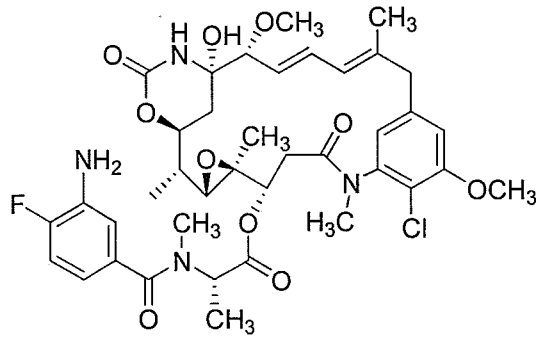
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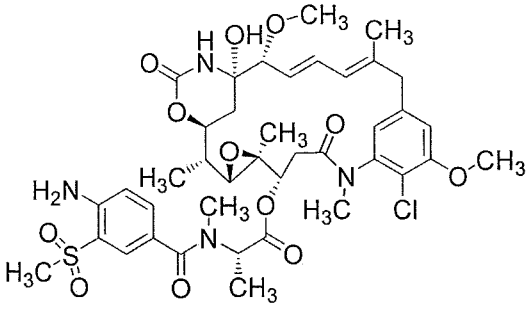
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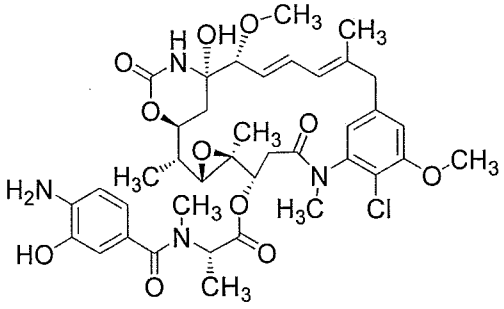


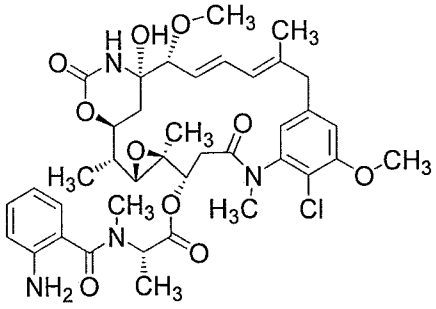
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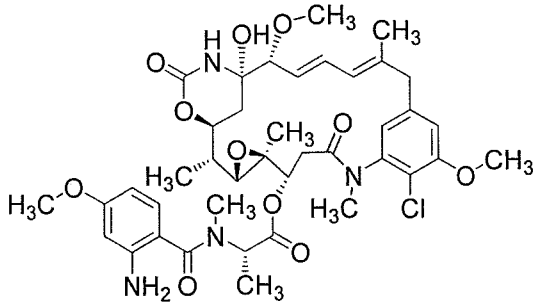


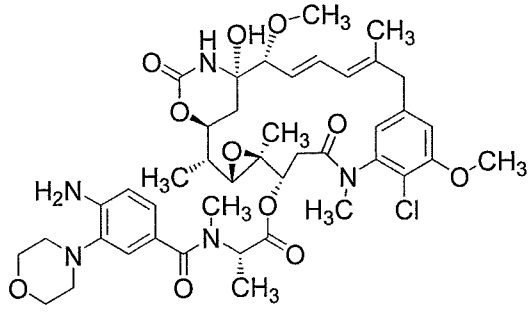
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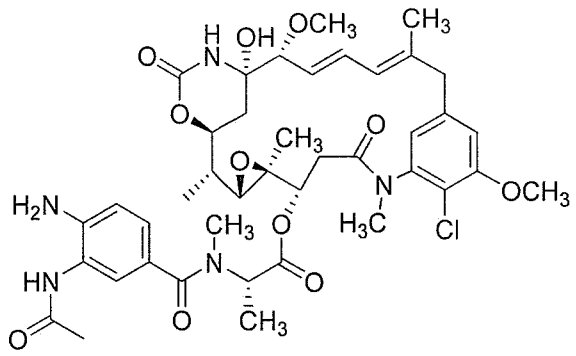

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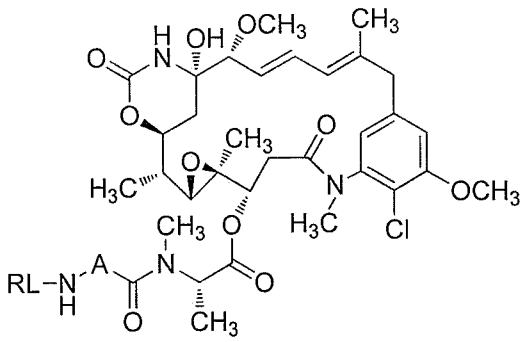

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49. A compound comprising an antibody or antigen binding fragment thereof conjugated to a compound of Formula P1

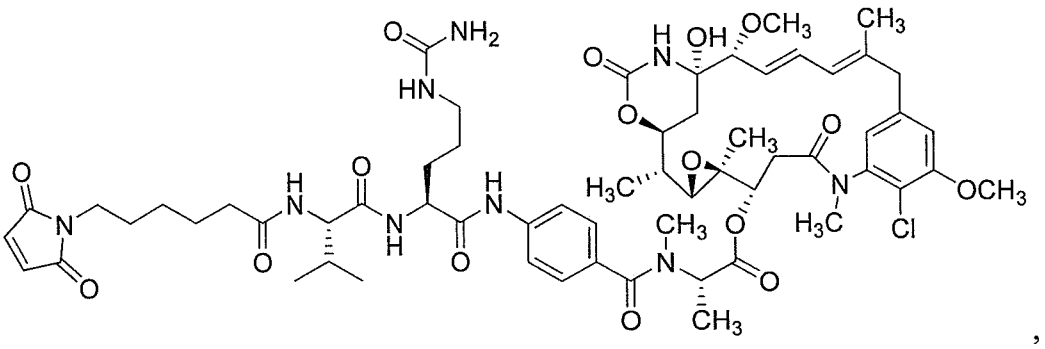


wherein

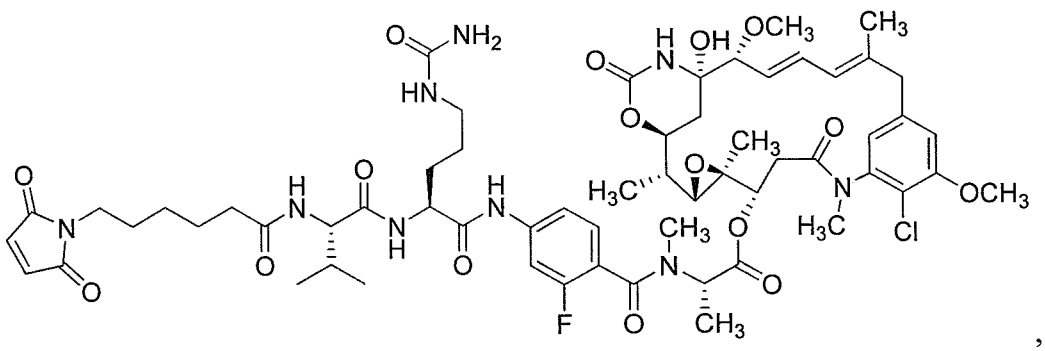
RL is a reactive linker; and

A is arylene or heteroarylene.

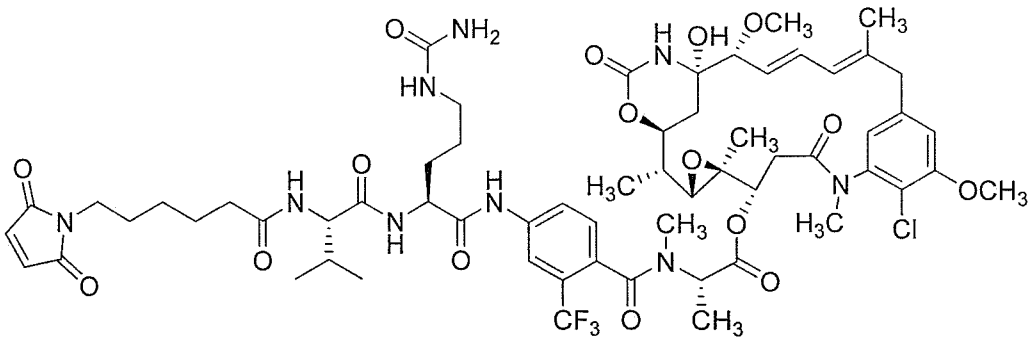
50. The compound of claim 49 wherein the compound of Formula P1 is selected from the group consisting of



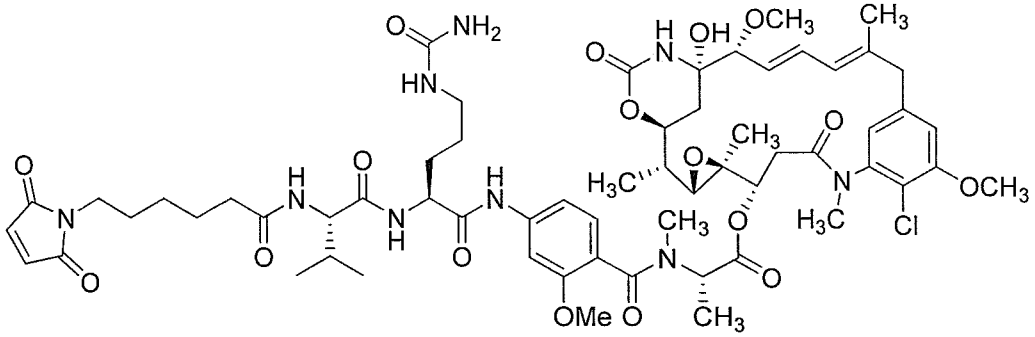
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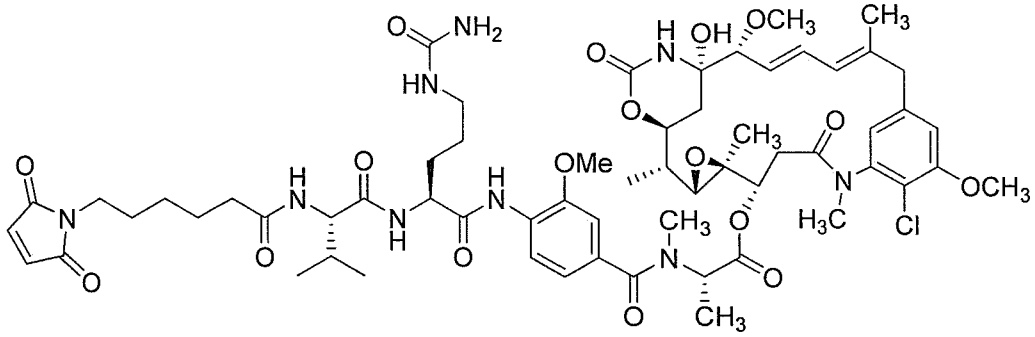
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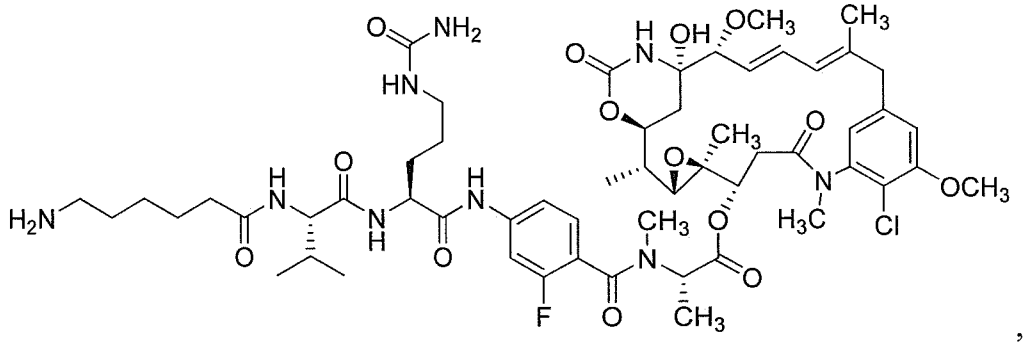
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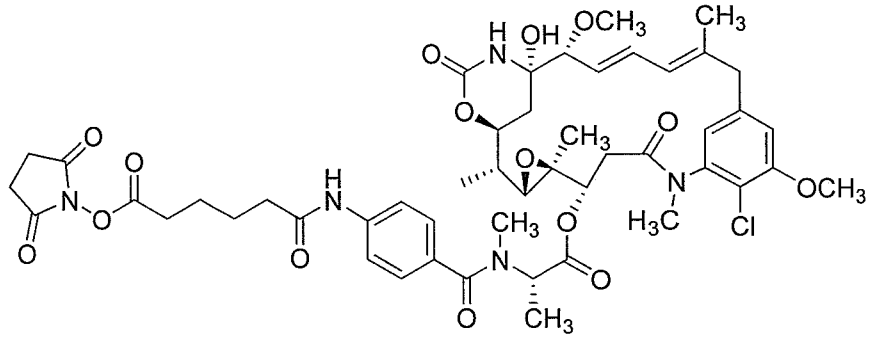
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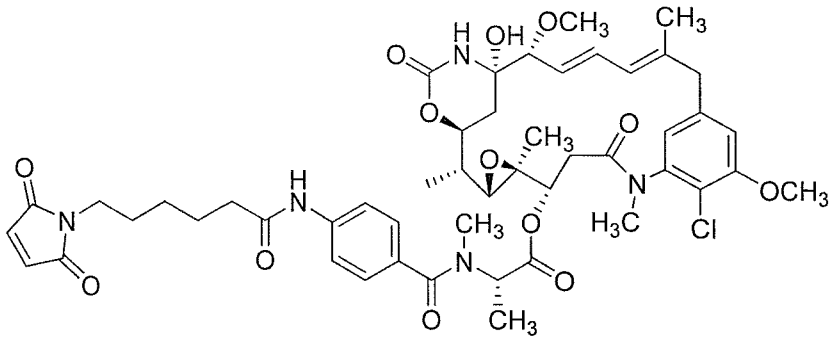
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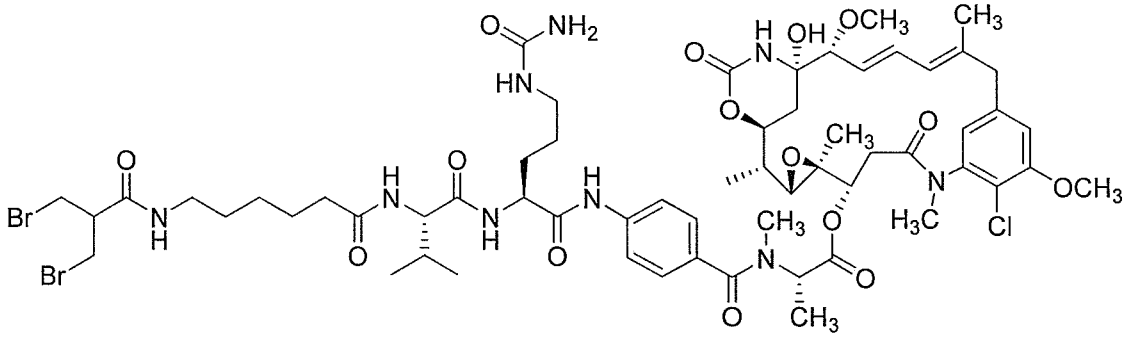
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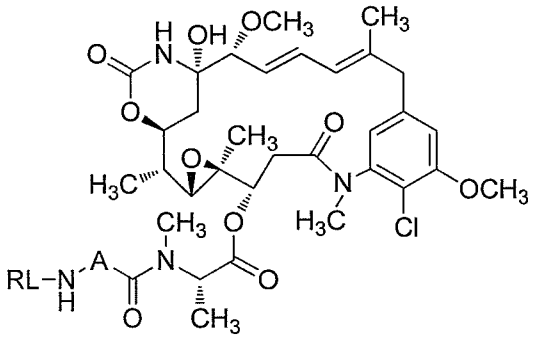
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51. The compound of Formula I in claim 1, wherein BA is anti-PSMA, anti-MUC16, anti-EGFRvIII, or anti-STEAP-2 antibody.

52. A compound prepared by the process of contacting a compound of Formula P1 with an antibody or antigen binding fragment thereof under conjugation conditions,



P1

wherein A is arylene or heteroarylene;

RL is a reactive linker; and

wherein Formula P1 is coupled to one or more cysteine or lysine residues of the antibody or antigen binding fragment thereof.

53. The compound of any one of claims 1, 24, 25, 34, 37, 44, 45, or 47 wherein the antibody

or antigen binding fragment thereof binds a tumor antigen.

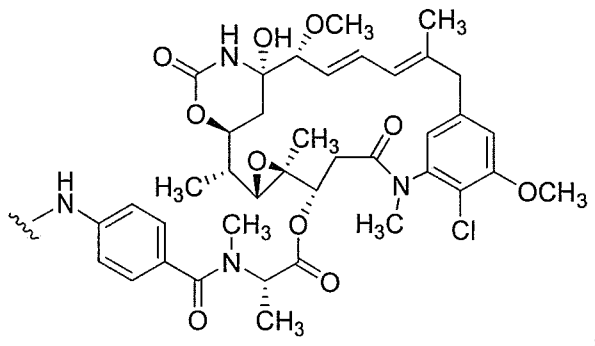
54. The use of claim 45, wherein the condition is cancer.

55. The use claim 54, wherein the cancer is ovarian cancer, prostate cancer, or breast cancer.

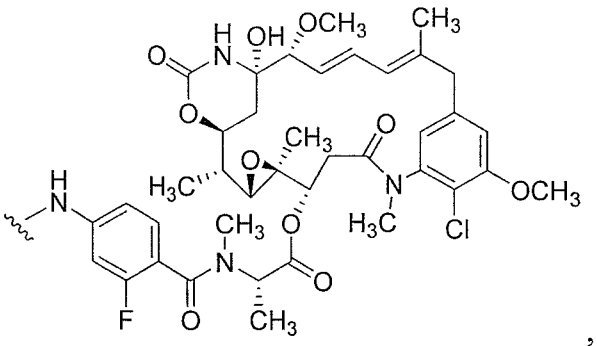
56. The use of claim 54, wherein the cancer is a tumor that expresses PSMA, PRLR, or MUC16.

57. The compound of any one of claims 1-12, wherein the antibody or antigen binding fragment thereof is selected from the group consisting of an anti-EGFR antibody, anti-ErbB2 antibody, anti-ErbB3 antibody, anti-ErbB4 antibody, antibody that specifically binds EGFRvIII, anti-cMET antibody, anti-IGF1R antibody, anti-PDGFR-α antibody, anti-PDGFR-β antibody, anti-PDGF-A, anti-PDGF-B, anti-PDGF-C, anti-PDGF-D antibody,anti-VEGF antibody, anti-DLL4 antibody, anti-Ang2 antibody, anti-FOLH1 antibody, anti-STEAP1 antibody, anti-STEAP2 antibody, anti-TMPRSS2 antibody, anti-MSLN antibody, anti-CA9 antibody, anti-uroplakin or anti-UPK3A antibody, anti-MUC16 antibody, anti-Tn antibody, anti-CLEC12A antibody, anti-TNFRSF17 antibody, anti-LGR5 antibody, a monovalent anti-CD20 antibody, anti-PRLR antibody, anti-PSMA antibody, and antibodies that bind to cytokines comprising IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-9, IL-11, IL-12, IL-13, IL-17, IL-18, or to their respective receptors.

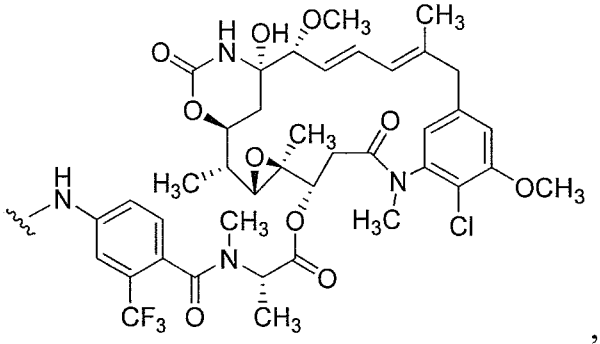
58. An antibody-drug conjugate comprising an antibody or antigen-binding fragment thereof conjugated to a payload selected from the group consisting of



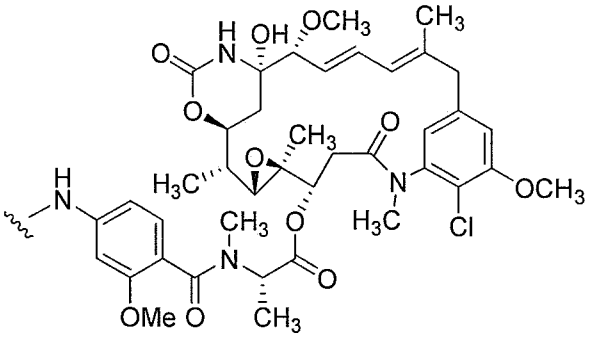
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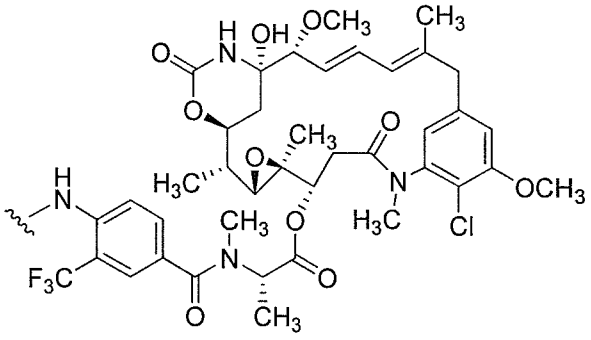
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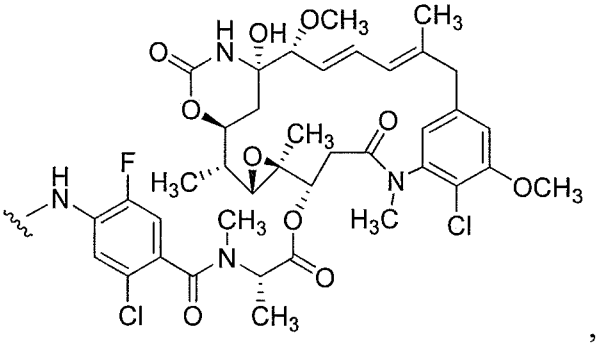
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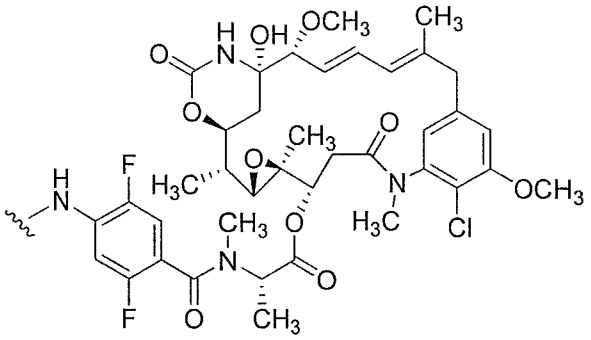
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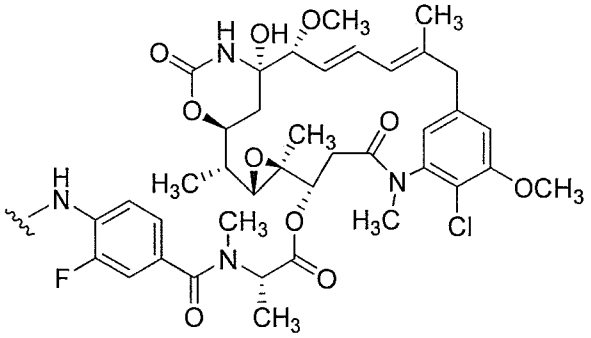
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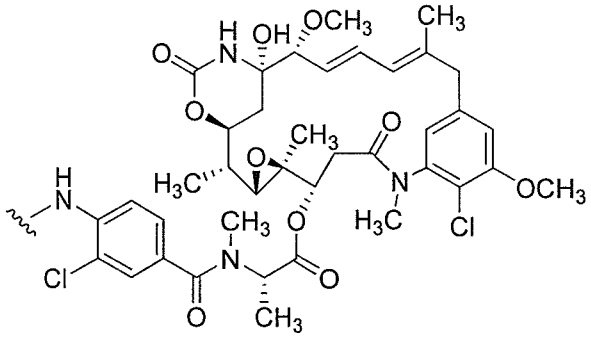
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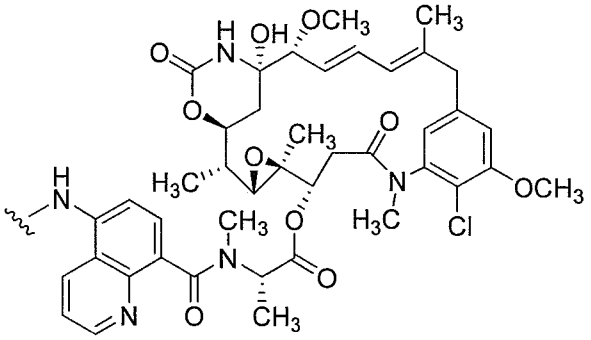
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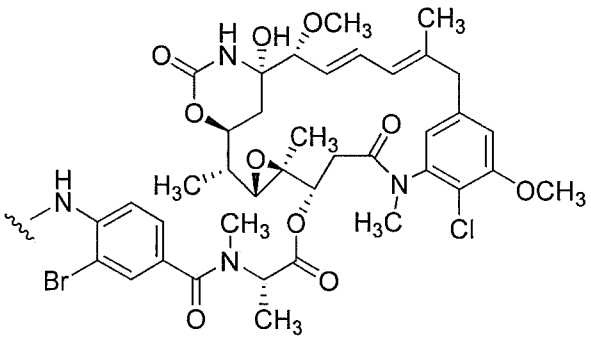
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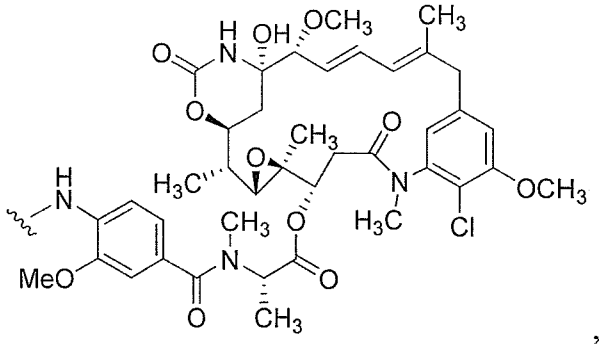
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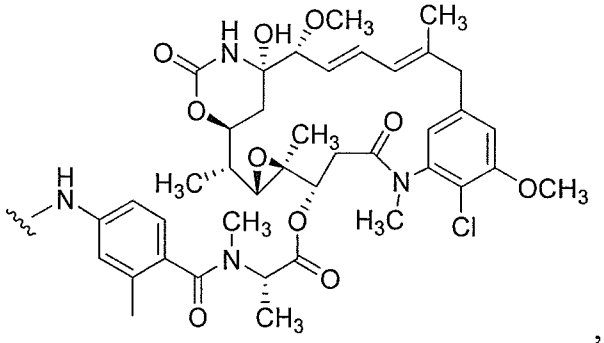
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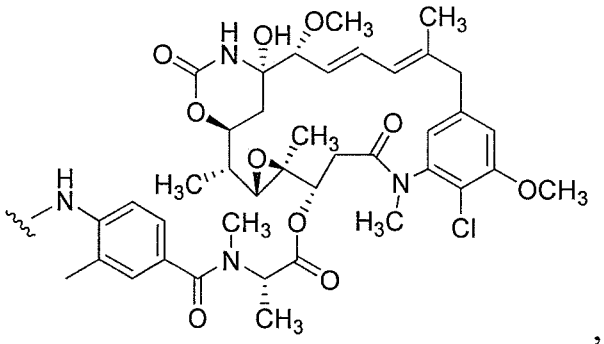
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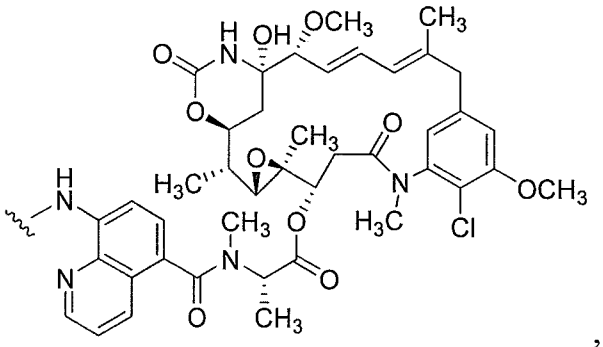
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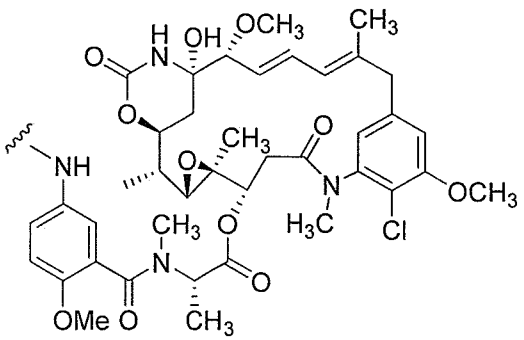
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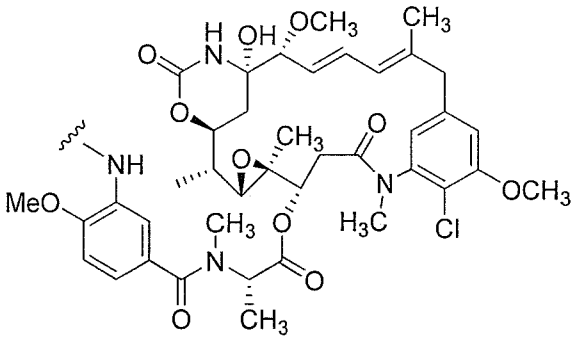
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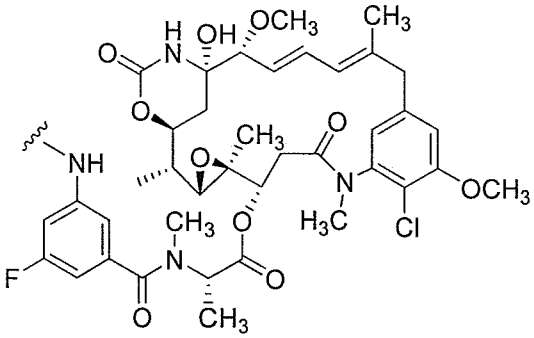
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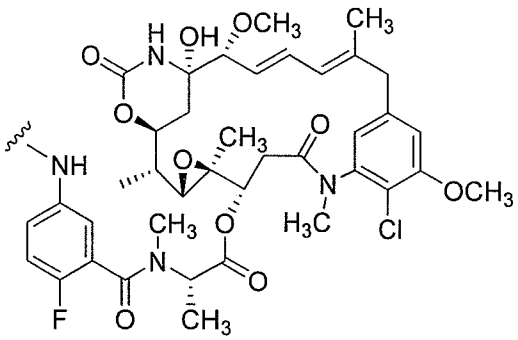
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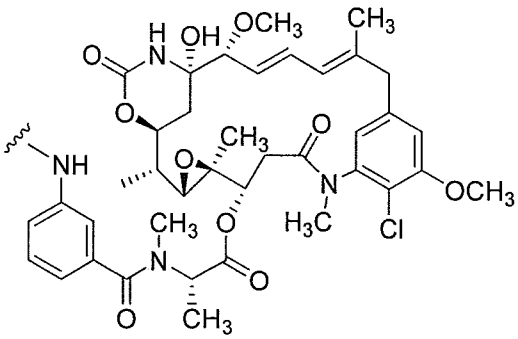
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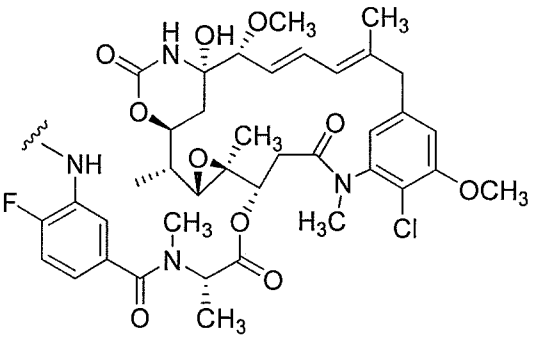
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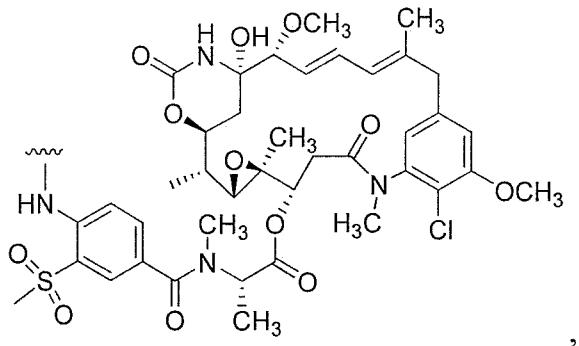
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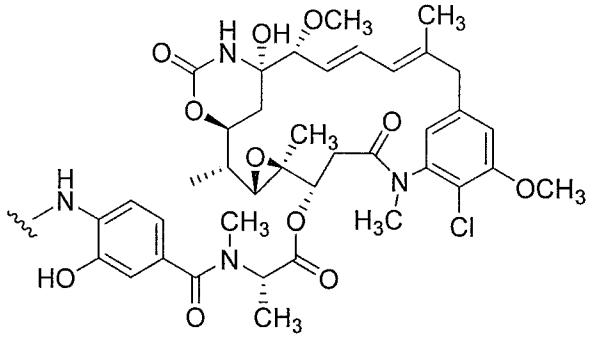
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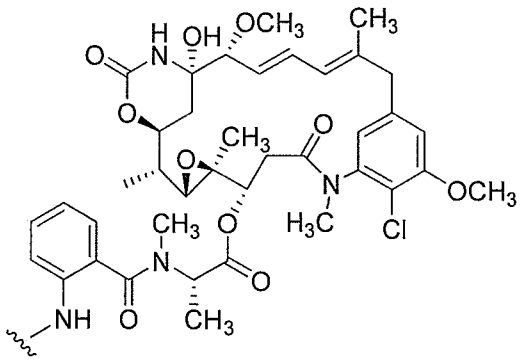
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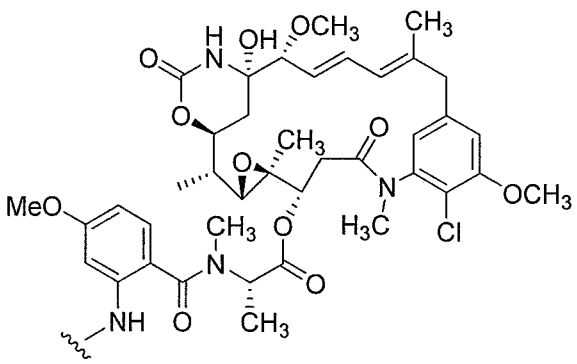
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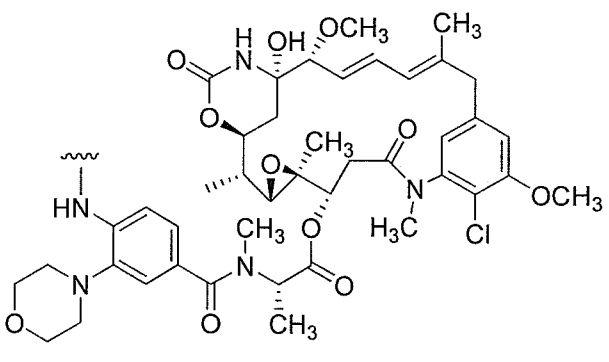
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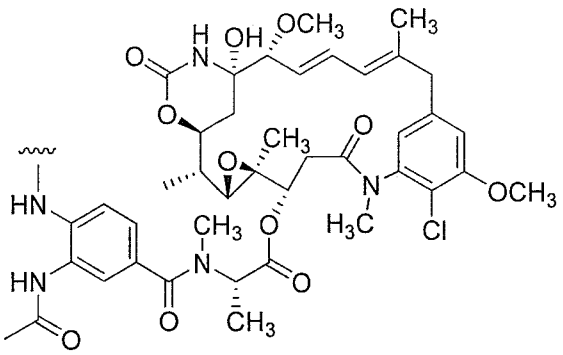
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, and



59. The antibody-drug conjugate of claim 58, wherein the payload is conjugated to the antibody-drug conjugate through a cleavable linker.