Claims

1. A compound of Formula (I):

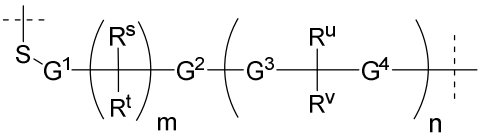
(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is a peptide;

R^2 is a radical of monomethyl auristatin E; and

L is a linker having the structure:



;

wherein the terminal S atom of the linker is bonded with a cysteine residue of the peptide to form a disulfide bond; and wherein:

G^1 is selected from a bond, phenyl, and C_{3-14} cycloalkyl;

G^2 is selected from -OC(O)- and -OC(O)NR^G-;

G^3 is C_{6-10} aryl;

G^4 is -OC(O)-;

each R^s and R^t are independently selected from H, halo, C_{1-6} alkyl, and C_{1-6} haloalkyl;

or each R^s and R^t, together with the C atom to which they are attached, form a C_{3-6} cycloalkyl ring;

R^u and R^v are independently selected from H, halo, C_{1-6} alkyl, and C_{1-6} haloalkyl;

each R^G is independently selected from H and C_{1-4} alkyl;

m is 0, 1, or 2; and

n is 0 or 1.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is a peptide having 5 to 50 amino acids, or

wherein R^1 is a peptide capable of selectively delivering R^2L- across a cell membrane having an acidic or hypoxic mantle, or

wherein R^1 is a peptide capable of selectively delivering R^2L- across a cell membrane having an acidic or hypoxic mantle having a pH less than about 6.0.

3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is a peptide comprising at least one of the following sequences:

ADDQNPWRAYLDLLFPTDTLLLDLLWCG (SEQ ID NO. 1; Pv1),

AEQNPIYWARYADWLFTTPLLLLDLALLVDADECG (SEQ ID NO. 2; Pv2), and/or

ADDQNPWRAYLDLLFPTDTLLLDLLWDADECG (SEQ ID NO. 3; Pv3).

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein G^1 is a bond.

5. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein G^1 is C_{3-14} cycloalkyl, or

wherein G^1 is cyclopentyl or cyclohexyl, wherein said cyclopentyl and cyclohexyl are each optionally fused with a phenyl group.

6. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein G^1 is phenyl.

7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein:

(a) each R^s and R^t are independently selected from H and C_{1-6} alkyl; and/or

(b) each R^s and R^t are independently selected from H and isopropyl; and/or

(c) each R^s and R^t are independently selected from H, methyl, and isopropyl, or

R^s and R^t together with the C atom to which they are attached form a cyclobutyl ring.

8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein m is 0, or wherein m is 2.

9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein G^2 is -OC(O)-.

10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein G^3 is phenyl.

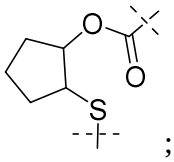
11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein R^u and R^v are each H.

12. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein n is 0.

13. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein n is 1.

14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein each R^G is independently selected from H and methyl, or wherein each R^G is H.

15. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein L has one of the following structures:



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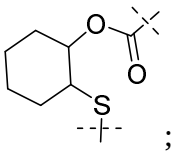

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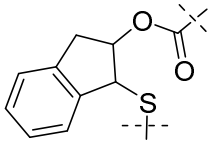

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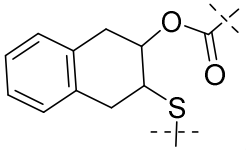

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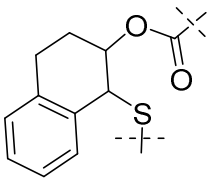
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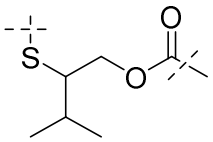
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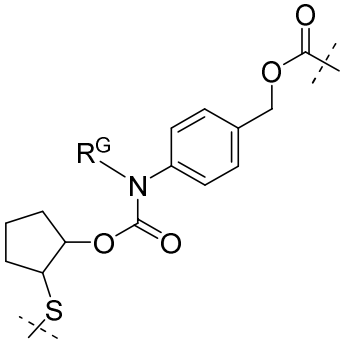
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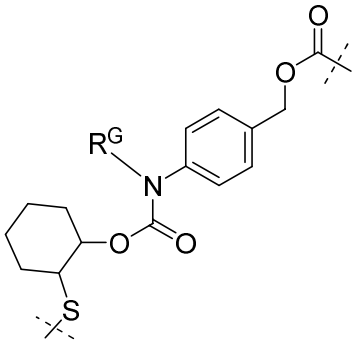
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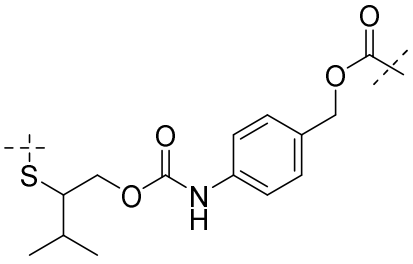
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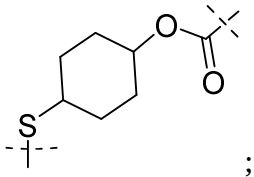
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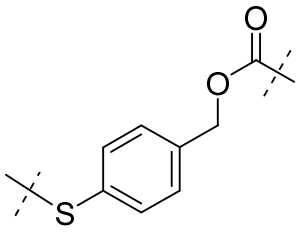
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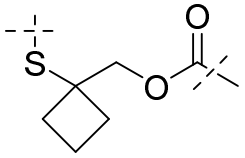

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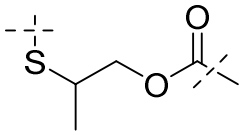

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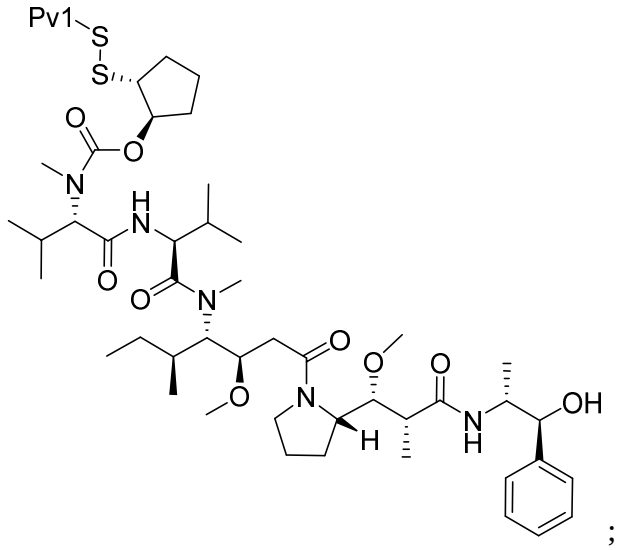
16. The compound of claim 1, wherein the compound is selected from one of the following:



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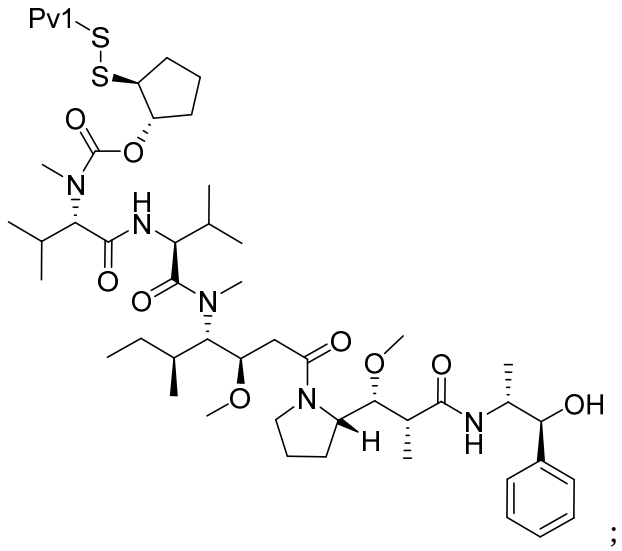

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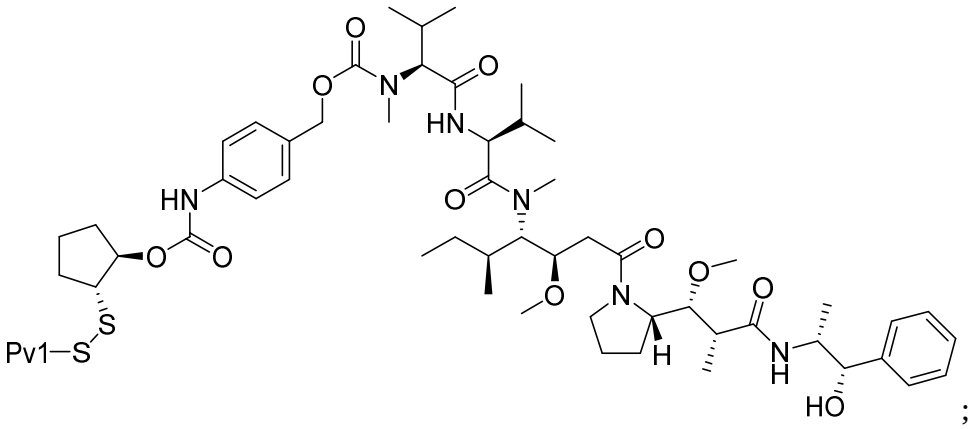
Pv1—S
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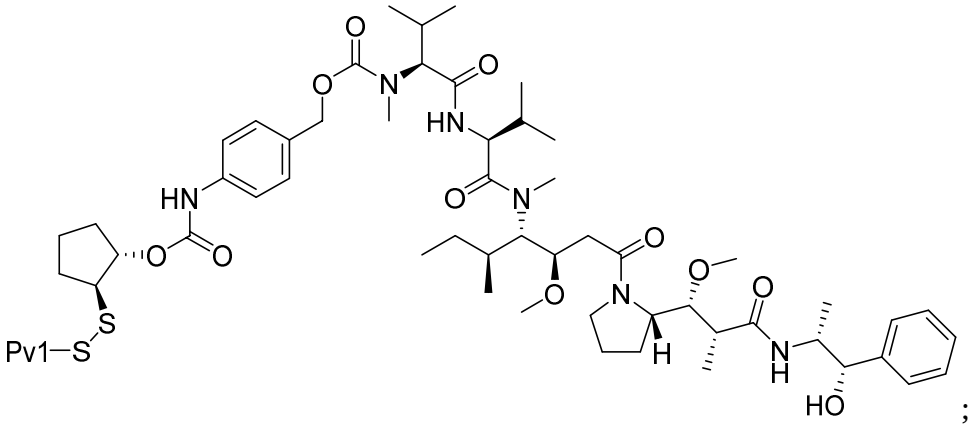
Pv1—S
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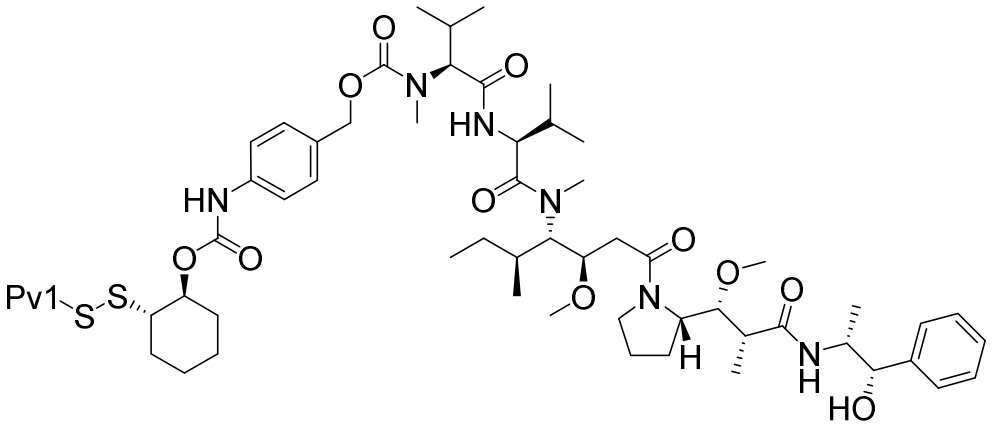
Pv1
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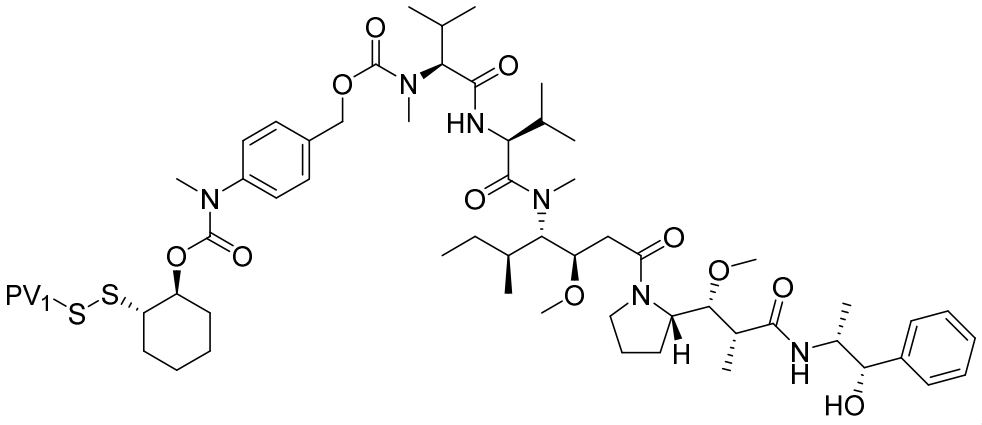
PV1
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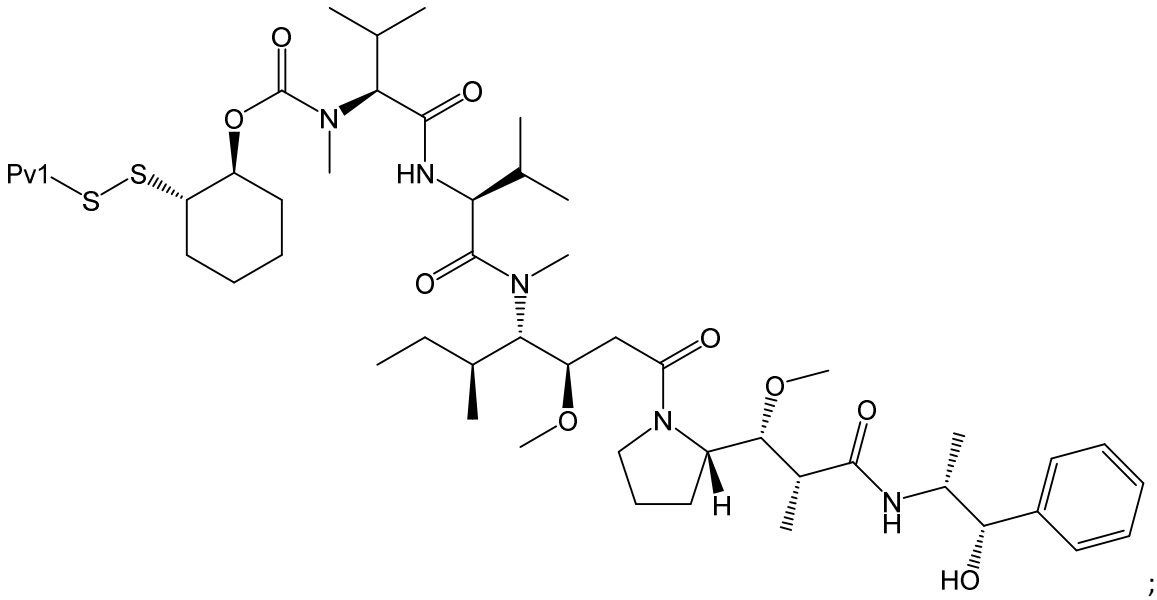
Pv1
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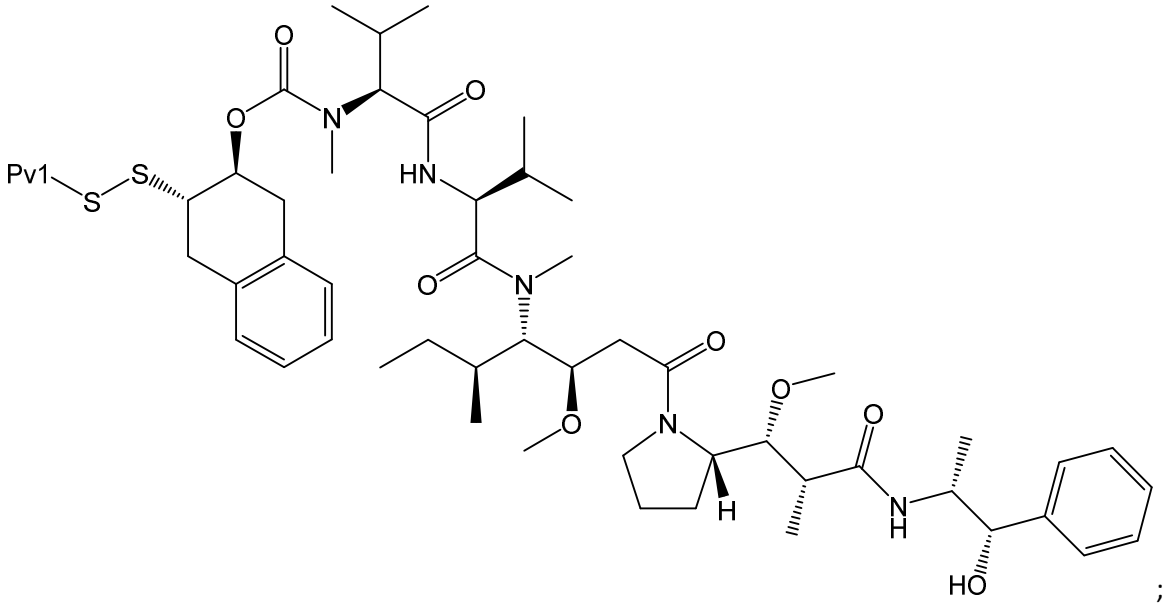
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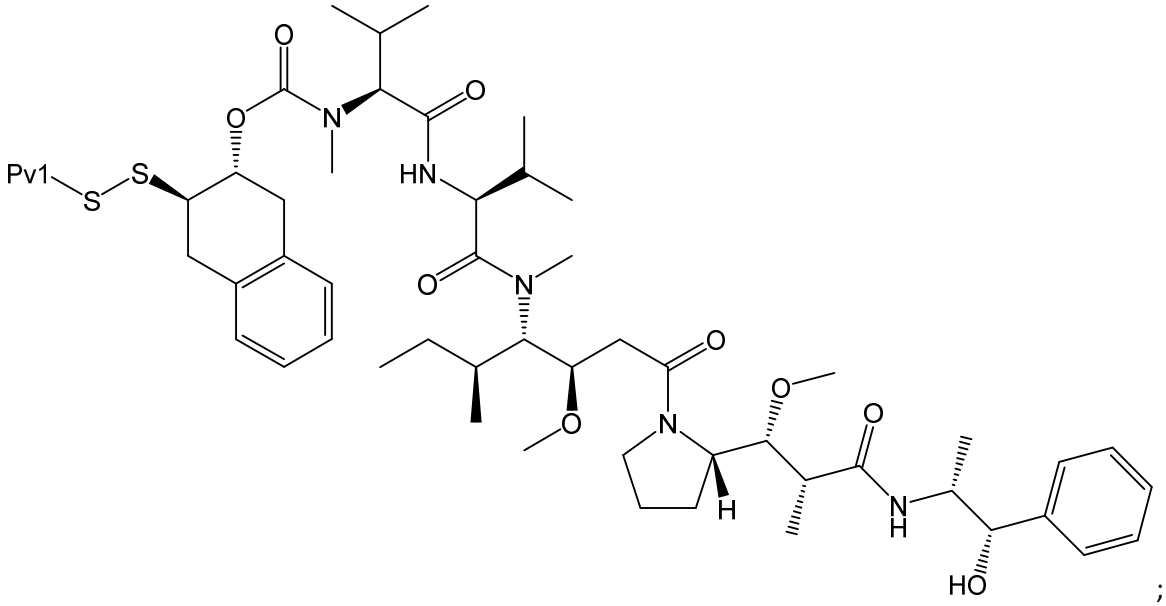
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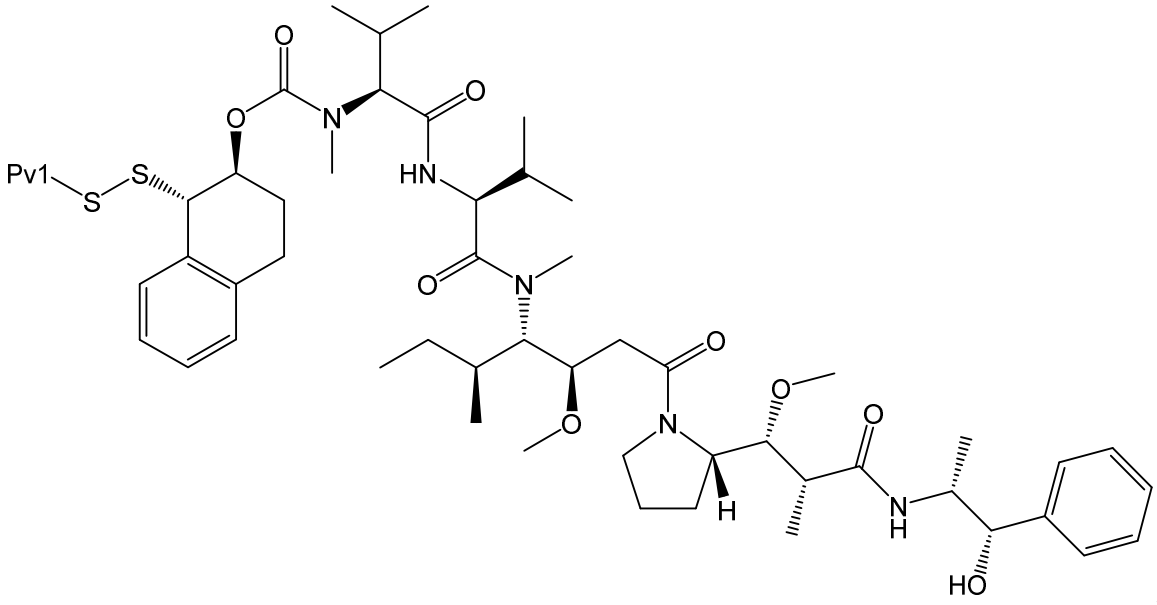
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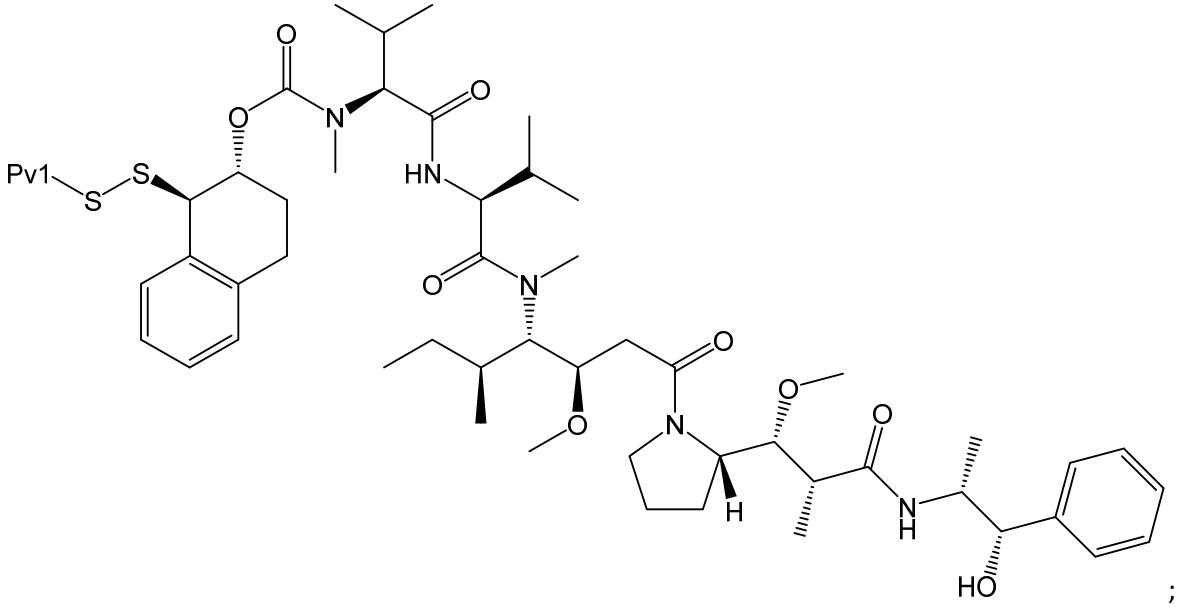
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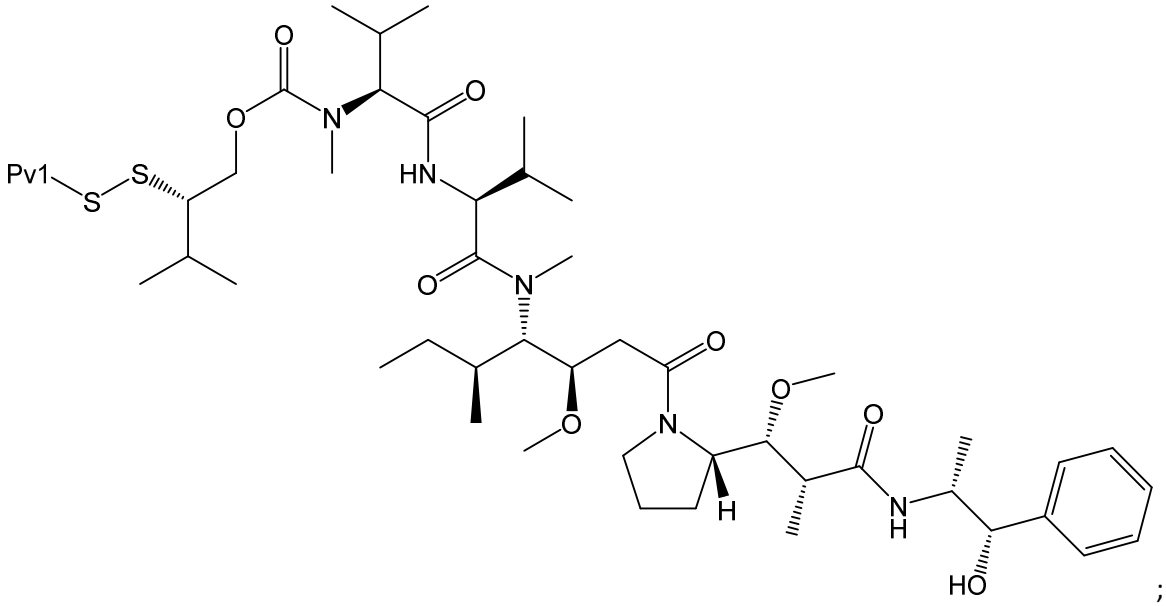
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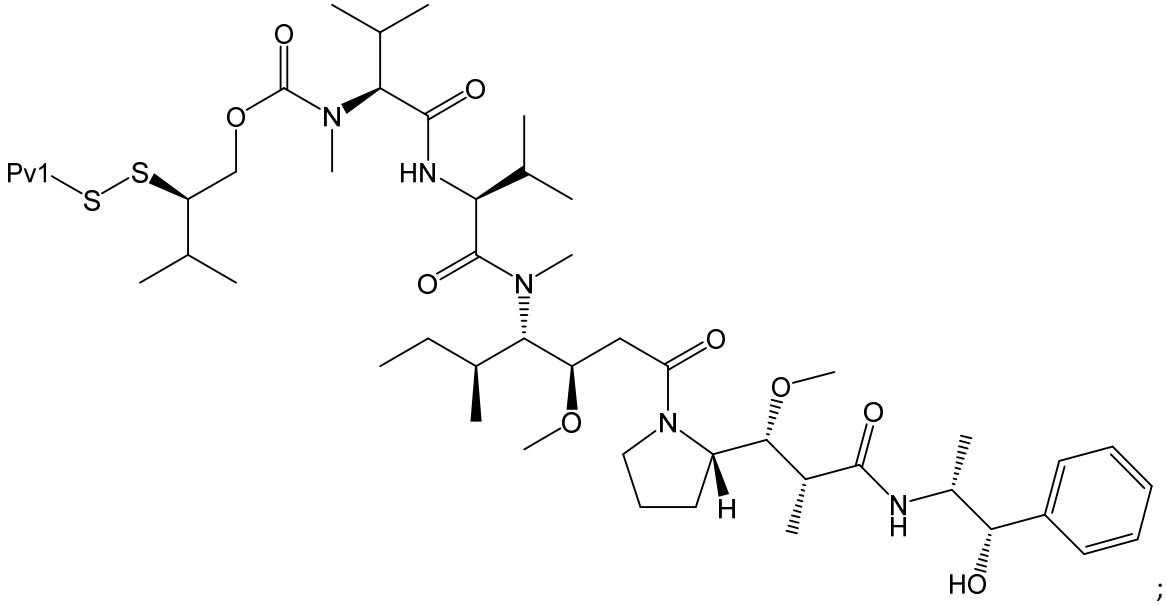
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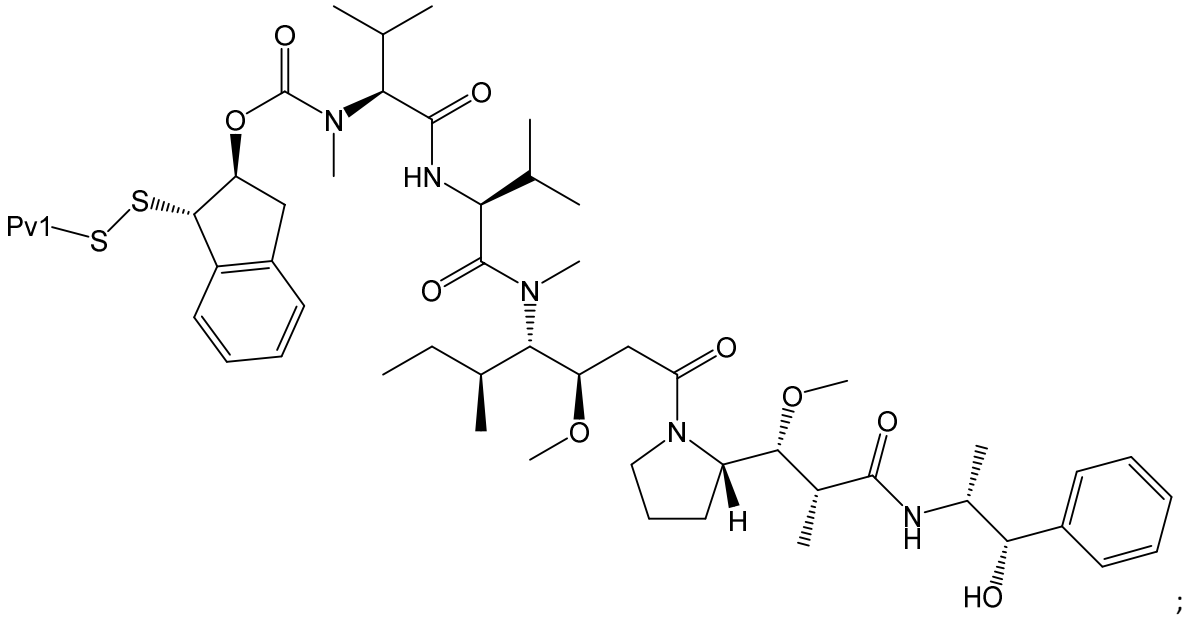
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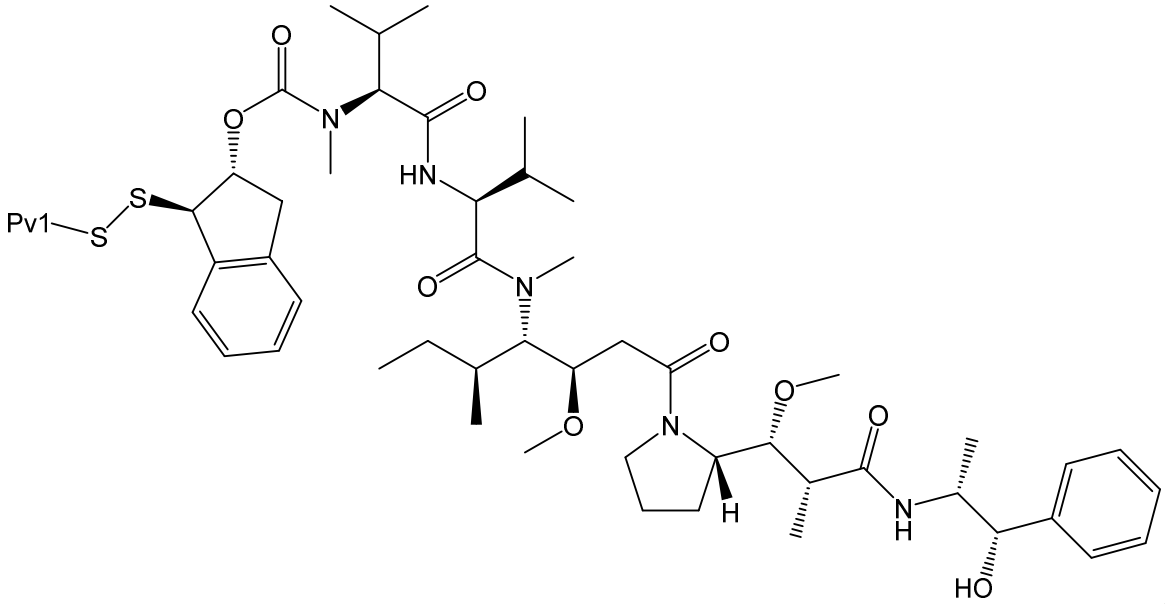
Pv1
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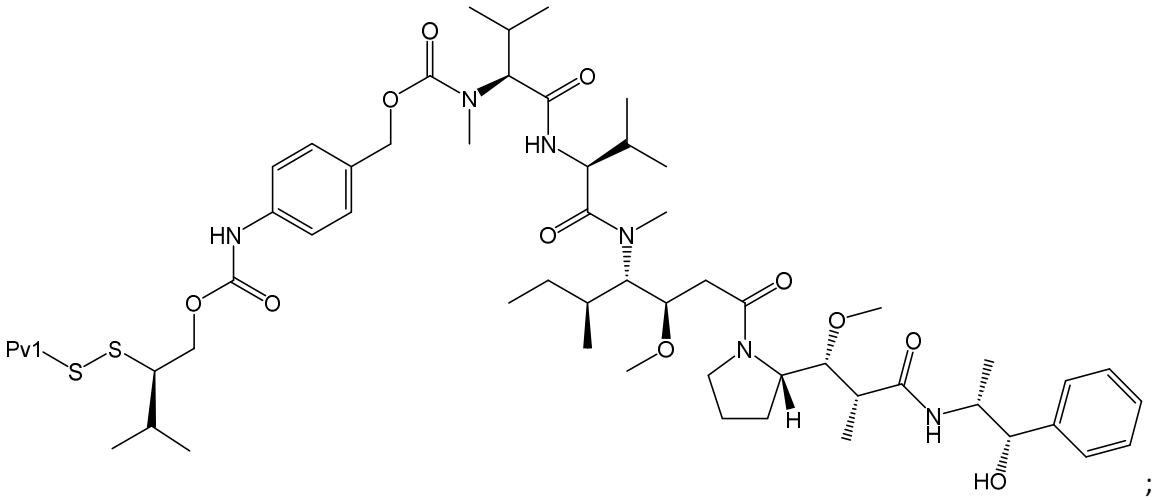
Pv1
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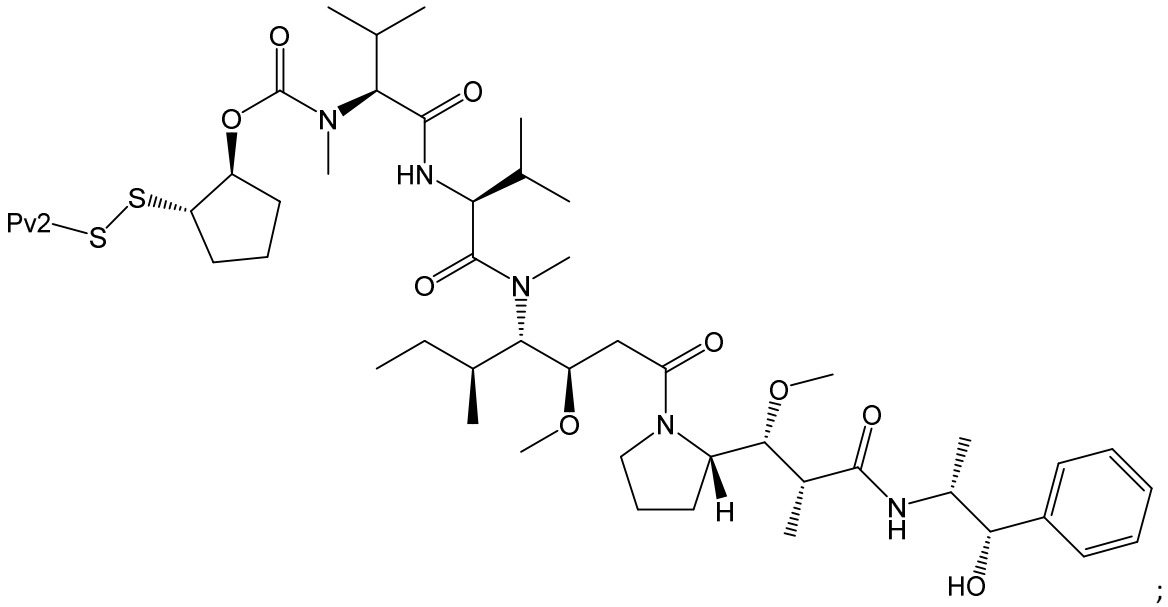
Pv2
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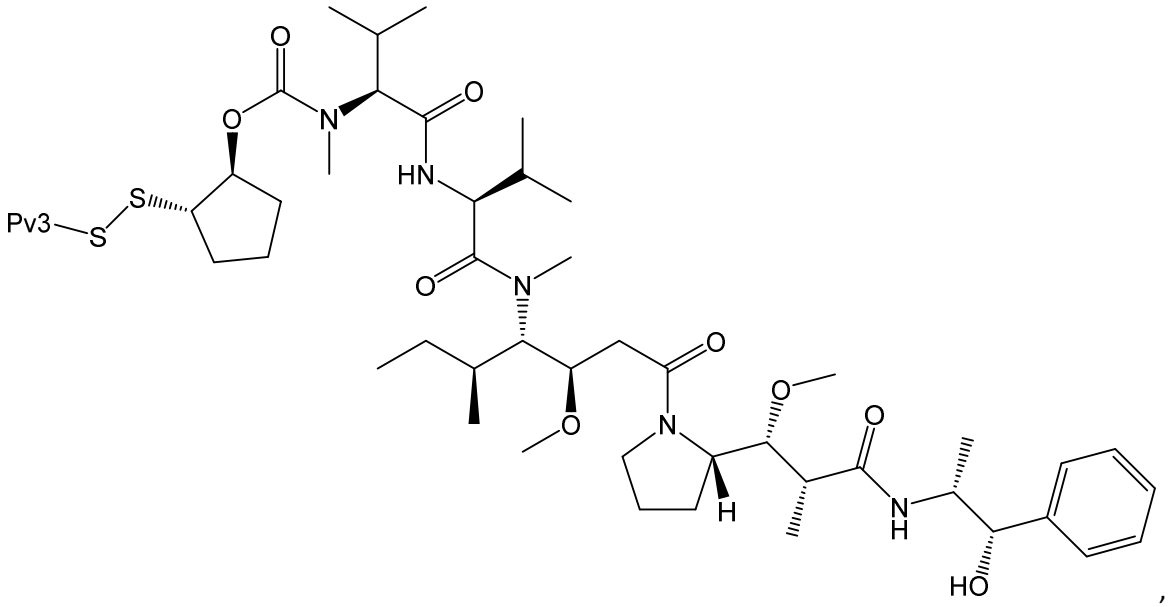
Pv3
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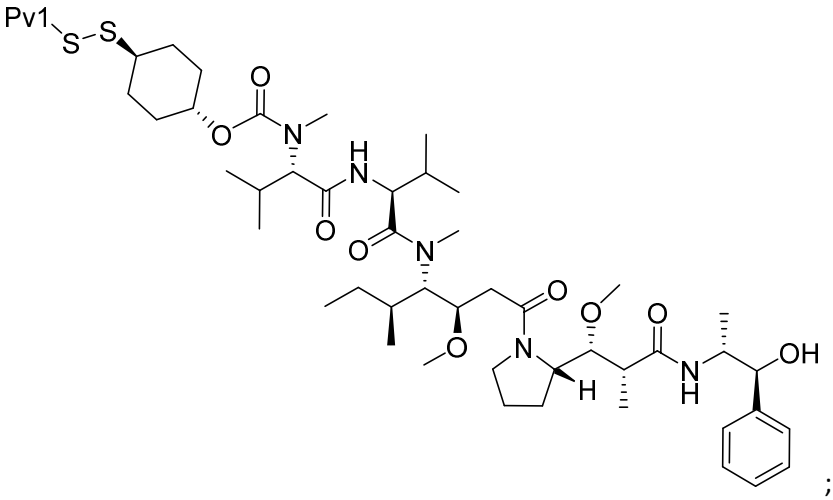
Pv1
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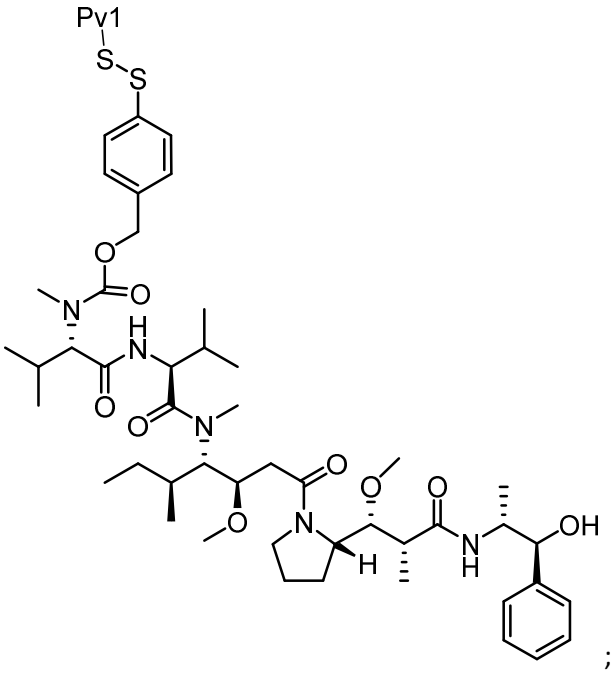
Pv1
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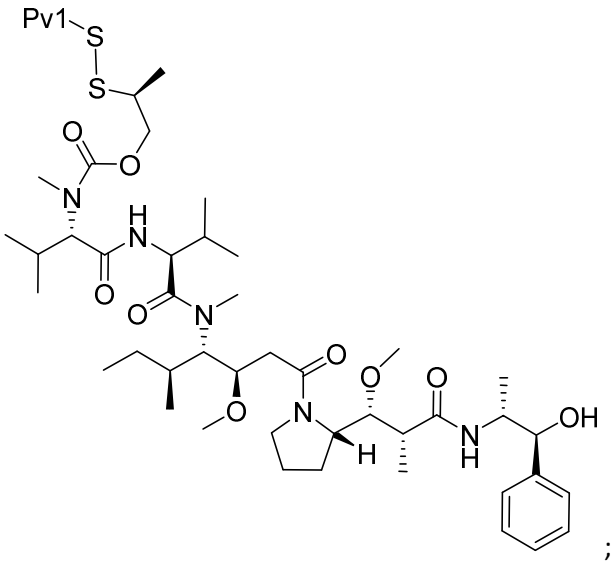
Pv1
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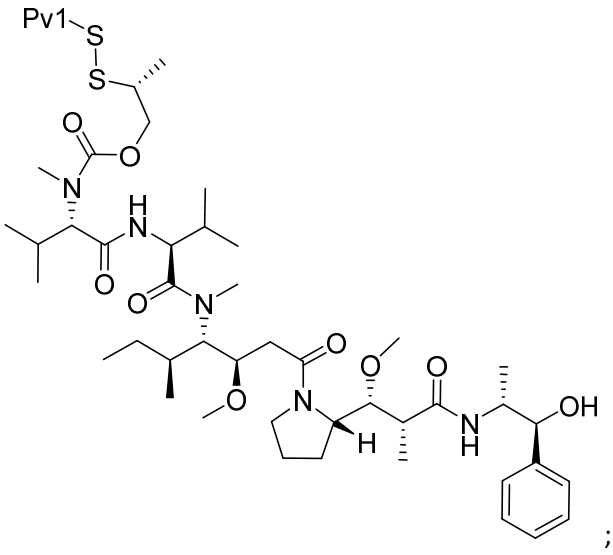
Pv1
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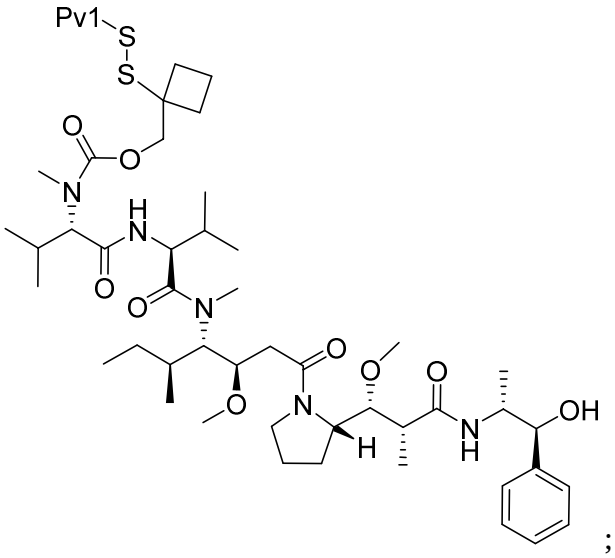


;

or a pharmaceutically acceptable salt of any of the aforementioned, wherein:

Pv1 is a peptide comprising the sequence:

ADDQNPWRAYLDLLFPTDTLLLDLLWCG (SEQ ID NO: 1);

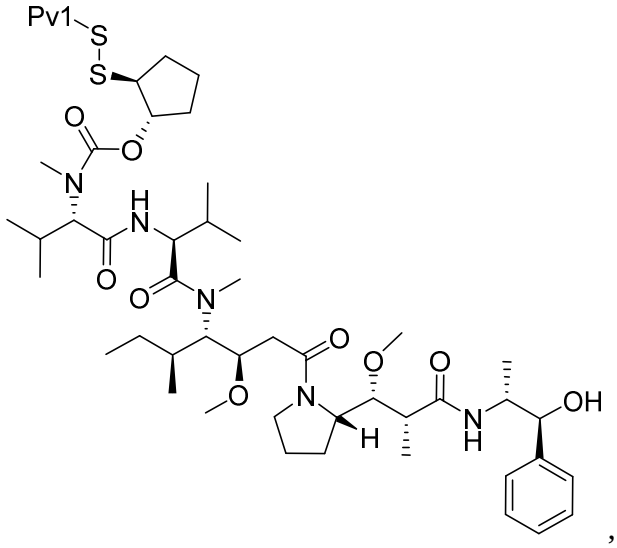
Pv2 is a peptide comprising the sequence:

AEQNPIYWARYADWLFTTPLLLLDLALLVDADECG (SEQ ID NO: 2); and

Pv3 is a peptide comprising the sequence:

ADDQNPWRAYLDLLFPTDTLLLDLLWDADECG (SEQ ID NO: 3).

17. The compound of claim 1, wherein the compound is



,

or a pharmaceutically acceptable salt thereof,

wherein:

Pv1 is a peptide comprising the sequence:

ADDQNPWRAYLDLLFPTDTLLLDLLWCG (SEQ ID NO: 1).

18. A pharmaceutical composition that comprises a compound of any one of claims 1-17, or a pharmaceutically acceptable salt thereof.

19. Use of the compound of any one of claims 1-17, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a patient in need thereof.

20. The use of claim 19, wherein the cancer is selected from bladder cancer, bone cancer, glioma, breast cancer, cervical cancer, colon cancer, colorectal cancer, endometrial cancer, epithelial cancer, esophageal cancer, Ewing's sarcoma, pancreatic cancer, gallbladder cancer, gastric cancer, gastrointestinal tumors, head and neck cancer, intestinal cancers, Kaposi's sarcoma, kidney cancer, laryngeal cancer, liver cancer, lung cancer, melanoma, prostate cancer, rectal cancer, renal clear cell carcinoma, skin cancer, stomach cancer, testicular cancer, thyroid cancer, and uterine cancer, or

wherein the cancer is selected from Hodgkin lymphoma, anaplastic large cell lymphoma (ALCL), diffuse large B-cell lymphoma (DLBCL), ovarian cancer, urothelial cancer, non-small cell lung cancer (NSCLC), triple-negative breast cancer, squamous non-small cell lung cancer (sqNSCLC), squamous head and neck cancer, Non-Hodgkin lymphoma, pancreatic cancer, chronic myeloid leukemia (CML), acute myeloid leukemia (AML), fallopian tube cancer, and peritoneal cancer.

21. The use of claim 19, wherein the cancer is selected from lung cancer, colorectal cancer, and prostate cancer, optionally

wherein the lung cancer is non-small cell lung cancer.