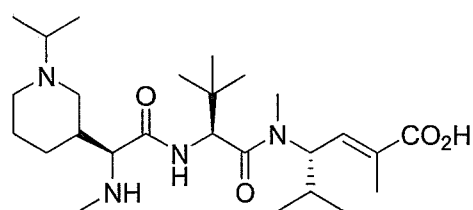
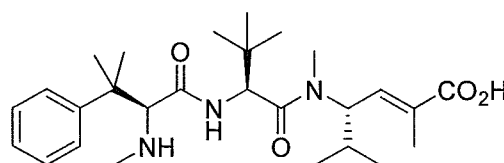


in patients with solid malignancies," presented at American Society of Clinical Oncology Annual Meeting; June 1-5, 2007; Chicago, Ill; both summarized in Rocha-Lima *et al.*, *Cancer*, September 1, 2012 pp. 4262-4270). However, no results have been reported for HTI-286 to date.



(E7974)



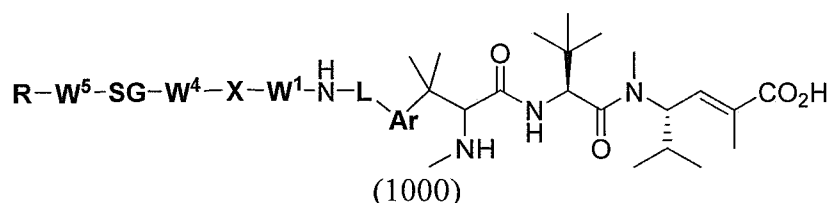
(HTI-286)

[0005] In addition, conjugation of HTI-286 at the C-terminus to a gastrin decapeptide VLALAEEEAYGWNleDF-NH₂ for tumor targeting is described in Tarsova *et al.*, United States patent application publication number US 2005/0171014 A1. Reported activity, however, was very weak.

SUMMARY

[0006] Provided herein are hemiasterlin derivatives, conjugates thereof, compositions comprising the derivatives or conjugates thereof, methods of producing the derivatives and conjugates thereof, and methods of using the derivatives, conjugates, and compositions for the treatment of cell proliferation. The derivatives, conjugates, and compositions are useful in methods of treatment and prevention of cell proliferation and cancer, methods of detection of cell proliferation and cancer, and methods of diagnosis of cell proliferation and cancer.

[0007] The present disclosure provides a compound according to Formula 1000:

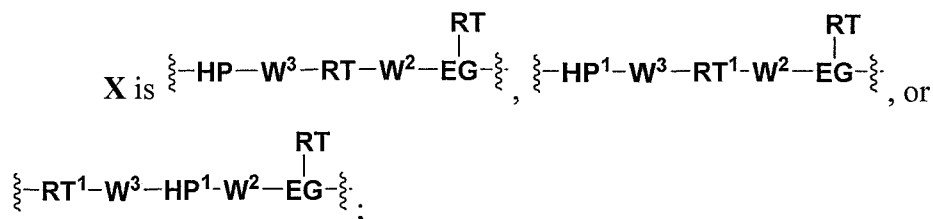


(1000)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein:

Ar is a divalent five- or six-membered, substituted or unsubstituted, monocyclic aryl or heteroaryl ring or a divalent eight-, nine- or ten-membered, substituted or unsubstituted, fused bicyclic aryl or heteroaryl ring;

L is absent or -CH₂-;



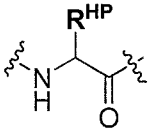
W^1 , W^2 , W^3 , W^4 , and W^5 are each independently a single bond, absent, or a divalent attaching group;

EG is absent or an eliminator group;

each RT is a release trigger group, in the backbone of Formula 1000 or bonded to EG , wherein each RT is optional;

RT^1 is a release trigger group, or a cleavable linker, or RT^1 is absent;

HP is a single bond, absent, or a divalent hydrophilic group;

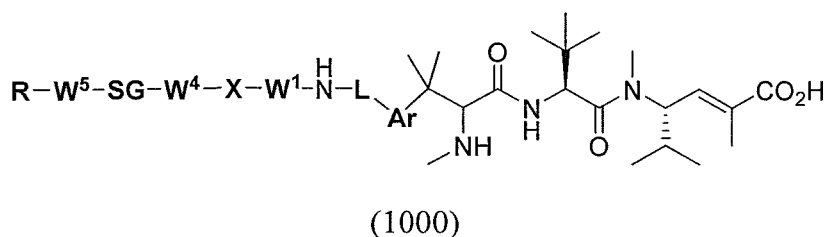
HP^1 is a single bond, absent, a divalent hydrophilic group, or  where R^{HP} is a monovalent hydrophilic group;

SG is a single bond, absent, or a divalent spacer group; and

R is hydrogen, a terminal conjugating group, or a divalent residue of a terminal conjugating group;

or, in the alternative, W^1 , W^2 , W^3 , W^4 , W^5 , EG , RT , HP , SG , and R combine to form $-\text{H}$.

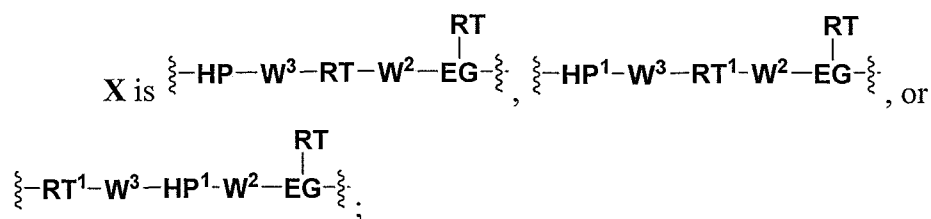
[0007a] According to an aspect there is provided a compound according to Formula 1000:



or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein:

Ar is a divalent six-membered substituted or unsubstituted, monocyclic aryl, a divalent five- or six-membered, substituted or unsubstituted, heteroaryl or a divalent eight-, nine- or ten-membered, substituted or unsubstituted, fused heteroaryl;

L is absent or $-\text{CH}_2-$;



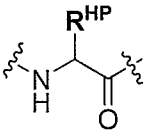
W^1 , W^2 , W^3 , W^4 , and W^5 are each independently a single bond, absent, or a divalent attaching group;

EG is absent or an eliminator group;

each **RT** is a release trigger group, in the backbone of Formula 1000 or bonded to **EG**, wherein each **RT** is optional;

RT^1 is a release trigger group, or a cleavable linker, or RT^1 is absent;

HP is a single bond, absent, or a divalent hydrophilic group;

HP^1 is a single bond, absent, a divalent hydrophilic group, or  where R^{HP} is a monovalent hydrophilic group;

SG is a single bond, absent, or a divalent spacer group; and
R is hydrogen, or a terminal conjugating group.

[0008] The present disclosure also provides a conjugate comprising the compound as described herein, or a pharmaceutically acceptable salt, solvate, or tautomer thereof, linked to a second compound. In one example, there is disclosed a conjugate comprising a compound described herein (*e.g.*, a compound according to any of Formulas 1000-1000b, 1001-1001b, 1002-1002b, and I-XIXb-2, 101-111b, or 1-8b) linked to a second compound.

[0008a] In another aspect there is provided a conjugate comprising the compound as described herein, or a pharmaceutically acceptable salt, solvate, or tautomer thereof, linked to a second compound.

[0009] In another aspect, there is provided a pharmaceutical composition comprising the compound or conjugate as described herein; and a pharmaceutically acceptable excipient, carrier, or diluent. In one example, there is disclosed a pharmaceutical composition comprising:

a compound (*e.g.*, a compound according to any of Formulas 1000-1000b, 1001-1001b, 1002-1002b, and I-XIXb-2, 101-111b, or 1-8b) or conjugate (*e.g.*, a conjugate according to any of Formulas C1-C17b, E1, F1-F17b, and G1-G17b) as described herein; and

a pharmaceutically acceptable excipient, carrier, or diluent.

[0010] The present disclosure also provides the compound, conjugate, or pharmaceutical composition as described herein for use in therapy. In a further aspect, the present invention refers to use of an effective amount of the compound, conjugate, or pharmaceutical composition as described herein in the manufacture of a medicament for inhibiting tubulin polymerization. In one example, there is disclosed a method of inhibiting tubulin polymerization in a subject in need thereof comprising administering an effective amount of a compound (*e.g.*, a compound according to any of Formulas 1000-1000b, 1001-1001b, 1002-1002b, and I-XIXb-2, 101-111b, or 1-8b), conjugate (*e.g.*, a conjugate according to any of Formulas C1-C17b, E1, F1-F17b, and G1-G17b), or composition comprising a compound or conjugate, as described herein, to the subject.

[0010a] In another aspect, there is provided use of an effective amount of the compound, conjugate, or pharmaceutical composition as described herein in the manufacture of a medicament for inhibiting tubulin polymerization associated with cell proliferation.

[0011] In another aspect, there is provided use of an effective amount of the compound, conjugate, or pharmaceutical composition as described herein in the manufacture of a medicament for treating cell proliferation or cancer. In one example, there is disclosed a method of treating cell proliferation or cancer in a subject in need thereof comprising administering an effective amount of a compound (*e.g.*, a compound according to any of Formulas 1000-1000b, 1001-1001b, 1002-1002b, and I-XIXb-2, 101-111b, or 1-8b), conjugate (*e.g.*, a conjugate according to any of Formulas C1-C17b, E1, F1-F17b, and G1-G17b), or composition comprising a compound or conjugate, as described herein, to the subject.

[0012] In another aspect, there is provided a method of producing a conjugate, comprising contacting the compound as described herein with a second compound under conditions suitable for conjugating the compound as described herein with the second compound; wherein the second compound comprises an alkyne, strained alkene, tetrazine, thiol, maleimide, carbonyl, oxyamine, or azide. In one example, there is disclosed a method of producing a conjugate, comprising contacting a compound described herein (*e.g.*, a compound according to any of Formulas 1000-1000b, 1001-1001b, 1002-1002b, and I-XIXb-2 or 101-111b) with a second compound under conditions suitable for conjugating the second compound with the compound described herein (*e.g.*, a compound according to any of Formulas 1000-1000b, 1001-1001b, 1002-1002b, and I-XIXb-2 or 101-111b); wherein the second compound comprises a modified amino acid comprising an alkyne, strained alkene, tetrazine, thiol, maleimide, carbonyl, oxyamine, or azide.

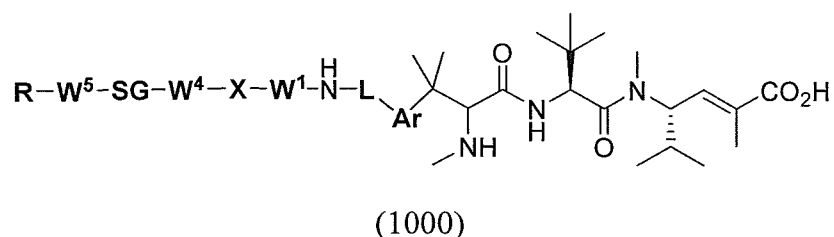
BRIEF DESCRIPTION OF THE FIGURES

[0013] Figure 1 provides results of a cell killing assay described in detail herein. Racemic [**R/S,S,S**] Compound **1** is evaluated as a conjugate on the trastuzumab heavy chain at F404 and also on the light chain at S7. All other conjugates in Figure 1 are on the trastuzumab heavy chain at F404. The relative cell viability of SKBR3 cells is plotted against concentration for trastuzumab (exes), trastuzumab **F404** [**S,S,S**] Compound **1** conjugate (filled squares), trastuzumab **F404** racemic [**R/S,S,S**] Compound **1** conjugate (split squares), trastuzumab **S7** racemic [**R/S,S,S**] Compound **1** conjugate (split circles), and a trastuzumab auristatin (MMAF) conjugate (open triangles).

[0014] Figure 2a provides results of a cell killing assay described in detail herein. In Figure 2a relative cell viability is plotted against concentration of [**S,S,S**] Compound **1** (filled

WHAT IS CLAIMED IS:

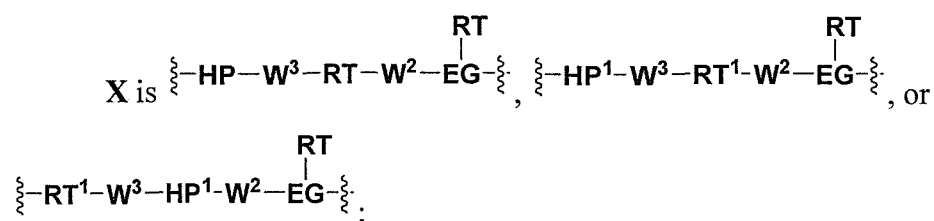
1. A compound according to Formula 1000:



or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein:

Ar is a divalent six-membered substituted or unsubstituted, monocyclic aryl, a divalent five- or six-membered, substituted or unsubstituted, heteroaryl or a divalent eight-, nine- or ten-membered, substituted or unsubstituted, fused heteroaryl;

L is absent or $-\text{CH}_2-$;



W¹, **W**², **W**³, **W**⁴, and **W**⁵ are each independently a single bond, absent, or a divalent attaching group;

EG is absent or an eliminator group;

each **RT** is a release trigger group, in the backbone of Formula 1000 or bonded to **EG**, wherein each **RT** is optional;

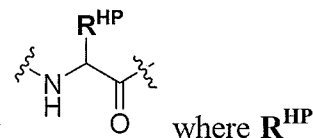
RT¹ is a release trigger group, or a cleavable linker, or **RT**¹ is absent;

HP is a single bond, absent, or a divalent hydrophilic group;

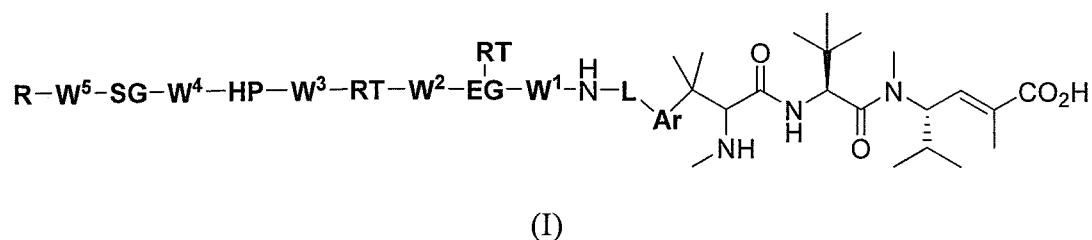
HP¹ is a single bond, absent, a divalent hydrophilic group, or is a monovalent hydrophilic group;

SG is a single bond, absent, or a divalent spacer group; and

R is hydrogen, or a terminal conjugating group.

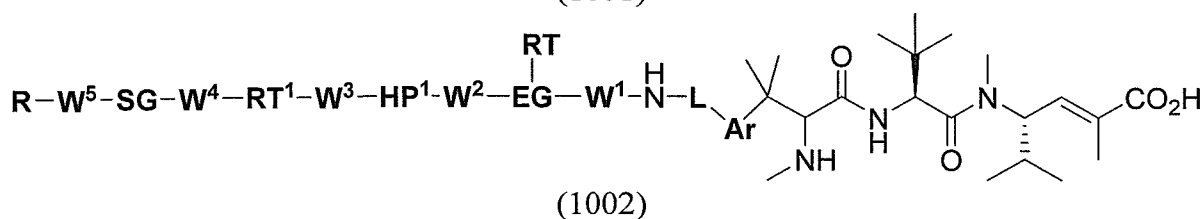
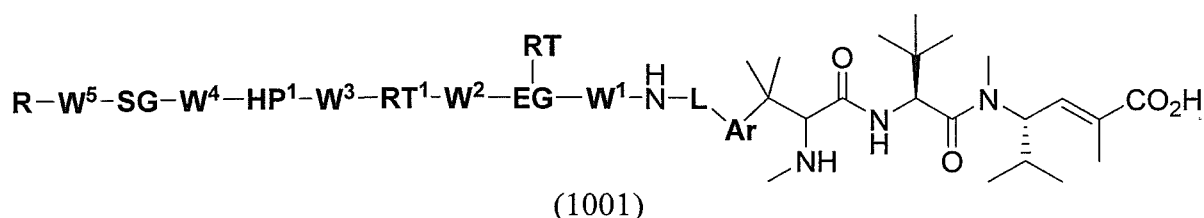


2. The compound of Claim 1 according to Formula I:



or a pharmaceutically acceptable salt, solvate, or tautomer thereof, wherein **EG** is an eliminator group.

3. The compound of claim 1 according to Formula 1001 or 1002:



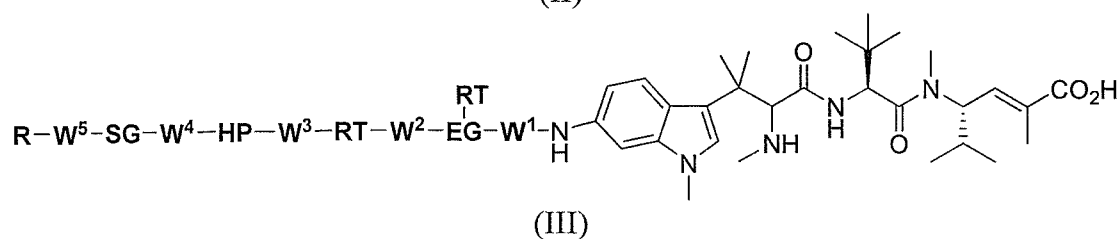
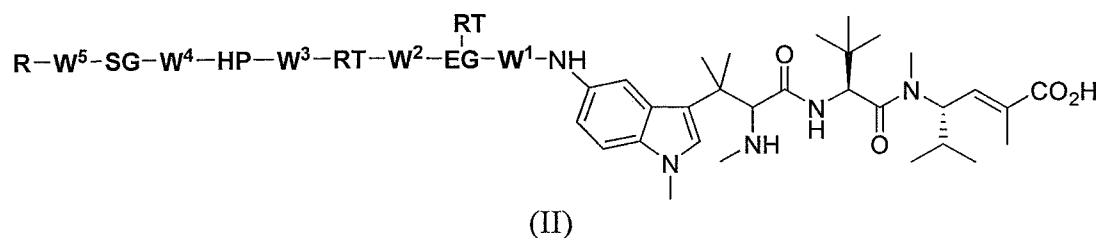
or a pharmaceutically acceptable salt, solvate, or tautomer thereof, wherein

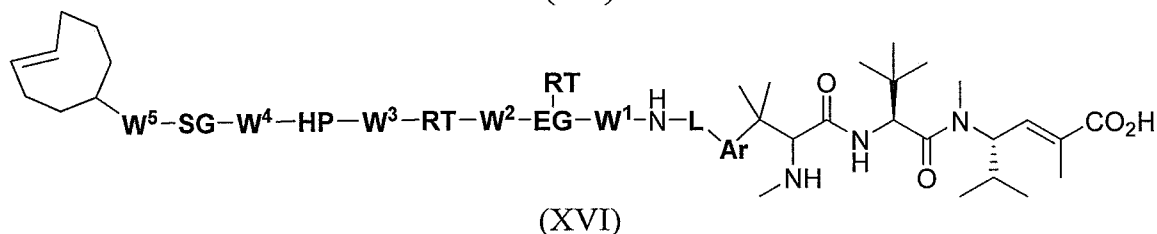
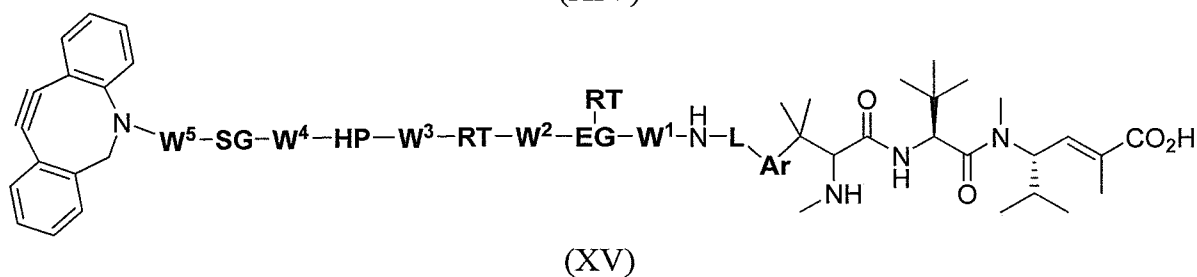
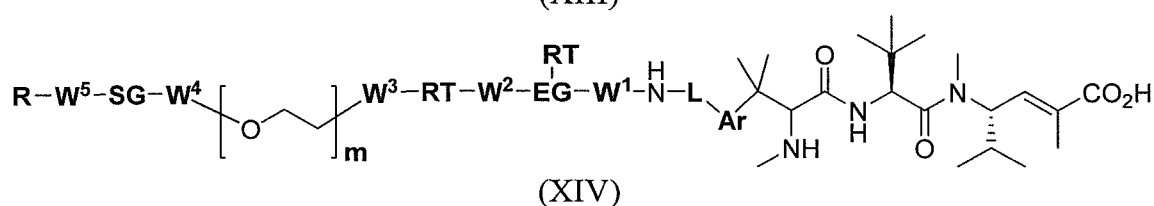
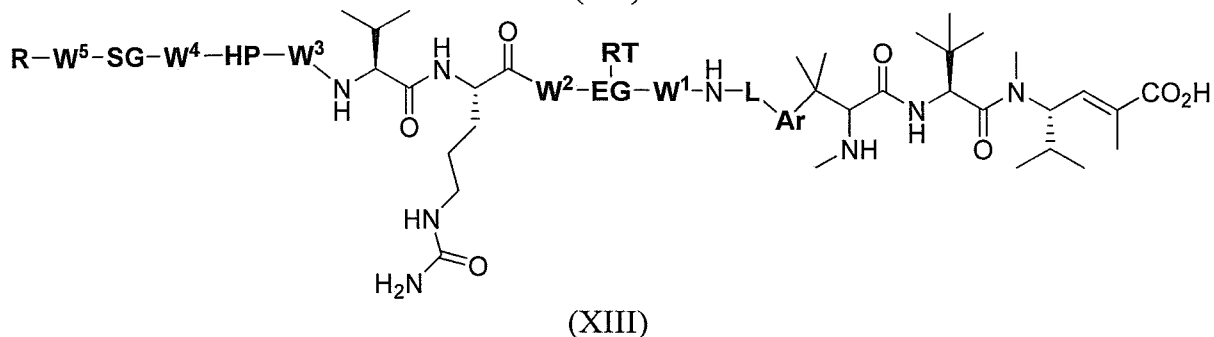
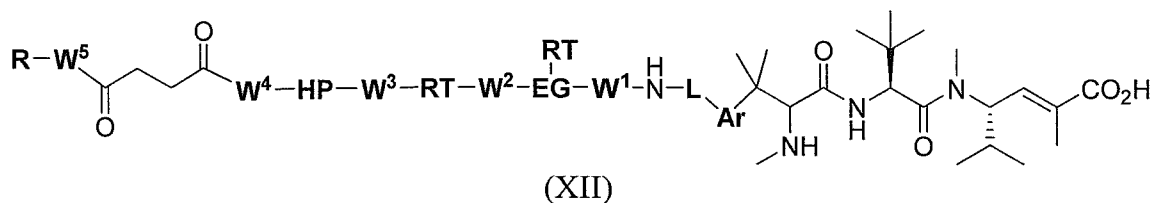
RT¹ is a release trigger group or a cleavable linker;

RT is a release trigger group bonded to **EG**; and **RT** is optional;

R is hydrogen or a terminal conjugating group.

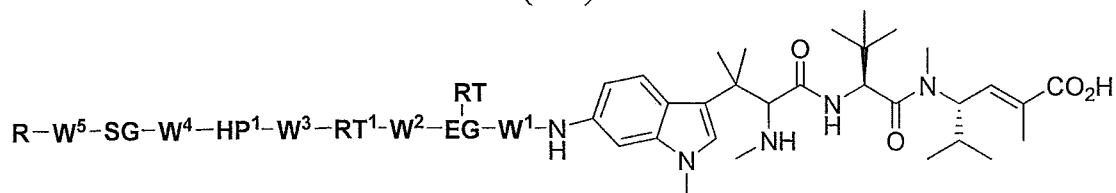
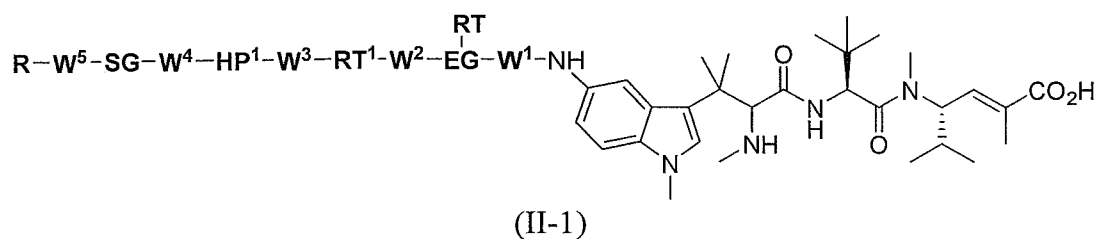
4. The compound of claim 1 or 2, according to any of Formulas II-IX:

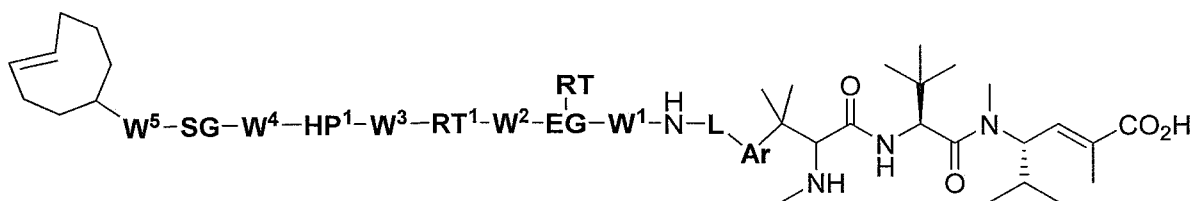




or a pharmaceutically acceptable salt, solvate, or tautomer thereof; wherein **m** is an integer selected from 1 to 12 and one **RT** is optional.

6. The compound of claim 1 or 3, according to any of the following Formula:



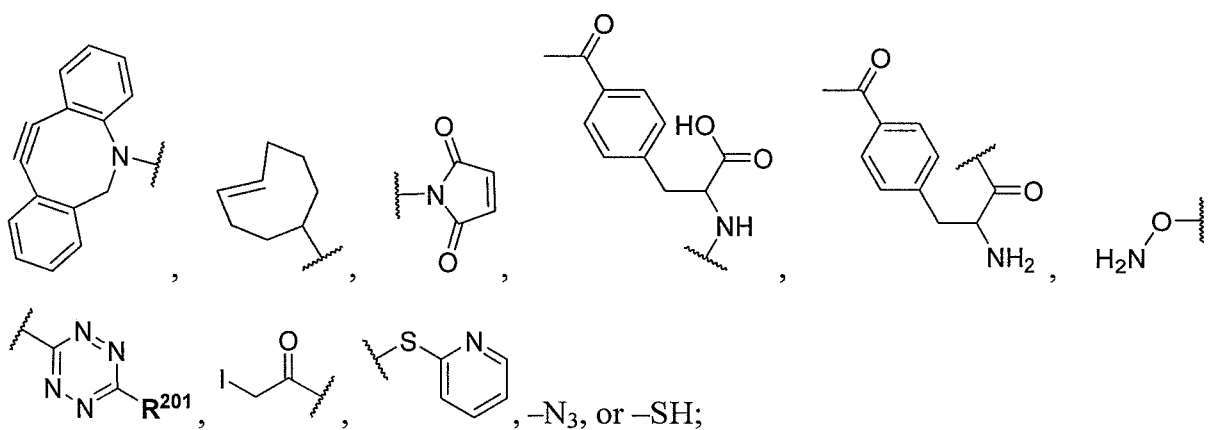


(XVI-2)

or a pharmaceutically acceptable salt, solvate, or tautomer thereof; wherein **m** is an integer selected from 1 to 12 and **RT** is optional.

8. The compound of any one of claims 1-7, wherein **R** comprises an alkyne, strained alkene, tetrazine, thiol, para-acetyl-phenylalanine residue, oxyamine, maleimide, carbonyl alkyl halide, aryl sulfide, or azide.

9. The compound of any one of claims 1-8, wherein **R** is:



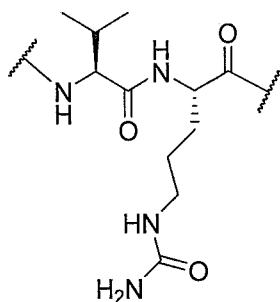
wherein **R**²⁰¹ is lower alkyl.

10. The compound of claim 9, wherein **R**²⁰¹ is methyl, ethyl, or propyl.

11. The compound of claim 9 or 10, wherein **R**²⁰¹ is methyl.

12. The compound of any of claims 1-11, wherein **EG** comprises phenylene, carboxylene, amino, or a combination thereof.

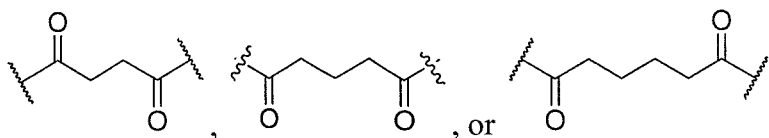
17. The compound of any one of claims 1, 3, and 6-16, wherein **RT**¹ is absent;



; valine-alanine; valine-glutamic acid; alanine-phenylalanine; phenylalanine-lysine; phenylalanine-homolysine; glycine-glycine-glycine; $\{\text{--HN--C}_1\text{--C}_6\text{--alkylene--C(O)--}\}$; $\{\text{--HN--C}_1\text{--C}_6\text{--alkylene--C(O)--aa--}\}$ where **aa** is a natural or non-natural amino acid residue; or $\{\text{--N--}\}$ $\text{--C(O)--}\}$ where the N ring is a 4-7 membered heterocyclic ring comprising 3-6 carbon atoms.

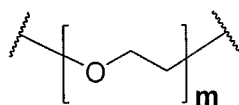
18. The compound of any one of claims 1-17, wherein **SG** comprises C₁-C₁₀ alkylene, -C(O)-, or a combination thereof.

19. The compound of any one of claims 1-18, wherein **SG** is:



20. The compound of any one of claims 1, 2, 4, 5, and 8-19, wherein **HP** comprises poly(ethylene glycol).

21. The compound of any one of claims 1, 2, 4, 5, and 8-20, wherein **HP** is:



wherein **m** is an integer selected from 1 to 12.

22. The compound of any one of claims 1, 3, and 6-19, wherein **HP**¹ is absent or

where **R**^{HP} is wherein **R** is -H or -CH₃ and **m** is an integer selected from 1 to 12 or **R**^{HP} is -C₁-C₆-alkylene-SO₃⁻.

23. The compound of any one of claims 1-22, wherein **W**¹, **W**², **W**³, **W**⁴, and **W**⁵ are each independently a single bond, absent, or comprise -C(O)-, -O-, -C(O)NH-, -C(O)NH-alkyl-,

–OC(O)NH–, –SC(O)NH–, –NH–, –NH-alkyl–, –N(CH₃)CH₂CH₂N(CH₃)–, –S–, –S–S–, –OCH₂CH₂O–, or a combination thereof.

24. The compound of any one of claims 1-23 where **W**¹, **W**², **W**³, **W**⁴, and **W**⁵ are independently absent or a bond; or a pharmaceutically acceptable salt, solvate, or tautomer thereof.

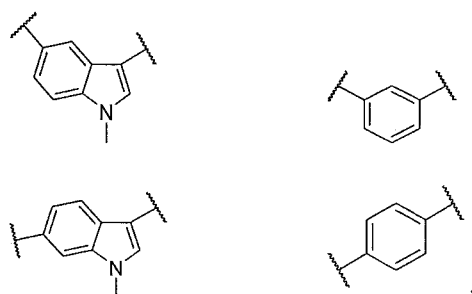
25. The compound of any one of claims 1-3, 5, and 7-24, wherein **Ar** is a divalent five- or six-membered, substituted or unsubstituted, monocyclic aryl or heteroaryl ring.

26. The compound of any one of claims 1-3, 5, and 7-25, wherein **Ar** is a divalent six-membered substituted or unsubstituted, monocyclic aryl, or a divalent six-membered, substituted or unsubstituted, heteroaryl.

27. The compound of any one of claims 1-3, 5, and 7-24, wherein **Ar** is a divalent six-membered substituted or unsubstituted, monocyclic aryl, or a divalent eight-, nine- or ten-membered, substituted or unsubstituted, fused bicyclic heteroaryl.

28. The compound of any one of claims 1-3, 5, 7-24, and 27, wherein **Ar** is a divalent nine-membered, substituted or unsubstituted, fused bicyclic heteroaryl.

29. The compound of any one of claims 1-3, 5, and 7-24, wherein **Ar** is any one of the following:

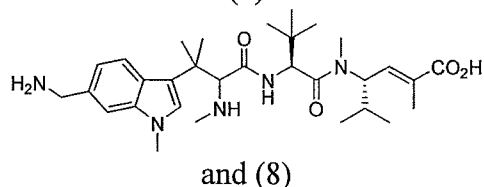
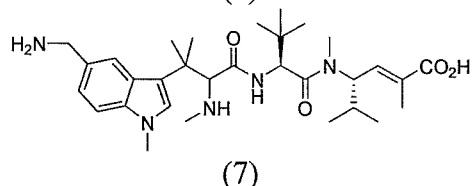
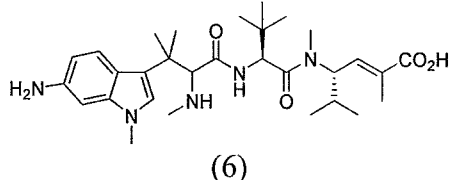
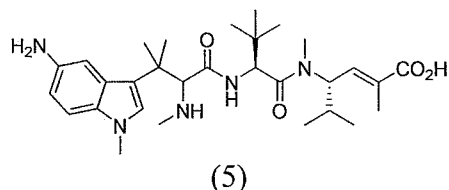
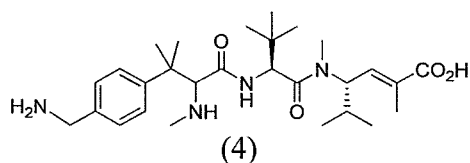
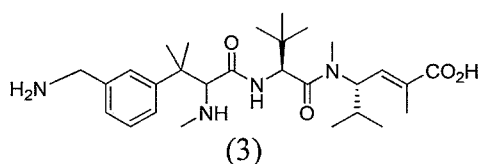
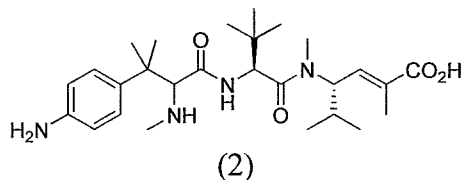
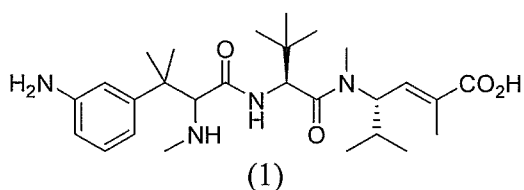


30. The compound of any one of claims 1-3, 5, and 7-29, wherein **L** is absent.

31. The compound of any one of claims 1-3, 5, and 7-29, wherein **L** is –CH₂–.

32. The compound of any one of claims 1, 2, and 4, wherein **W**¹, **W**², **W**³, **W**⁴, **W**⁵, **EG**, **RT**, **HP**, **SG**, and **R** combine to form –H.

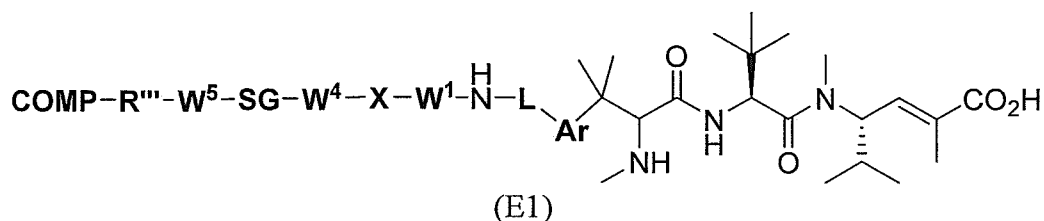
33. The compound of claim 1, according to any one of the following Formula:



or a pharmaceutically acceptable salt, solvate, or tautomer thereof.

34. A conjugate comprising a residue of the compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, or tautomer thereof, linked to a second compound.

35. The conjugate of claim 34 according to Formula (E1):

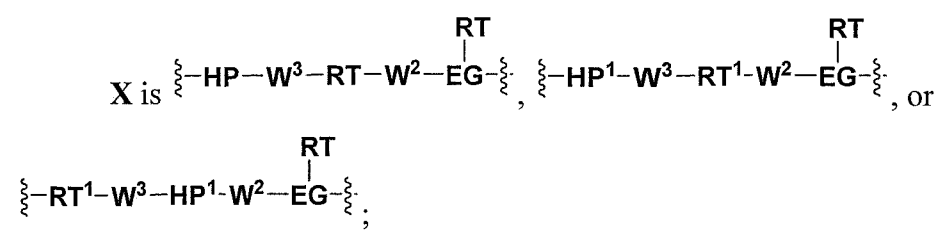


or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein:

COMP is a residue of a second compound;

Ar is a divalent six-membered substituted or unsubstituted, monocyclic aryl, a divalent five- or six-membered, substituted or unsubstituted, heteroaryl or a divalent eight-, nine- or ten-membered, substituted or unsubstituted, fused heteroaryl;

L is absent or $-\text{CH}_2-$;



W¹, **W²**, **W³**, **W⁴**, and **W⁵** are each independently a single bond, absent, or a divalent attaching group;

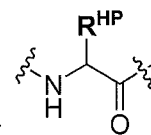
EG is absent or an eliminator group;

each **RT** is a release trigger group, in the backbone of Formula E1 or bonded to **EG**, wherein **RT** is optional;

RT¹ is a release trigger group, or a cleavable linker, or **RT¹** is absent;

HP is a single bond, absent, or a divalent hydrophilic group;

HP¹ is a single bond, absent, a divalent hydrophilic group, or is a monovalent hydrophilic group;

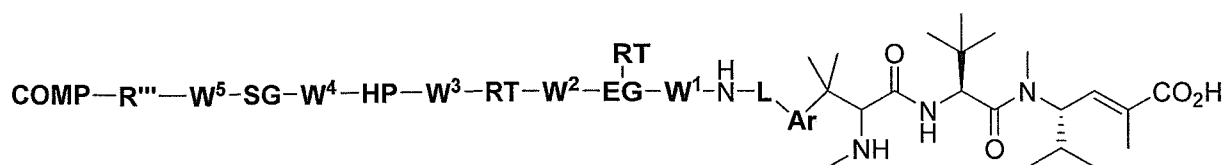


where **R^{HP}**

SG is a single bond, absent, or a divalent spacer group; and

R''' is a divalent residue of a terminal conjugating group.

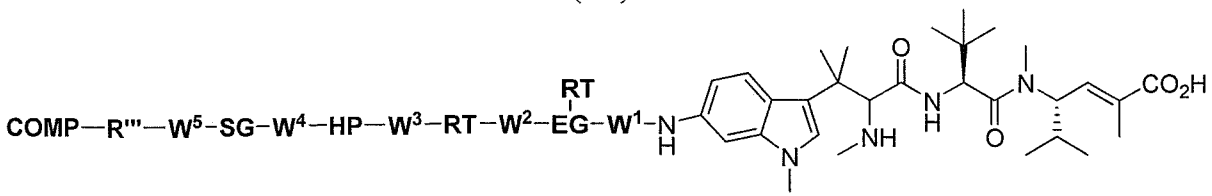
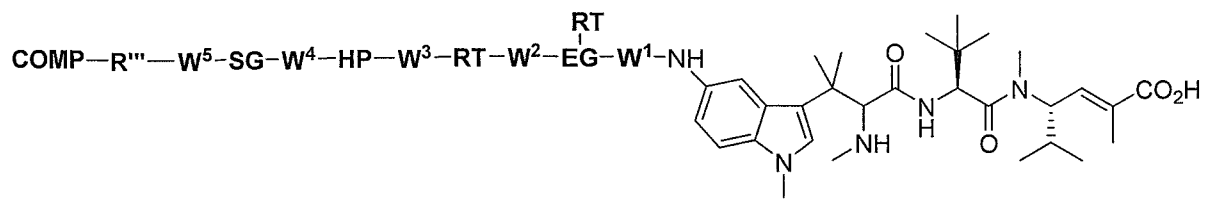
36. The conjugate of claim 35, according to Formula C1:

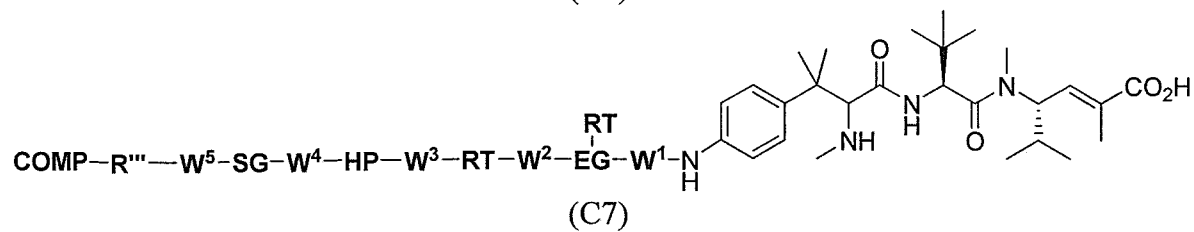
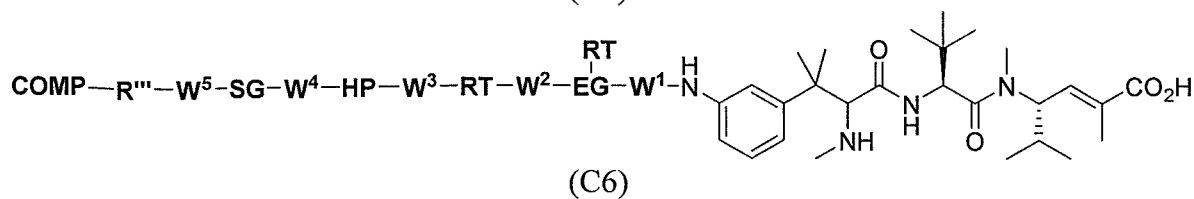
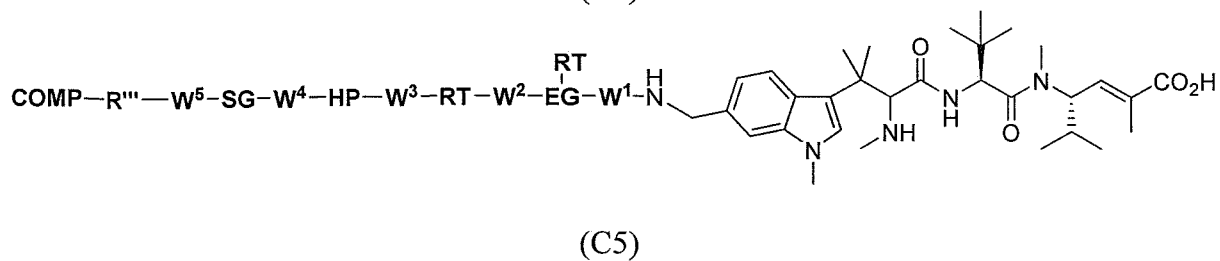
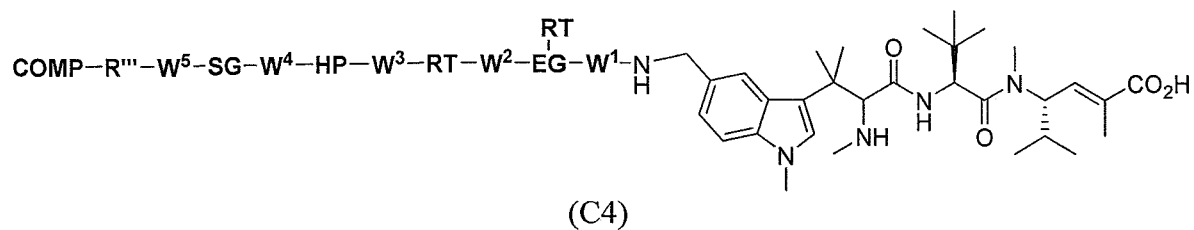


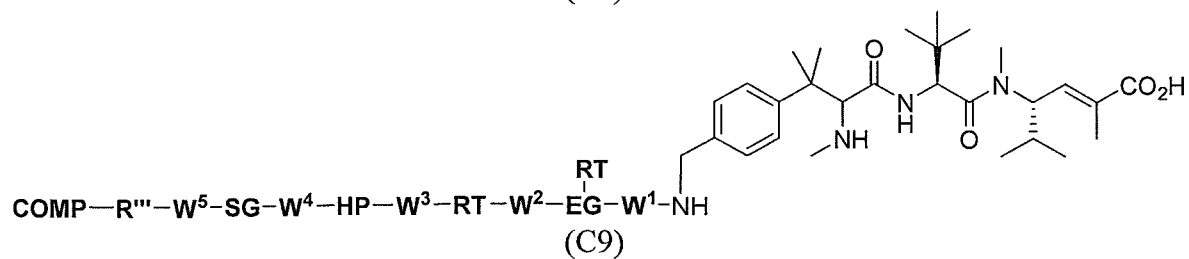
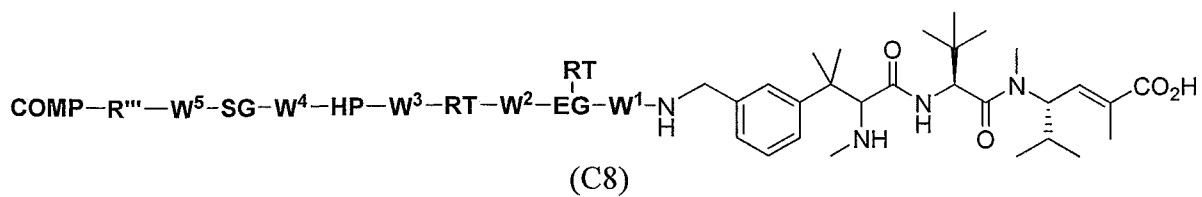
(C1)

or a pharmaceutically acceptable salt, solvate, or tautomer thereof, wherein **EG** is an eliminator group; and each **RT** is a release trigger group, and one **RT** is optional.

37. The conjugate of claim 35 or 36 according to any one of Formulas C2-C9:

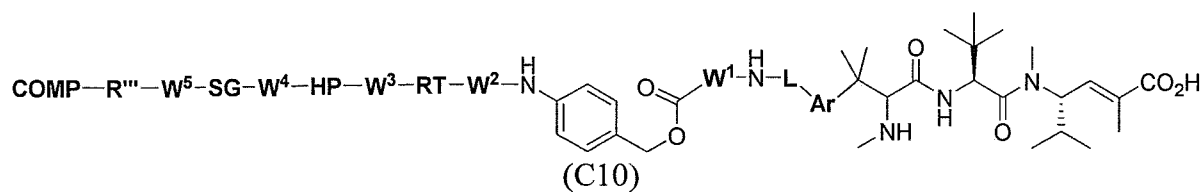


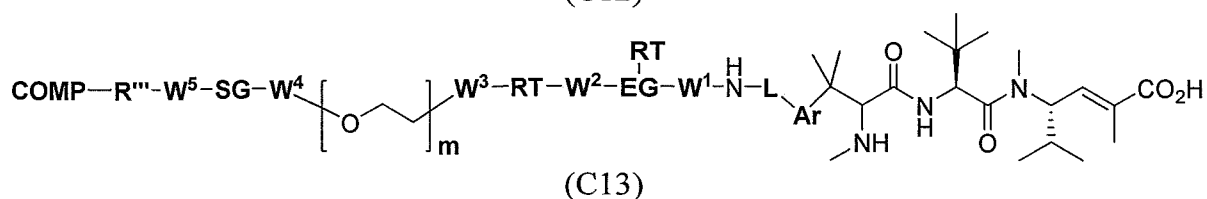
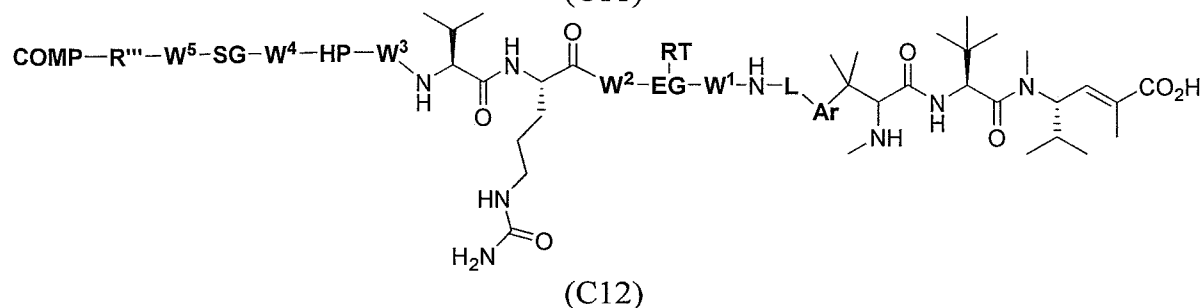
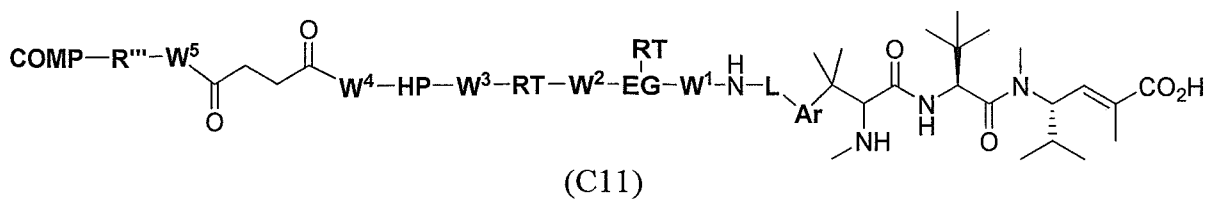




or a pharmaceutically acceptable salt, solvate, or tautomer thereof wherein one **RT** is optional.

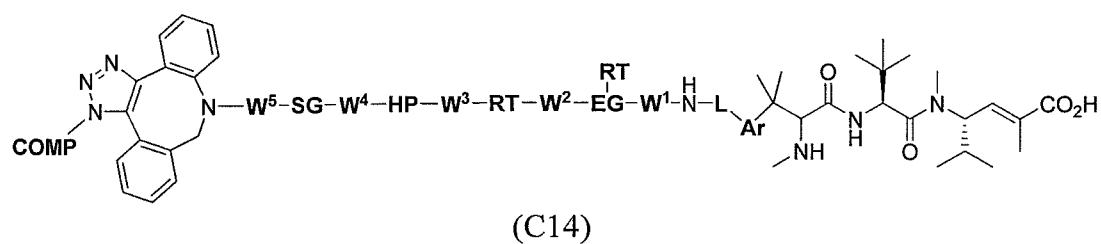
38. The conjugate of claim 35 or 36 according to any one of Formulas C10-C13:

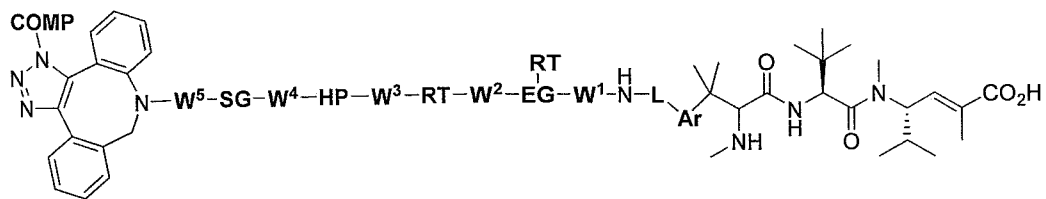




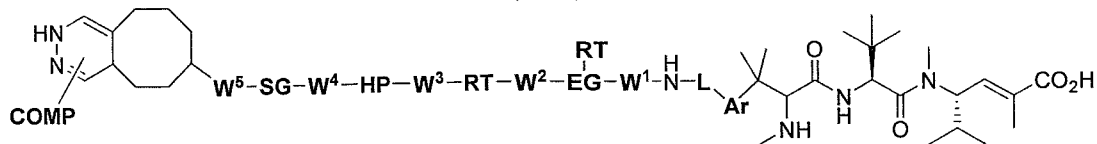
or a pharmaceutically acceptable salt, solvate, or tautomer thereof, wherein **m** is an integer selected from 1 to 12 and one **RT** is optional.

39. The conjugate of claim 35 or 36 according to any one of Formulas C14-C17:

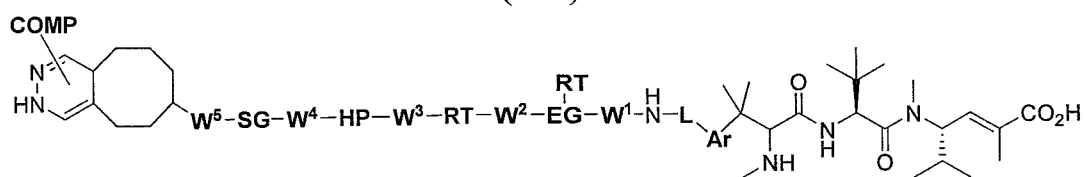




(C15)



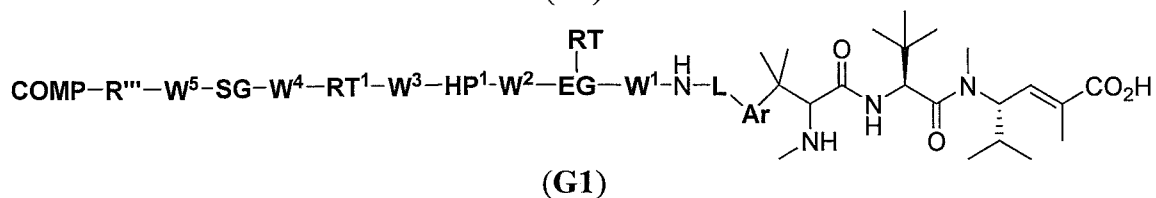
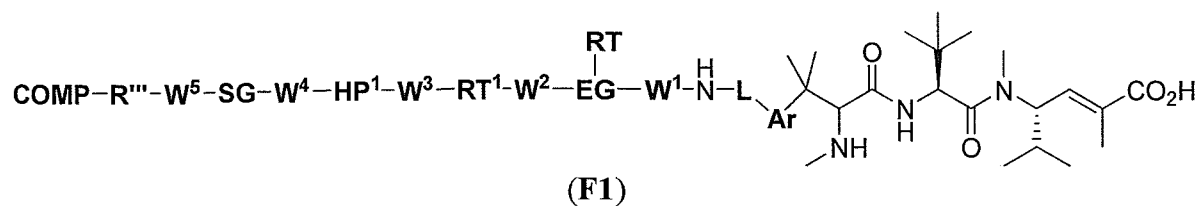
(C16)



(C17)

or a pharmaceutically acceptable salt, solvate, or tautomer thereof, wherein one **RT** is optional.

40. The conjugate of claim 35 according to Formula (F1) or (G1):

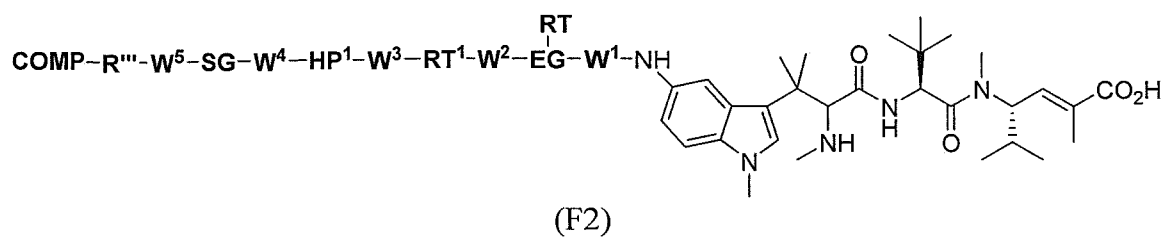


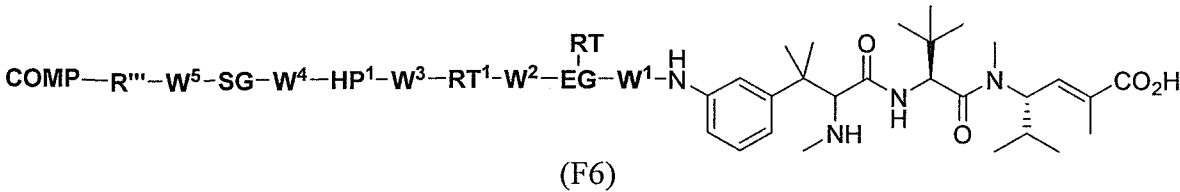
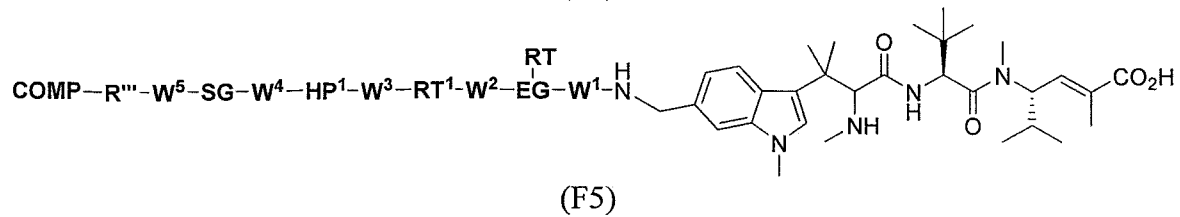
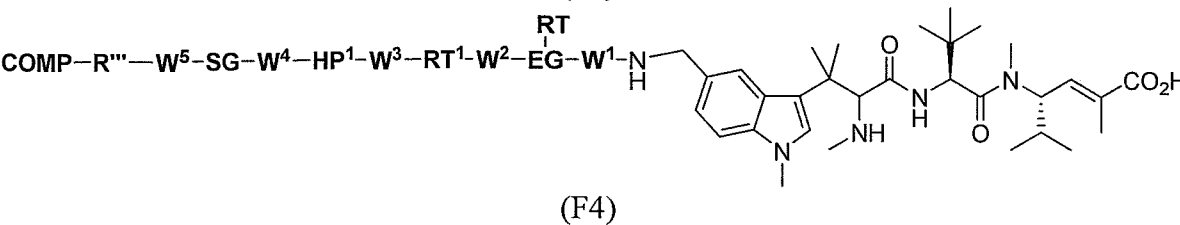
or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein:

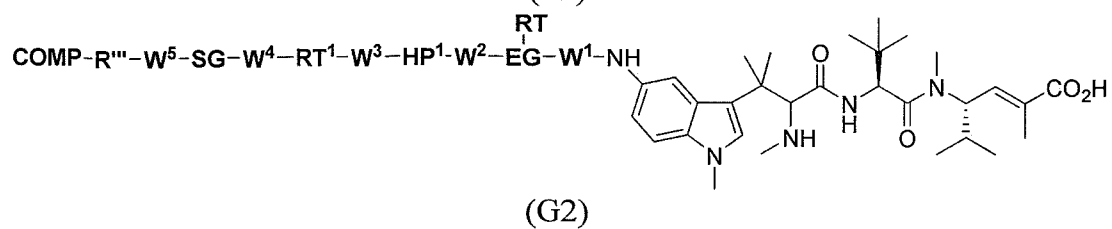
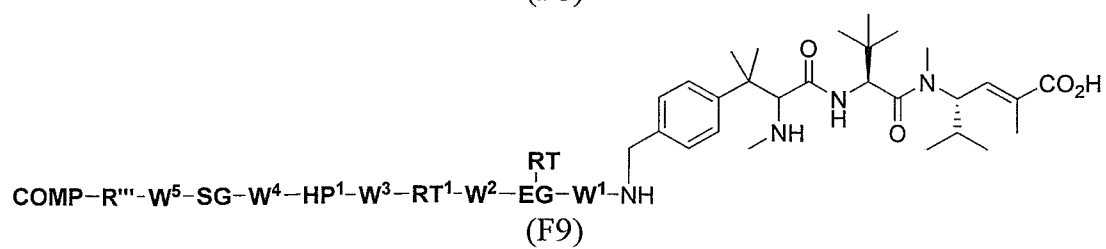
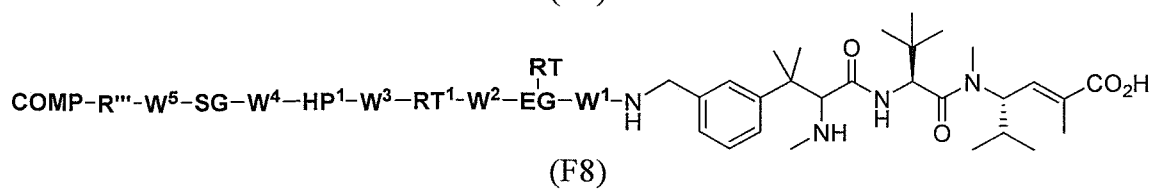
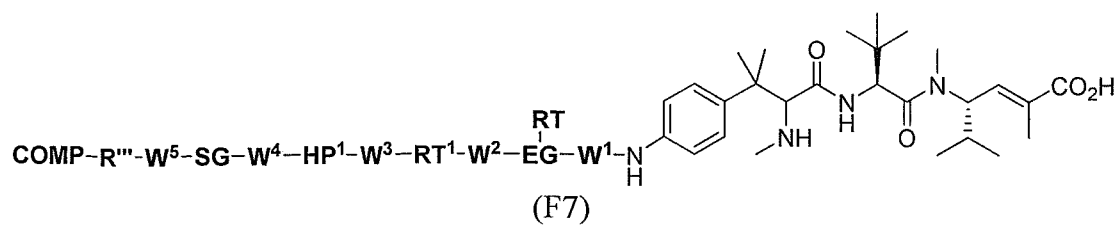
RT¹ is a release trigger group or a cleavable linker group; and

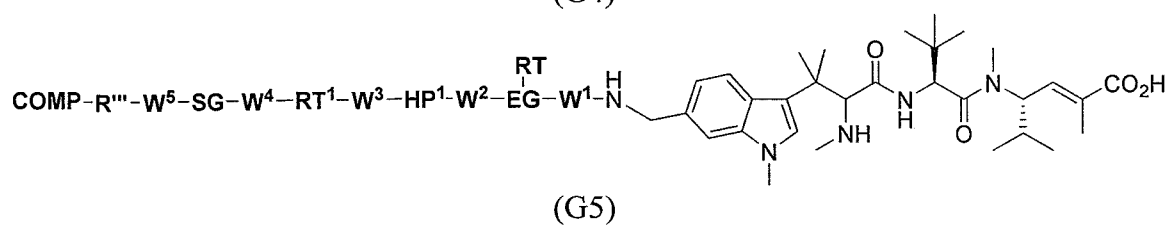
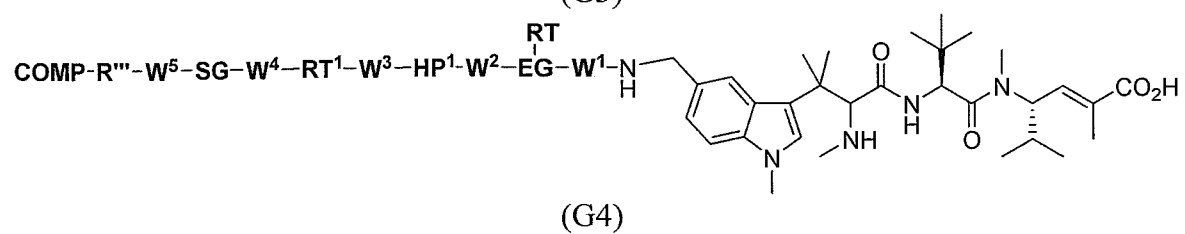
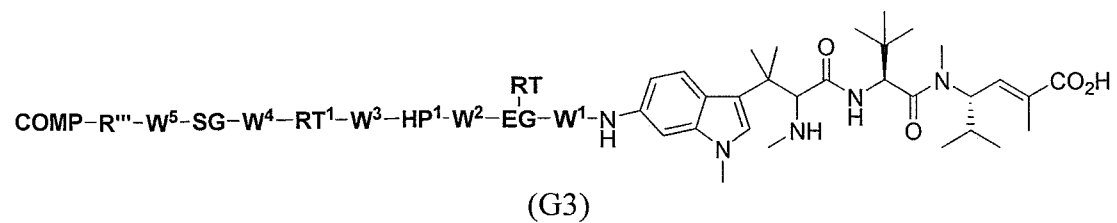
RT is a release trigger group bonded to **EG**; wherein **RT** is optional.

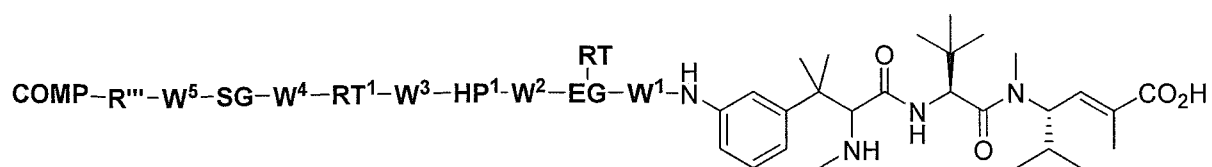
41. The conjugate of claim 35 or 40 according to any one of the following Formulas:



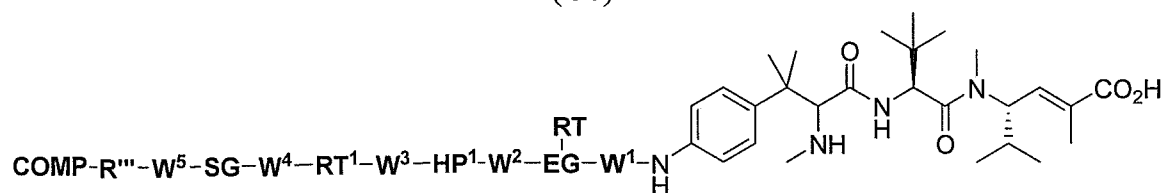




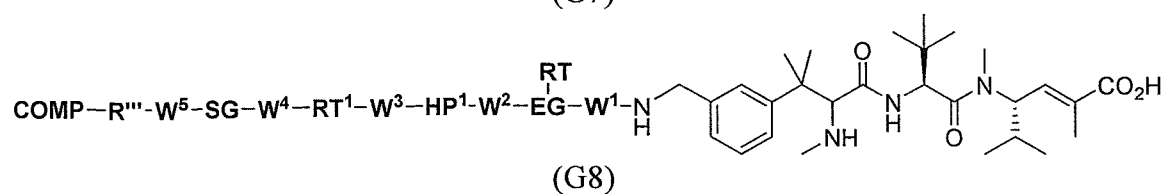




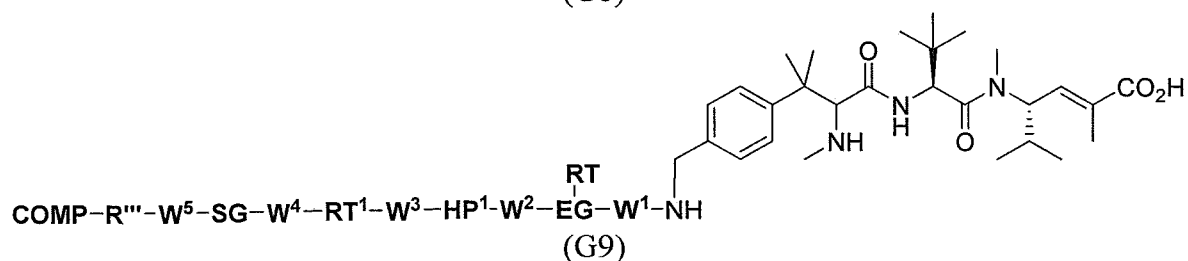
(G6)



(G7)



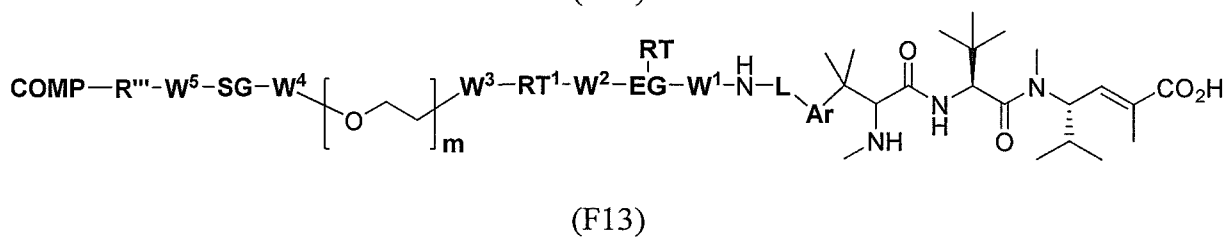
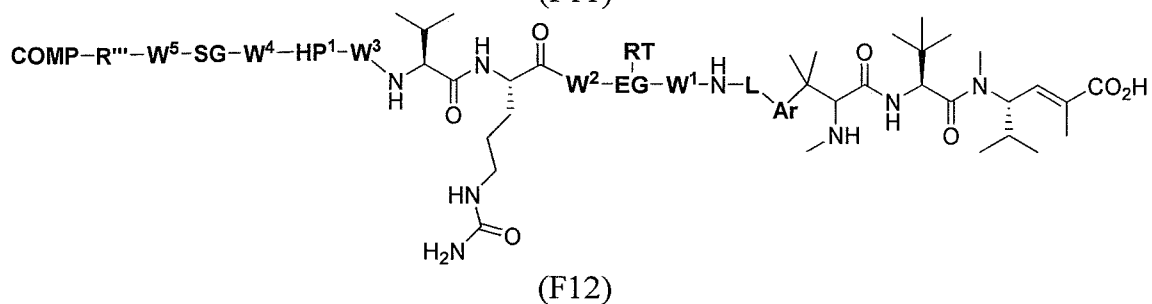
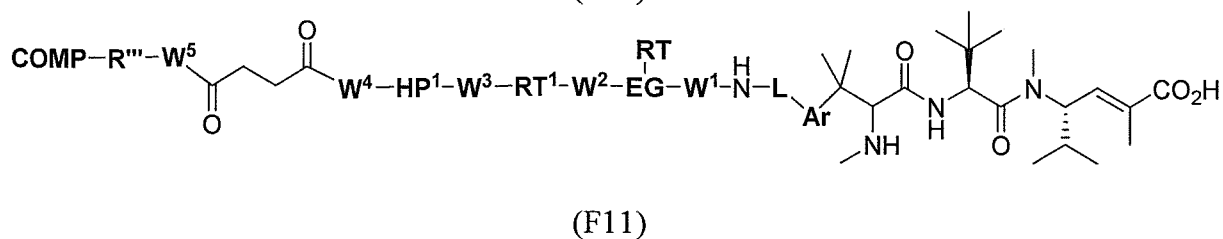
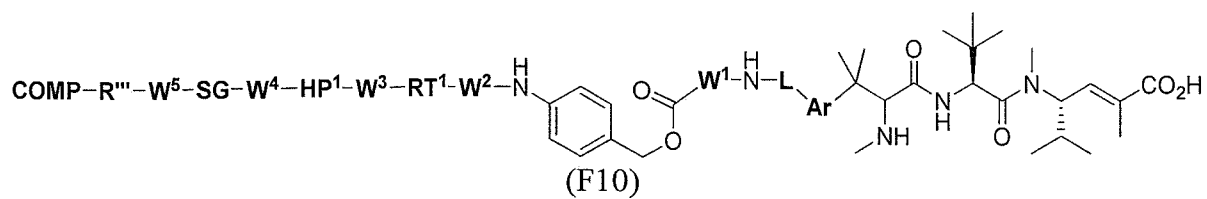
(G8)

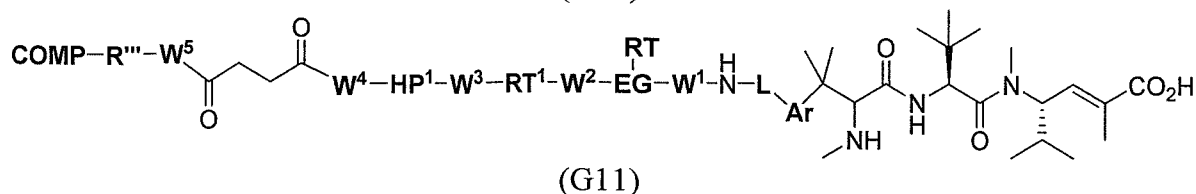
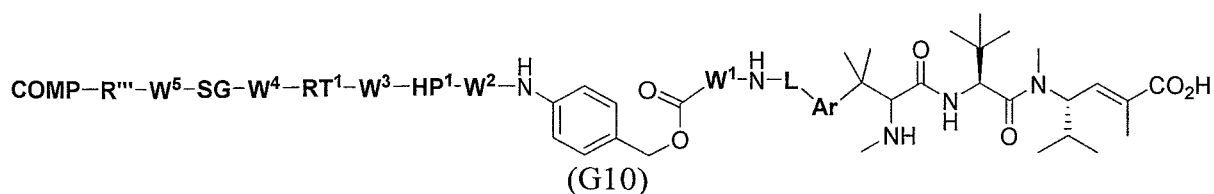


(G9)

or a pharmaceutically acceptable salt, solvate, or tautomer thereof wherein **RT** is optional.

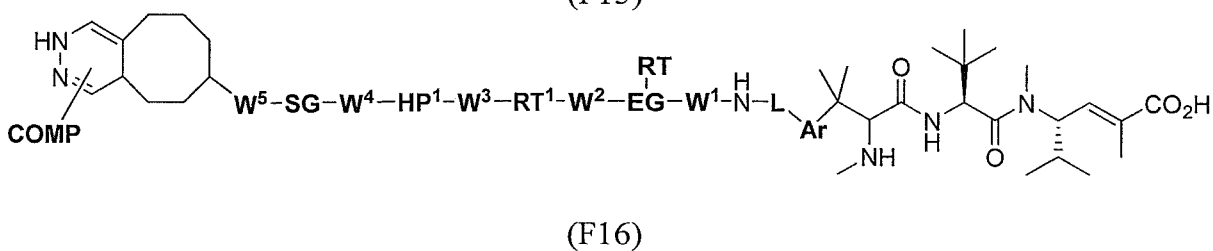
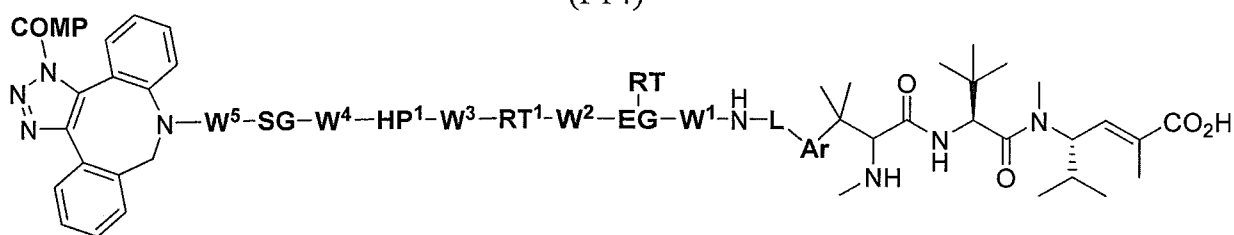
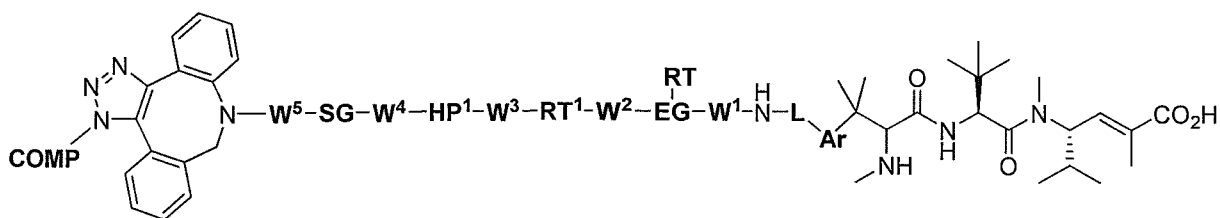
42. The conjugate of claim 35 or 40 according to any one of the following Formulas:

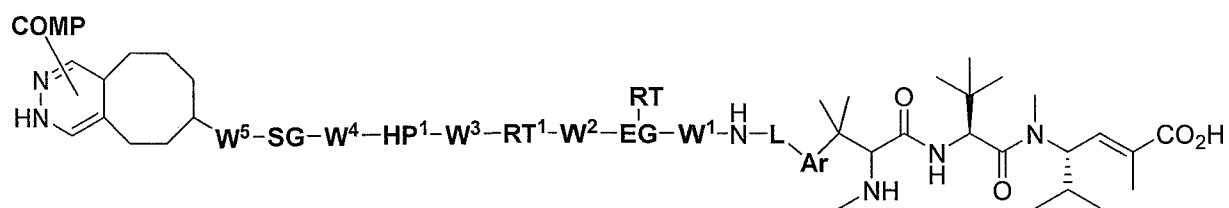




or a pharmaceutically acceptable salt, solvate, or tautomer thereof, wherein **m** is an integer selected from 1 to 12 and **RT** is optional.

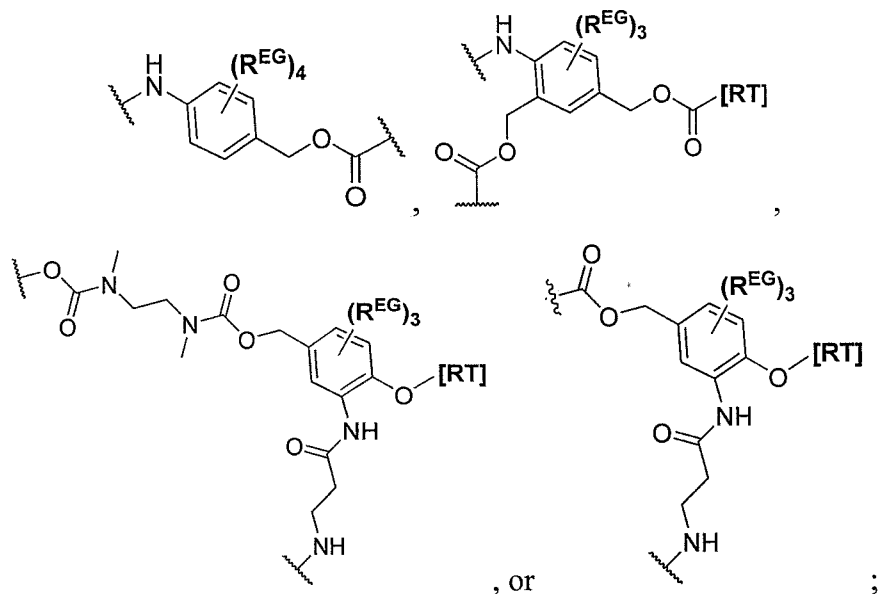
43. The conjugate of claim 35 or 40 according to any one of the following Formulas:





(F17)

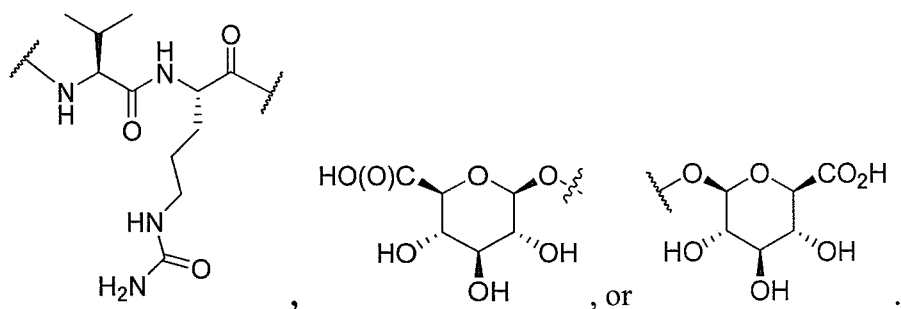
45. The conjugate of any one of claims 35-44, wherein **EG** is:



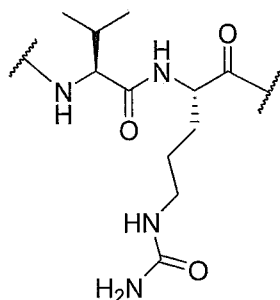
wherein each **R^{EG}** is independently selected from the group consisting of hydrogen, alkyl, biphenyl, -CF₃, -NO₂, -CN, fluoro, bromo, chloro, alkoxy, alkylamino, dialkylamino, alkyl-C(O)O-, alkylamino-C(O)- and dialkylaminoC(O)-.

46. The conjugate of any one of claims 35-45, wherein **RT** comprises a residue of a natural or non-natural amino acid or a residue of a sugar.

47. The conjugate of any one of claims 35-46, wherein **RT** is:



48. The conjugate of any one of claims 35 and 40-47, wherein **RT¹** is absent;

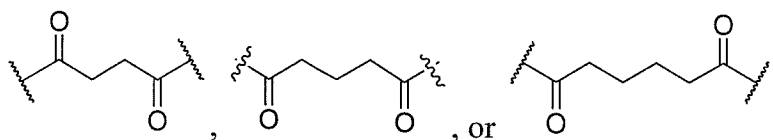


; valine-alanine; valine-glutamic acid; alanine-phenylalanine; phenylalanine-lysine; phenylalanine-homolysine; glycine-glycine-glycine;

$\text{--}\{\text{--}\text{HN--C}_1\text{--C}_6\text{--alkylene--C(O)--}\{\text{--}\}$, $\text{--}\{\text{--}\text{HN--C}_1\text{--C}_6\text{--alkylene--C(O)--aa--}\{\text{--}\}$ where **aa** is a natural or non-natural amino acid residue; or $\text{--}\{\text{--}\text{N}\bigcirc\text{--C(O)--}\{\text{--}\}$ where the $\text{N}\bigcirc$ ring is a 4-7 membered heterocyclic ring comprising 3-6 carbon atoms.

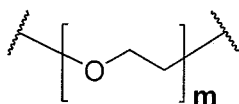
49. The conjugate of any one of claims 35-48, wherein **SG** comprises $\text{C}_1\text{--C}_{10}$ alkylene, $\text{C}_4\text{--C}_6$ alkylene, --C(O)-- , or combination thereof.

50. The conjugate of any one of claims 35-49, wherein **SG** is:



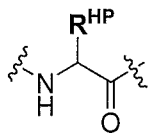
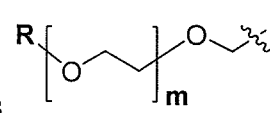
51. The conjugate of any of claims 35-39 and 44-50, wherein **HP** comprises poly(ethylene glycol).

52. The conjugate of any one of claims 35-39 and 44-51, wherein **HP** is:



wherein **m** is an integer selected from 1 to 12.

53. The conjugate of any one of claims 35, 40-43, and 44-50, wherein **HP¹** is absent

or  where **R^{HP}** is  wherein **R** is --H or --CH_3 and **m** is an integer selected from 1 to 12 or **R^{HP}** is $\text{--C}_1\text{--C}_6\text{--alkylene--SO}_3^-$.

54. The conjugate of any one of claims 35-53, wherein **W¹**, **W²**, **W³**, **W⁴**, and **W⁵** are each independently a single bond, absent, or comprise --C(O)-- , --O-- , --C(O)NH-- , --C(O)NH-alkyl-- , --OC(O)NH-- , --SC(O)NH-- , --NH-- , --NH-alkyl-- , $\text{--N(CH}_3\text{)CH}_2\text{CH}_2\text{N(CH}_3\text{)--}$, --S-- , --S--S-- , $\text{--OCH}_2\text{CH}_2\text{O--}$, or a combination thereof.

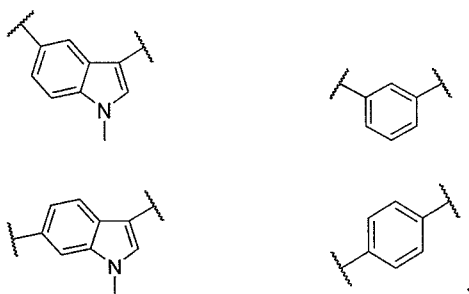
55. The conjugate of any one of claims 35, 36, 38-40, and 42-54, wherein **Ar** is a divalent six-membered substituted or unsubstituted, monocyclic aryl, or a divalent five- or six-membered, substituted or unsubstituted, heteroaryl.

56. The conjugate of any one of claims 35, 36, 38-40, and 42-55, wherein **Ar** is a divalent six-membered substituted or unsubstituted, monocyclic aryl, or a divalent six-membered, substituted or unsubstituted, heteroaryl.

57. The conjugate of any one of claims 35, 36, 38-40, and 42-54, wherein **Ar** is a divalent eight-, nine- or ten-membered, substituted or unsubstituted, fused bicyclic heteroaryl.

58. The conjugate of any one of claims 35, 36, 38-40, 42-54, and 57, wherein **Ar** is a divalent nine-membered, substituted or unsubstituted, fused bicyclic heteroaryl.

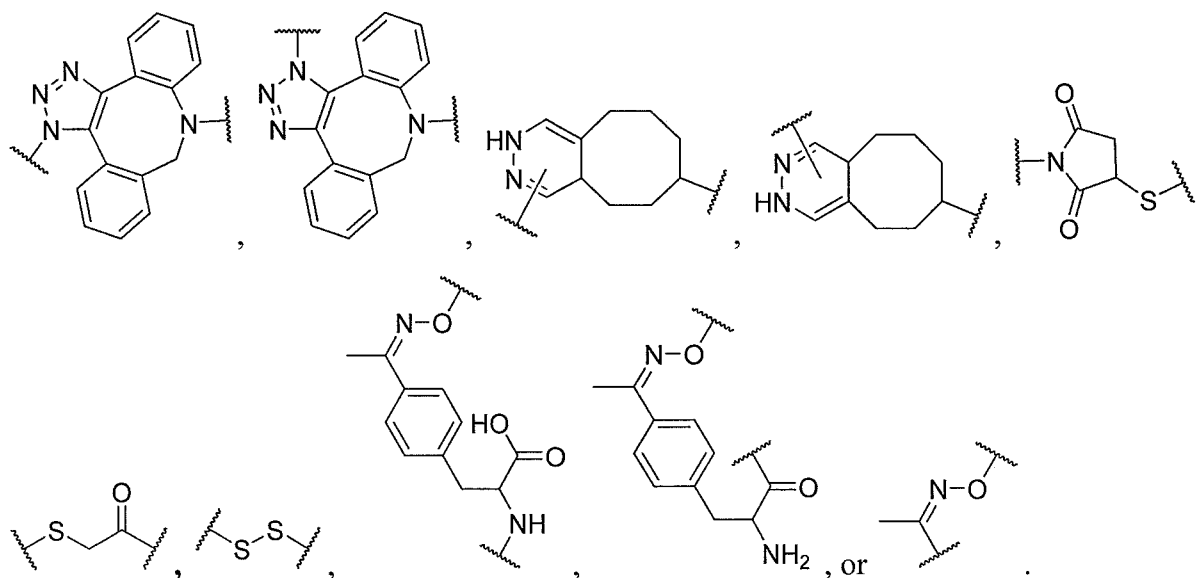
59. The conjugate of any one of claims 35, 36, 38-40, and 42-54, wherein **Ar** is any of the following:



60. The conjugate of any one of claims 35, 36, 38-40, and 42-59, wherein L is absent.

61. The conjugate of any one of claims 36, 38-40, and 42-59, wherein L is $-\text{CH}_2-$.

62. The conjugate of any one of claims 35-61-, wherein **R** is:



63. The conjugate of any one of claims 35-62, wherein **COMP** is a residue of a polypeptide.

64. The conjugate of any one of claims 35-62, wherein **COMP** is a residue of an antibody.

65. The conjugate of any one of claims 35-62, wherein **COMP** is a residue of an antibody chain.

66. A pharmaceutical composition comprising the compound of any one of claims 1-33 or conjugate of any one of claims 34-65; and a pharmaceutically acceptable excipient, carrier, or diluent.

67. The compound of any one of claims 1-33, conjugate of any one of claims 34-65, or pharmaceutical composition of claim 66 for use in therapy.

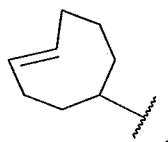
68. Use of an effective amount of the compound of any one of claims 1-33, conjugate of any one of claims 34-65, or pharmaceutical composition of claim 66 in the manufacture of a medicament for treating cell proliferation or cancer.

69. The use of claim 68 where the cancer is small cell lung cancer, non-small cell lung cancer, ovarian cancer, platinum-resistant ovarian cancer, ovarian adenocarcinoma, endometrial cancer, breast cancer, breast cancer which overexpresses Her2, triple-negative breast cancer, a lymphoma, large cell lymphoma; diffuse mixed histiocytic and lymphocytic lymphoma; follicular B cell lymphoma, colon cancer, colon carcinoma, colon adenocarcinoma, colorectal adenocarcinoma, melanoma, prostate cancer, or multiple myeloma.

70. A method of producing a conjugate, comprising contacting the compound of any one of claims 1-33 with a second compound under conditions suitable for conjugating the compound of any one of claims 1-33 with the second compound; wherein the second compound comprises an alkyne, strained alkene, tetrazine, thiol, maleimide, carbonyl, oxyamine, or azide.

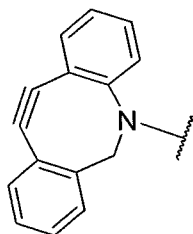
71. The method of claim 70, wherein the second compound comprises a tetrazine; and **R** comprises a strained alkene.

72. The method of claim 70 or 71, wherein **R** is:



73. The method of claim 70, wherein the second compound comprises an azide; and **R** comprises an alkyne.

74. The method of claim 70 or 73, wherein **R** is:

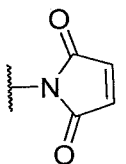


75. The method of claim 70, wherein the second compound comprises an alkyne; and **R** comprises an azide.

76. The method of claim 70, wherein the second compound comprises a strained alkene; and **R** comprises a tetrazine.

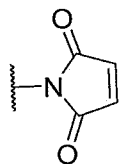
77. The method of claim 70, wherein the second compound comprises a thiol; and **R** comprises a maleimide.

78. The method of claim 70 or 77, wherein **R** is:



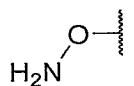
79. The method of claim 70, wherein the second compound comprises a maleimide; and **R** comprises a thiol.

80. The method of claim 70 or 79, wherein the second compound comprises:

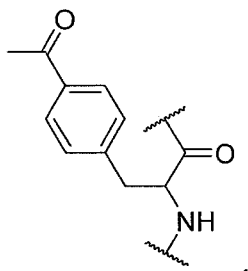


81. The method of claim 70, wherein the second compound comprises a carbonyl; and **R** comprises an oxyamine.

82. The method of claim 70 or 81, wherein **R** is:

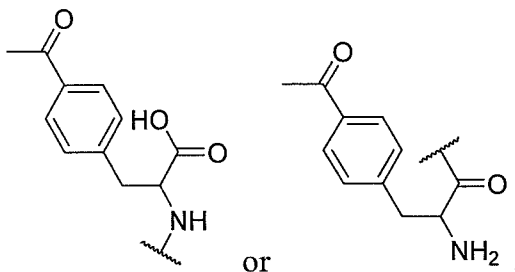


83. The method of claim 70, 81, or 82, wherein second compound comprises:

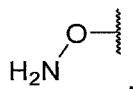


84. The method of claim 70, wherein the second compound comprises an oxyamine; and **R** comprises a carbonyl.

85. The method of claim 70 or 84, wherein **R** is:



86. The method of claim 70, 84, or 85, wherein the second compound comprises:



87. The method of any one of claims 70-86, wherein the second compound is a polypeptide.

88. The method of any one of claims 70-86, wherein the second compound is an antibody

89. The method of any one of claims 70-86, wherein the second compound is an antibody chain.