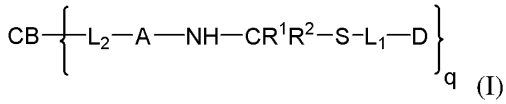
CLAIMS

What is claimed is:

1. A cell-binding agent-cytotoxic agent conjugate represented by the following formula:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

CB is a cell-binding agent;

L_2 is absent or a spacer;

A is an amino acid residue or a peptide comprising 2 to 20 amino acid residues;

R^1 and R^2 are each independently H or a C_{1-3}alkyl;

L_1 is a spacer;

D-L_1-SH is a cytotoxic agent; and

q is an integer from 1 to 20.

2. The conjugate of claim 1, wherein at least one of R^1 and R^2 is H.

3. The conjugate of claim 1, wherein R^1 and R^2 are each independently H or Me.

4. The conjugate of claim 3, wherein one of R^1 and R^2 is H, and the other one is Me.

5. The conjugate of claim 1, wherein R^1 and R^2 are both H.

6. The conjugate of any one of claims 1-5, wherein L_1 is $–L_1'–C(=O)-$; and L_1' is an alkylene or a cycloalkylene, wherein the –C(=O)- moiety in L_1 is connected to D.

7. The conjugate of claim 6, wherein L_1' is C_{1-10}alkylene.

8. The conjugate of claim 6, wherein L_1 is $–CR^3R^4-(CH_2)_{1-8}-C(=O)-$; R^3 and R^4 are each independently H or Me.

9. The conjugate of claim 8, wherein L_1 is $–CR^3R^4-(CH_2)_{3-5}-C(=O)-$.

10. The conjugate of claim 8 or 9, wherein R^3 and R^4 are both Me.

11. The conjugate of claim 6, wherein L_1 is $–(CH_2)_{4-6}-C(=O)-$.

12. The conjugate of any one of claims 1-11, wherein L_2 is represented by the following structural formula:

$$—J_{CB}—R^A—V—W—R^B—V'—R^C—J_A—;$$

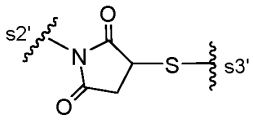
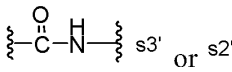
wherein:

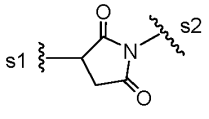
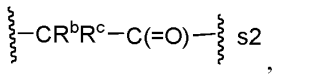
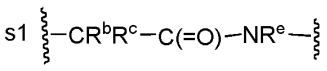
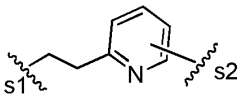
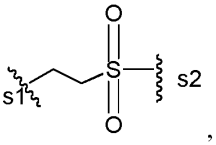
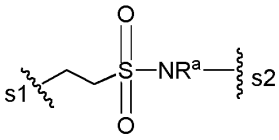
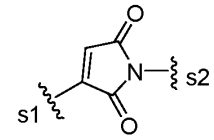
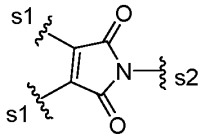
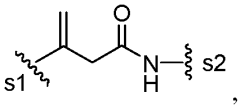
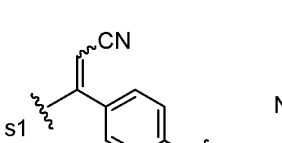
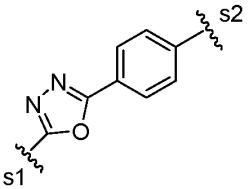
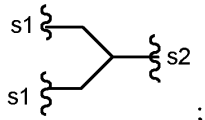
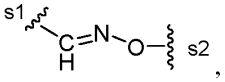
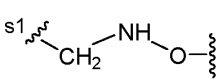
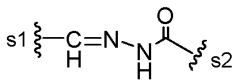
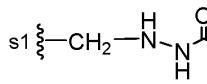
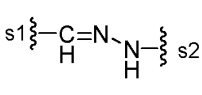
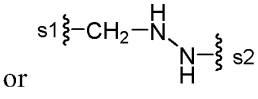
R^A is an alkylene, a cycloalkylalkylene or an arylene;

R^B and R^C are each independently absent, an alkylene, a cyclalkylene, or an arylene;

V and V' are each independently $-(O-CH_2-CH_2)_p-$, or $-(CH_2-CH_2-O)_p-$;

p is 0 or an integer from 1 to 10;

W is absent, ,  or , wherein s2' indicates the site connected to V, R^A or J_{CB} and s3' indicates the site connected to R^B, V', R^C or J_A;

J_{CB} is -C(=O)-, , , , , , , , , , , , , ; , , , ,  or , wherein s1 indicates the site connected to the cell-binding agent CB and s2 indicates the site connected to R^A;

R^a, R^b, R^c, and R^e, for each occurrence, are independently H or an alkyl; and

J_A is -C(=O)-.

13. The conjugate of any one of claims 1-12, wherein L_2 is represented by the following structural formula:

$$—J_{CB}—R^A—V—W—R^B—V'—R^C—J_A—;$$

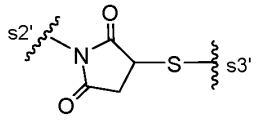
wherein:

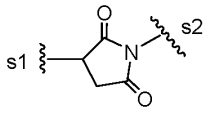
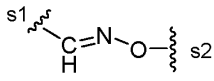
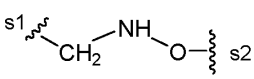
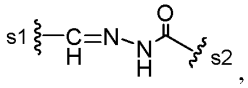
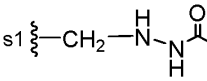
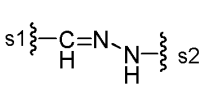
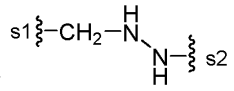
R^A is an alkylene, a cycloalkylalkylene or an arylene;

R^B and R^C are each independently absent, an alkylene, a cyclalkylene, or an arylene;

V and V' are each independently $-(O-CH_2-CH_2)_p-$, or $-(CH_2-CH_2-O)_p-$;

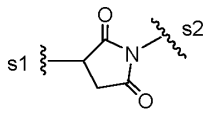
p is 0 or an integer from 1 to 10;

W is absent, or ;

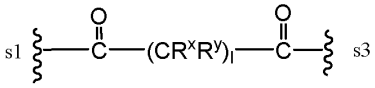
J_{CB} is -C(=O)-, , , , , , , , wherein s1 indicates the site connected to the cell-binding agent CB and s2 indicates the site connected to R^A; and

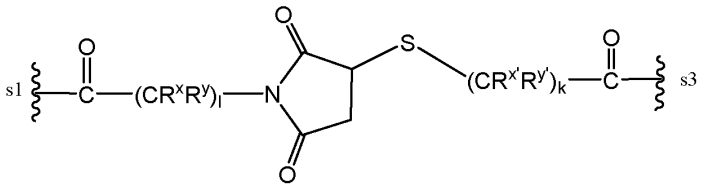
J_A is -C(=O)-.

14. The conjugate of claim 12 or 13, wherein p is 0 and R^C is absent.

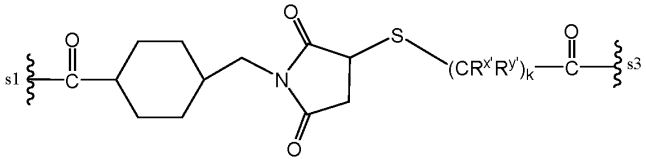
15. The conjugate of any one of claims 12-14, wherein J_{CB} is -C(=O)- or .

16. The conjugate of any one of claims 12-15, wherein L_2 is represented by the following structural formulas:

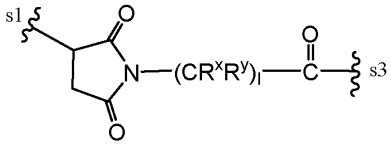
 (L2a);



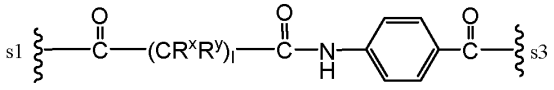
(L2b);



(L2c);



(L2d); or



(L2e);

wherein:

R^x, R^y, $R^{x'}$ and $R^{y'}$, for each occurrence, are independently H, -OH, halogen, -O-(C_{1-4} alkyl), -SO_3H, -$NR_{40}R_{41}R_{42}^+$, or a C_{1-4} alkyl optionally substituted with -OH, halogen, SO_3H or $NR_{40}R_{41}R_{42}^+$, wherein R_{40}, R_{41} and R_{42} are each independently H or a C_{1-4} alkyl;

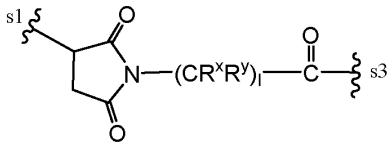
l and k are each independently an integer from 1 to 10; and

s1 indicates the site connected to the cell-binding agent CB and s3 indicates the site connected to the A group .

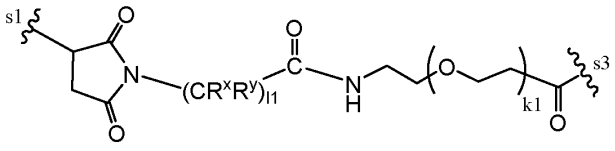
17. The conjugate of claim 16, wherein R^x, R^y, $R^{x'}$ and $R^{y'}$ are all H.

18. The conjugate of claim 16 or 17, wherein l and k are each independently an integer an integer from 2 to 6.

19. The conjugate of any one of claims 12-15, wherein L_2 is represented by the following structural formula:



(L2d), or



(L2f);

wherein:

R^x and R^y are both H;

l and l1 are each an integer from 2 to 6; and

k1 is an integer from 1 to 5.

20. The conjugate of any one of claims 1-19, wherein A is a peptide cleavable by a protease.

21. The conjugate of claim 20, wherein A is a peptide cleavable by a protease expressed in tumor tissue.

22. The conjugate of any one of claims 1-21 , wherein A is a peptide having an amino acid that is covalent linked with –NH-CR^1R^2-S-L_1-D selected from the group consisting of Ala, Arg, Asn, Asp, Cit, Cys, selino-Cys, Gln, Glu, Gly, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, each independently as L or D isomer.

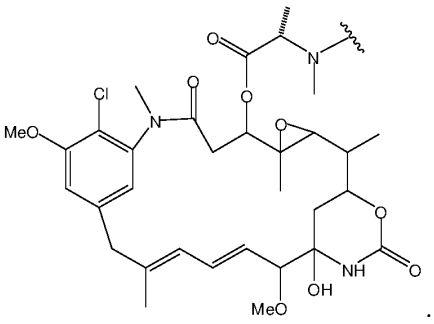
23. The conjugate of any one of claims 1-22, wherein the amino acid connected to –NH-CR^1R^2-S-L_1-D is an L amino acid.

24. The conjugate of any one of claims 1-19, wherein A is selected from the group consisting of Gly-Gly-Gly, Ala-Val, Val-Ala, D-Val-Ala, Val-Cit, D-Val-Cit, Val-Lys, Phe-Lys, Lys-Lys, Ala-Lys, Phe-Cit, Leu-Cit, Ile-Cit, Phe-Ala, Phe-N^9-tosyl-Arg, Phe-N^9-nitro-Arg, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Leu-Ala-Leu, Ile-Ala-Leu, Val-Ala-Val, Ala-Ala-Ala, D-Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala-D-Ala, Ala-Leu-Ala-Leu (SEQ ID NO: 1), β-Ala-Leu-Ala-Leu (SEQ ID NO: 2), Gly-Phe-Leu-Gly (SEQ ID NO: 3), Val-Arg, Arg-Arg, Val-D-Cit, Val-D-Lys, Val-D-Arg, D-Val-Cit, D-Val-Lys, D-Val-Arg, D-Val-D-Cit, D-Val-D-Lys, D-Val-D-Arg, D-Arg-D-Arg, Ala-Ala, Ala-D-Ala, D-Ala-Ala, D-Ala-D-Ala, Ala-Met, Gln-Val, Asn-Ala, Gln-Phe, Gln-Ala, D-Ala-Pro, and D-Ala-tBu-Gly, wherein the first amino acid in each peptide is connected to L_2 group and the last amino acid in each peptide is connected to –NH-CR^1R^2-S-L_1-D.

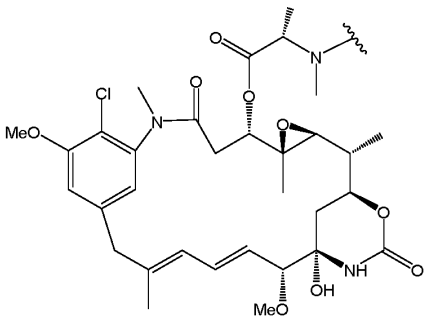
25. The conjugate of claim 24, wherein A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

26. The conjugate of any one of claims 1-25, wherein D is a maytansinoid.

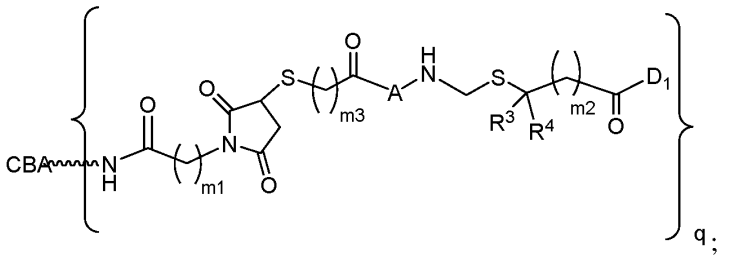
27. The conjugate of claim 26, wherein D is represented by the following formula:

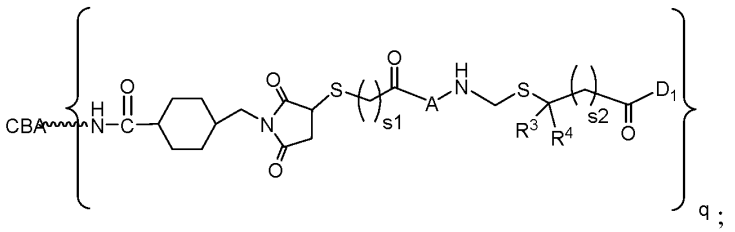


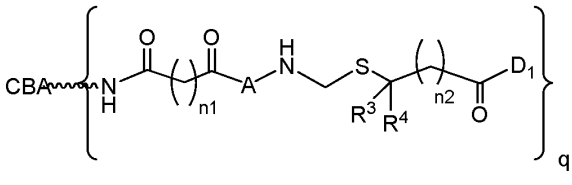
28. The conjugate of claim 27, wherein D is represented by the following formula:



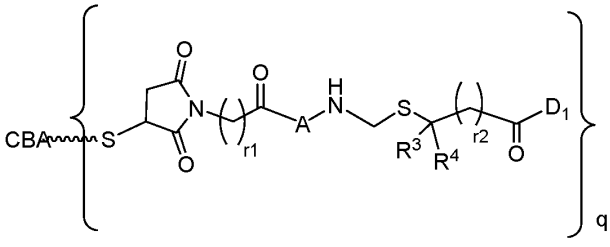
29. The conjugate of any one of claims 1-28, wherein the conjugate is represented by the following formula:



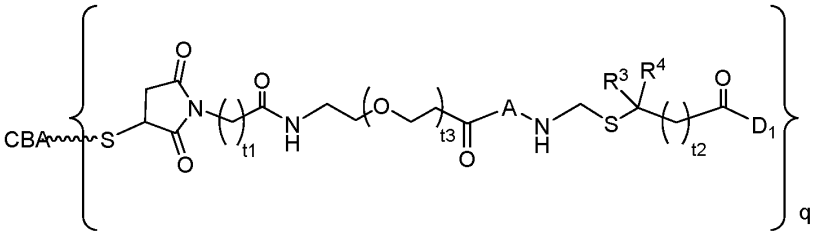




q;



q; or



or a pharmaceutically acceptable salt thereof, wherein:

 is the cell-binding agent connected to the L_2 group through a Lys amine group;

 is the cell-binding agent connected to the L_2 group through a Cys thiol group;

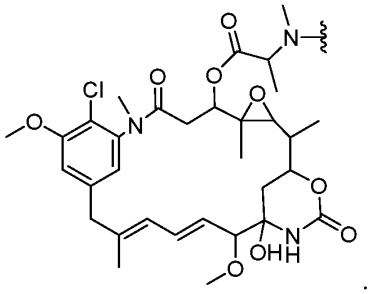
R^3 and R^4 are each independently H or Me;

m1, m3, n1, r1, s1 and t1 are each independently an integer from 1 to 6;

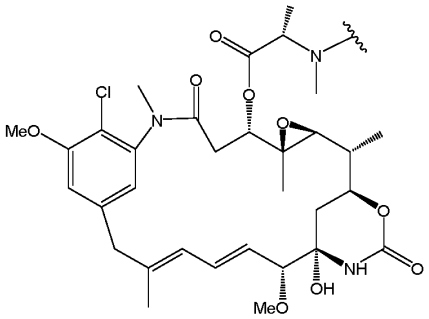
m2, n2, r2, s2 and t2 are each independently an integer from 1 to 7;

t3 is an integer from 1 to 12;

D_1 is represented by the following formula:



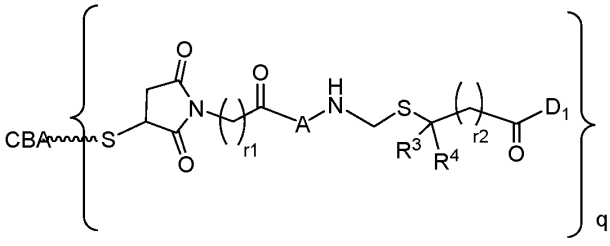
30. The conjugate of claim 29, wherein D_1 is represented by the following formula:



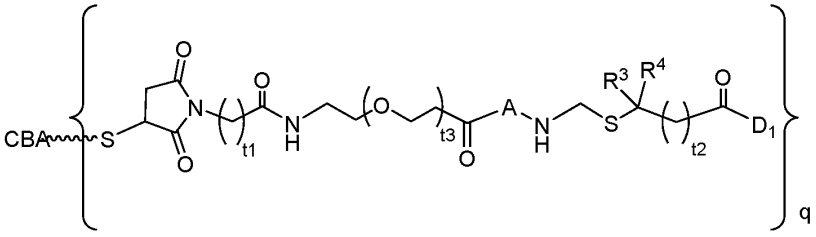
31. The conjugate of claim 29 or 30, wherein A is Ala-Ala-Ala,, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

32. The conjugate of any one of claims 29-31, wherein m1, r1, n1 and m3 are each independently an integer from 2 to 4; and m2, n2 and r2 are each independently an integer from 3 to 5.

33. The conjugate of any one of claims 29-31, wherein the conjugate is represented by the following formula:



; or



wherein:

r1 and t1 are each an integer from 2 to 6;

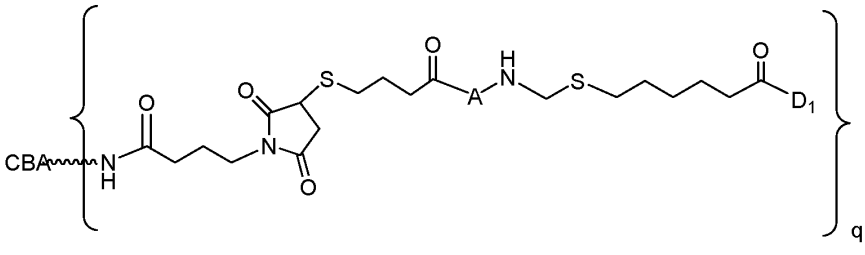
r2 and t2 are each an integer from 2 to 5; and

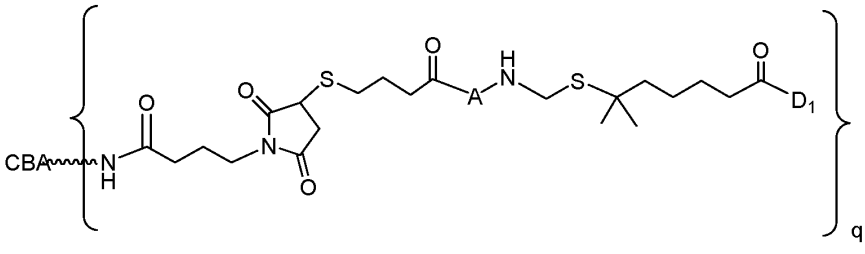
t3 is an integer from 2 to 12.

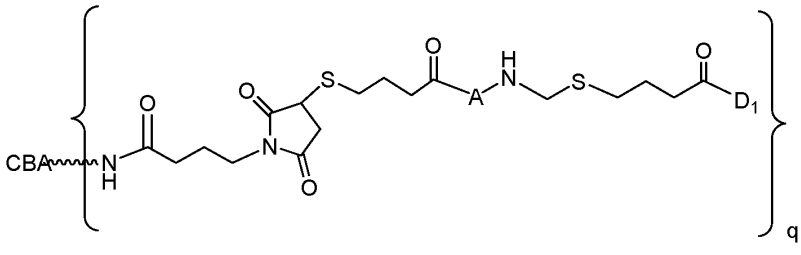
34. The conjugate of any one of claims 29-33, wherein R^3 and R^4 are both Me.

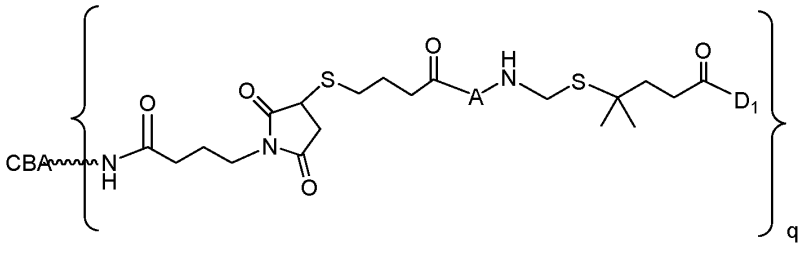
35. The conjugate of any one of claims 29-33, wherein R^3 and R^4 are both H.

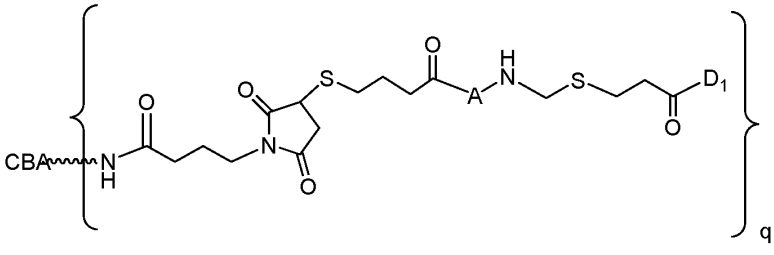
36. The conjugate of claim 29, wherein the conjugate is represented by the following formula:

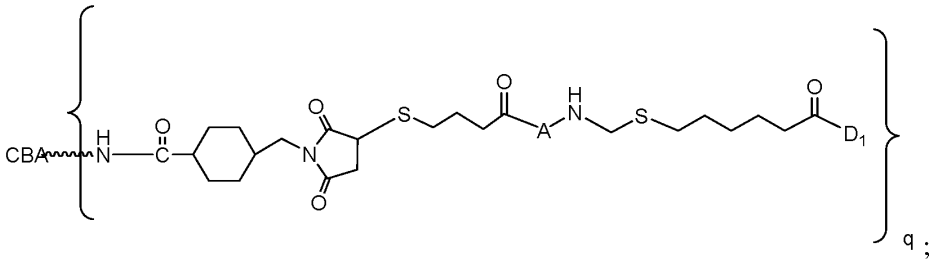




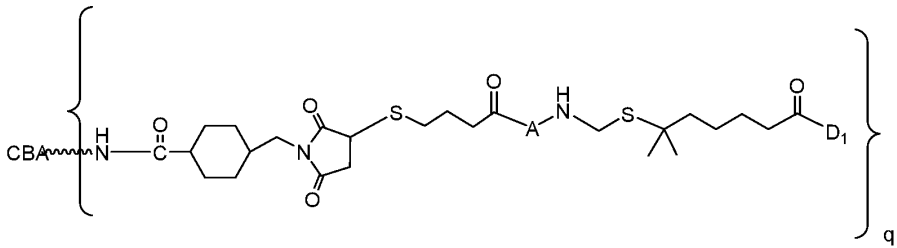




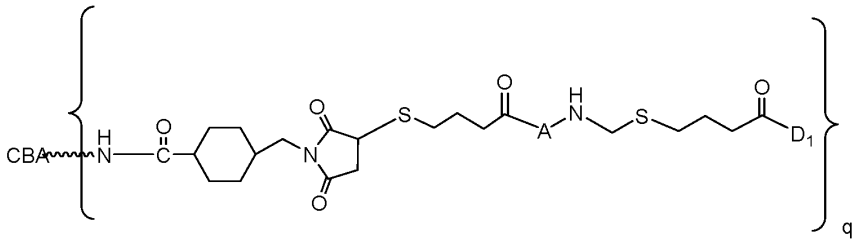




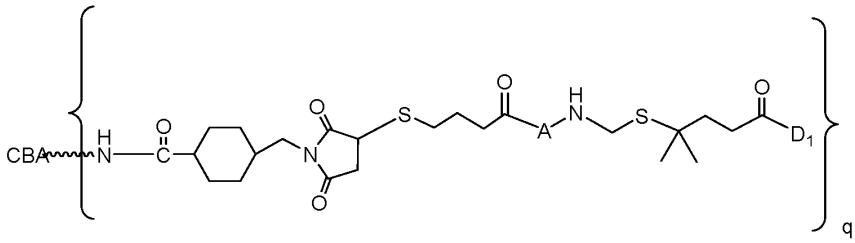
q ;



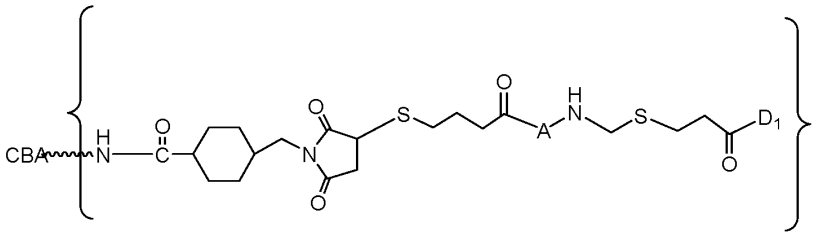
q ;



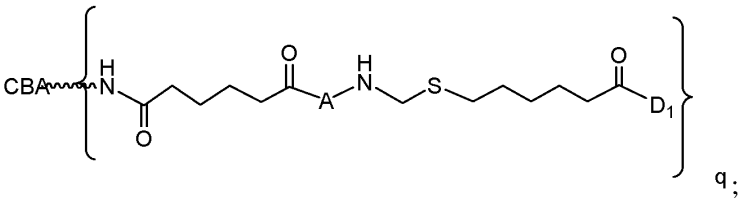
q ;



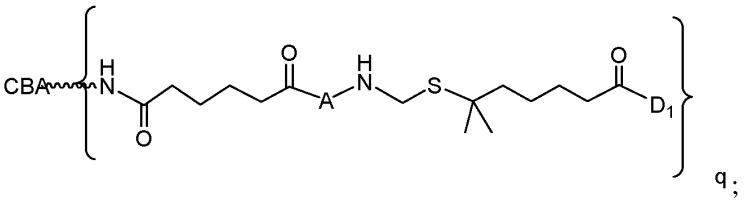
q ;



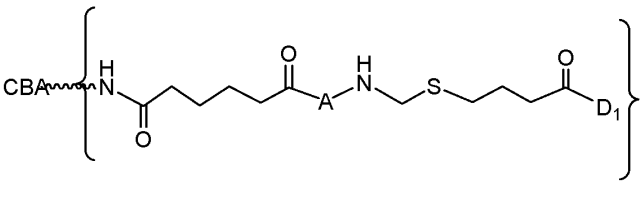
q ;



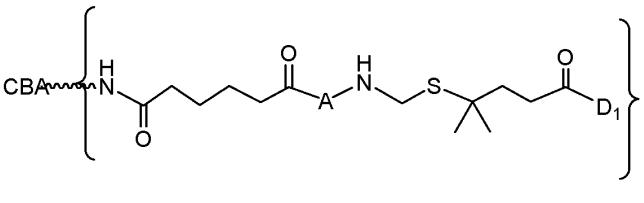
q;



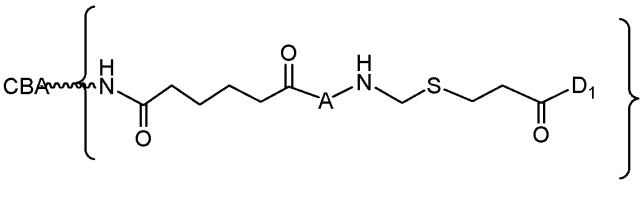
q;



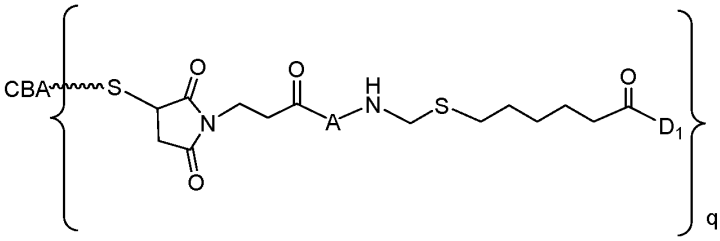
q;



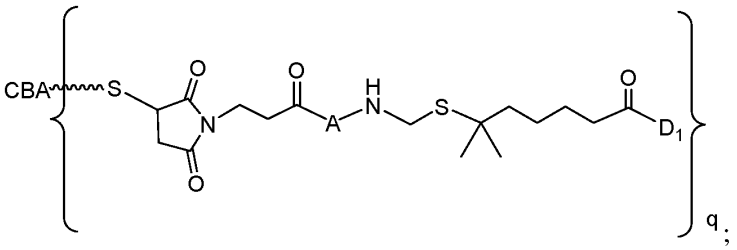
q;

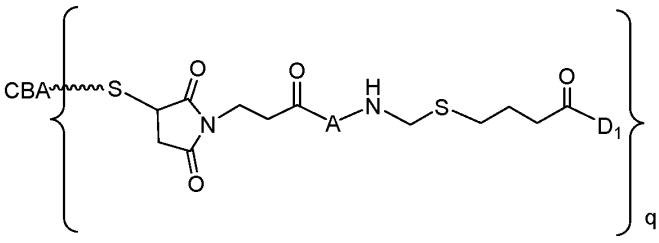


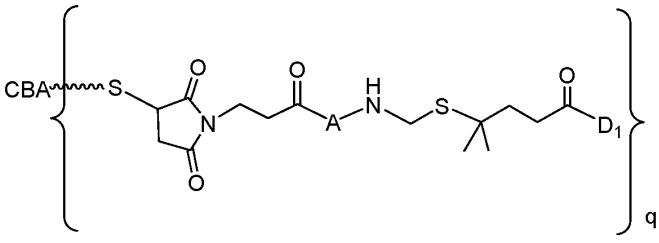
q;



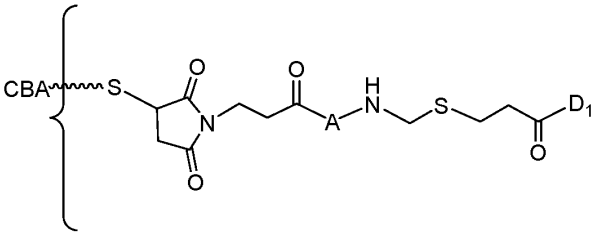
q;

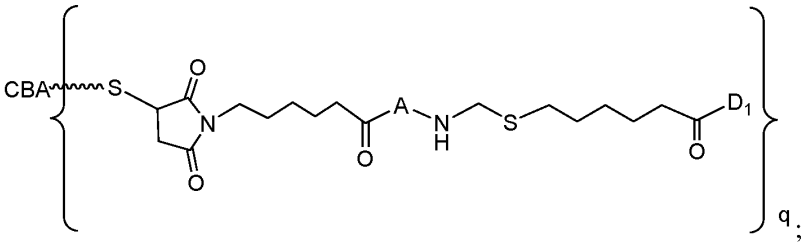


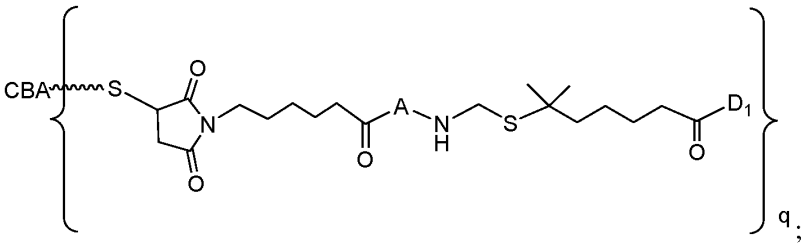


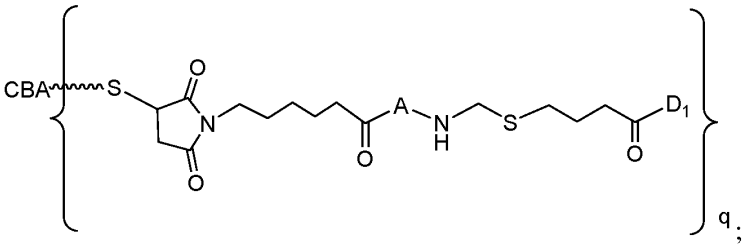


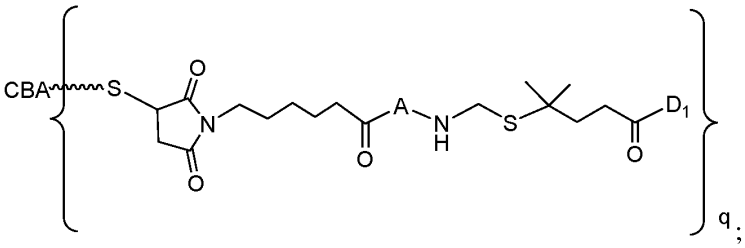
; or

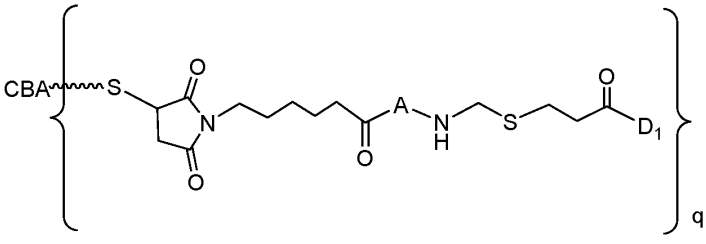


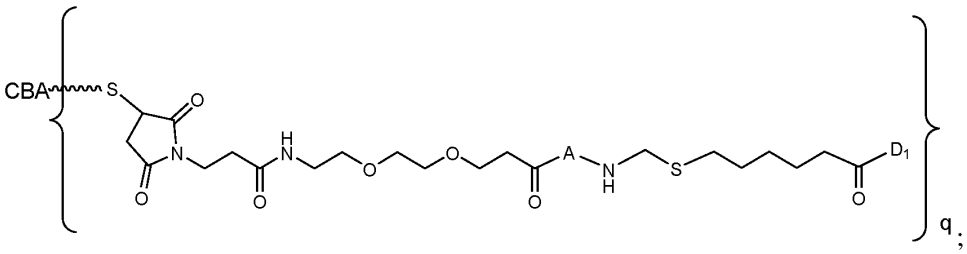


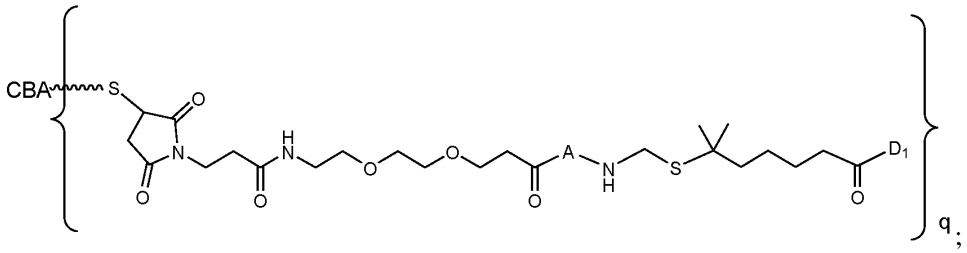


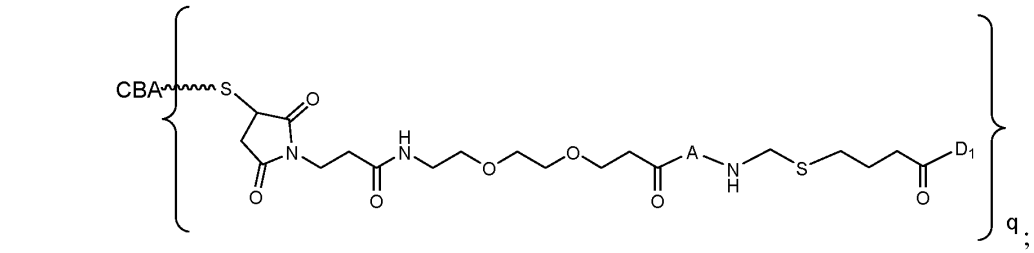


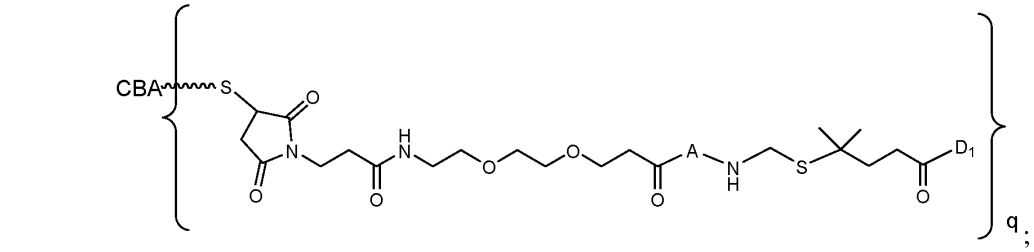


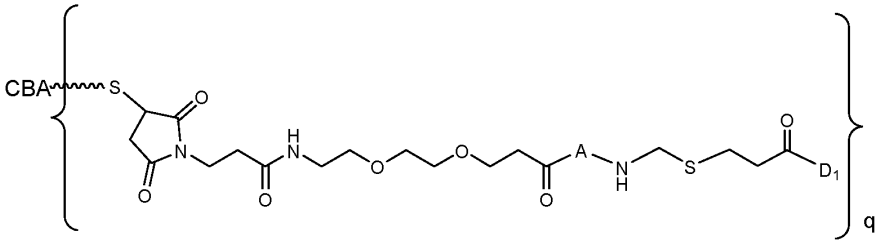


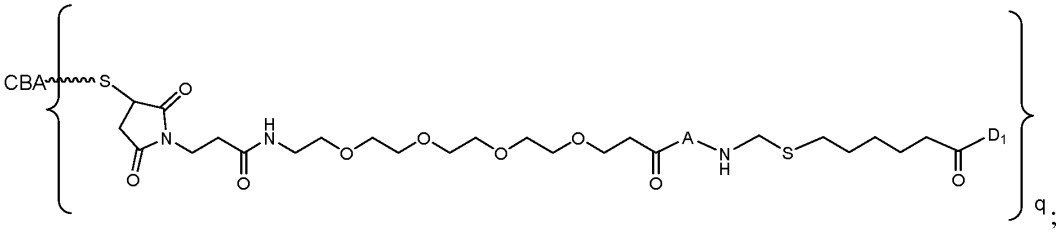


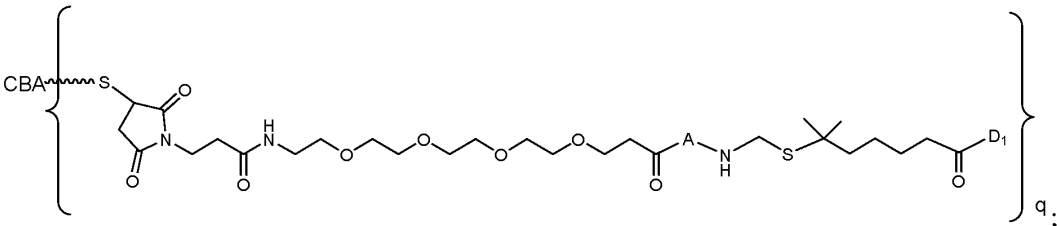


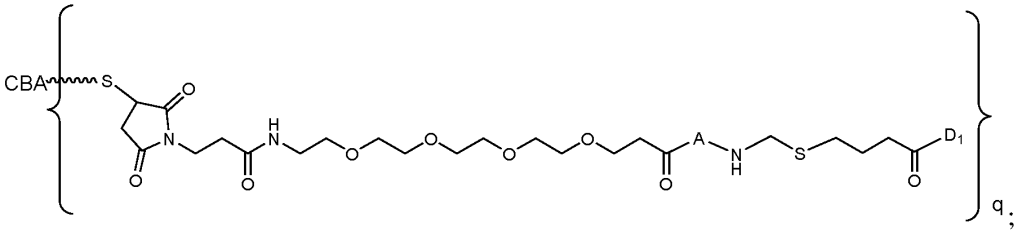


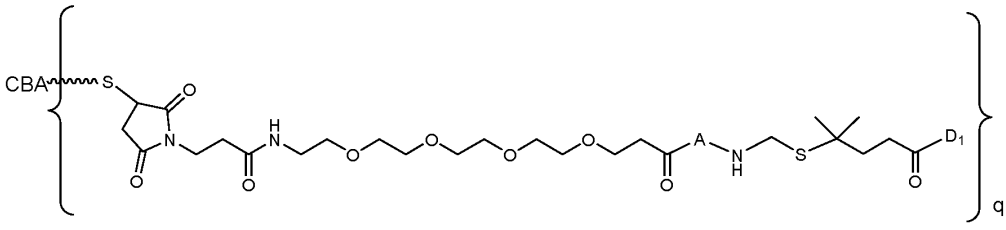




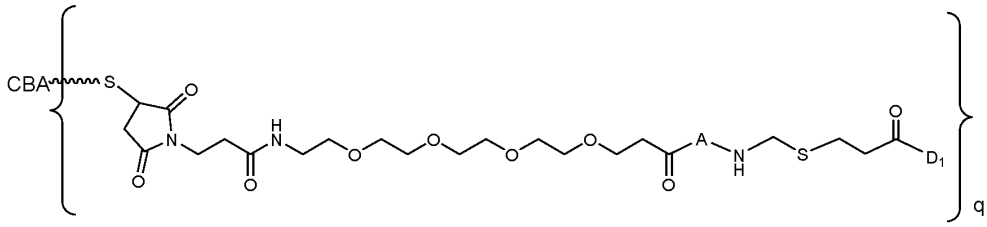








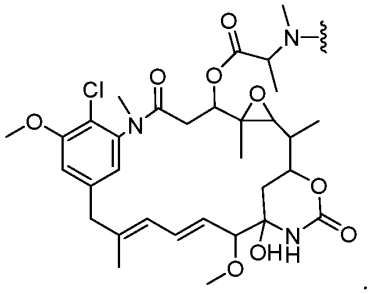
; or



or a pharmaceutically acceptable salt thereof, wherein:

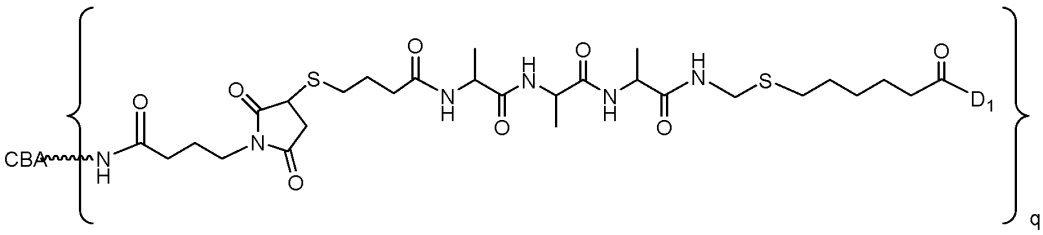
A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly, and

D_1 is represented by the following formula:

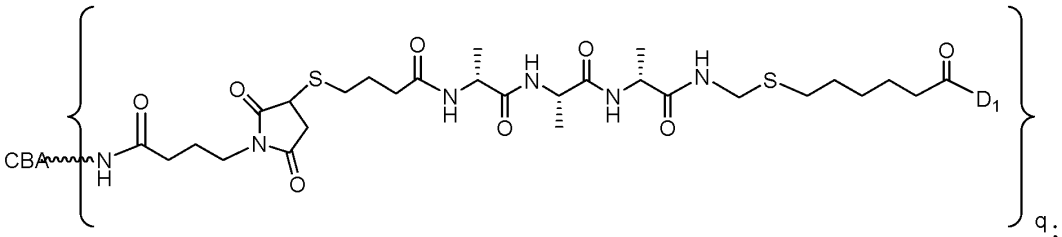


.

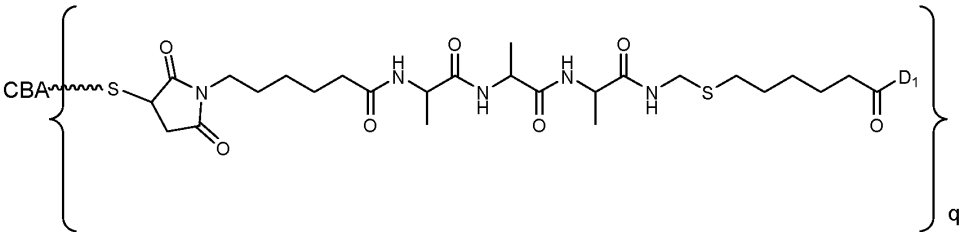
37. The conjugate of claim 36, wherein the conjugate is represented by the following formula:



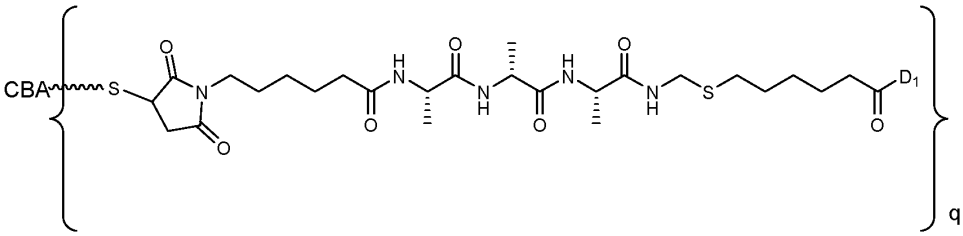
;



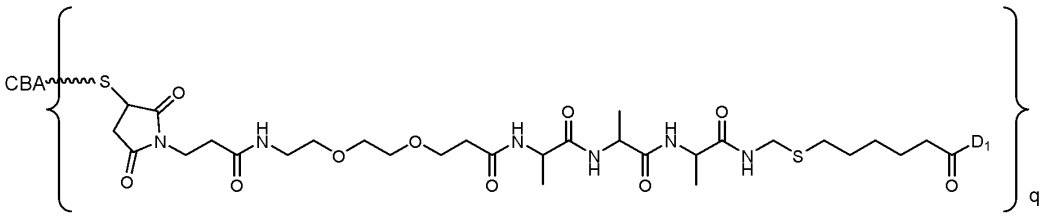
q;



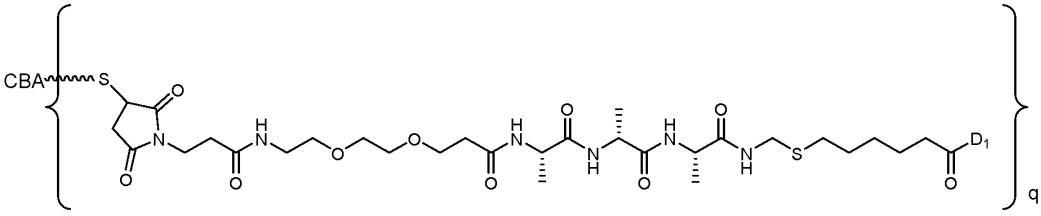
q;



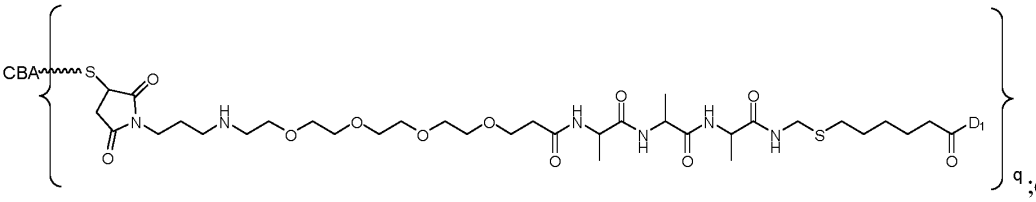
q;



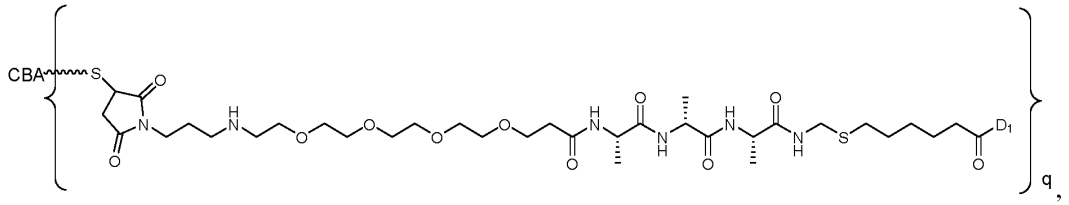
q;



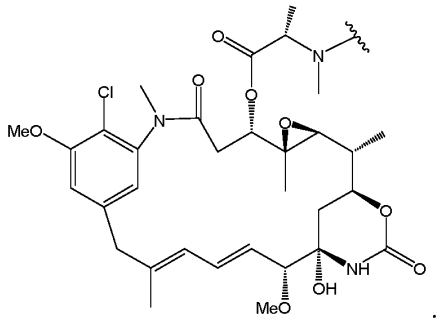
q;



q;or



wherein D_1 is represented by the following formula:



38. The conjugate of any one of claims 1-37, wherein, the cell-binding agent is an antibody or an antigen-binding fragment thereof, a single chain antibody, a single chain antibody fragment that specifically binds to a target cell, a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment that specifically binds to a target cell, a chimeric antibody, a chimeric antibody fragment that specifically binds to a target cell, a domain antibody, a domain antibody fragment that specifically binds to a target cell, a probody, a nanobody, a lymphokine, a hormone, a vitamin, a growth factor, a colony stimulating factor, a nutrient-transport molecule, a Bicycles® peptide, or a pentarin.

39. The conjugate of claim 38, wherein the cell-binding agent is an antibody or an antigen-binding fragment thereof.

40. The conjugate of claim 38, wherein the cell-binding agent is a resurfaced antibody or a resurfaced antibody fragment thereof.

41. The conjugate of claim 38, wherein the cell-binding agent is a monoclonal antibody or a monoclonal antibody fragment thereof.

42. The conjugate of claim 38, wherein the cell-binding agent is a humanized antibody or a humanized antibody fragment thereof.

43. The conjugate of claim 38, wherein the cell-binding agent is a chimeric antibody or a chimeric antibody fragment thereof.

44. The conjugate of claim 38, wherein the cell-binding agent is an anti-folate receptor antibody or an antibody fragment thereof, an anti-EGFR antibody or an antibody fragment thereof, an anti-CD33 antibody or an antibody fragment thereof, an anti-CD19 antibody or an antibody fragment thereof, an anti-Muc1 antibody or an antibody fragment thereof, or an anti-CD37 antibody or an antibody fragment thereof.

45. The conjugate of claim 38, wherein the cell-binding agent is an anti-CD123 antibody or an antibody fragment thereof.

46. The conjugate of claim 45, wherein the anti-CD123 antibody or antibody fragment thereof comprises a) a heavy chain a heavy chain variable region CDR1 having the amino acid sequence of SEQ ID NO:33, a heavy chain variable region CDR2 having the amino acid sequence of SEQ ID NO:34, and a heavy chain variable region CDR3 having the amino acid sequence of SEQ ID NO:35; and b) a light chain variable region CDR1 having the amino acid sequence of SEQ ID NO:36, a light chain variable region CDR2 having the amino acid sequence of SEQ ID NO:37, and a light chain variable region CDR3 having the amino acid sequence of SEQ ID NO:38.

47. The conjugate of claim 45, wherein the anti-CD123 antibody or antibody fragment thereof comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO. 39 and a light chain variable region having the amino acid sequence of SEQ ID NO. 40.

48. The conjugate of claim 47, wherein X (or Xaa), the second residue from the N-terminus of SEQ ID NO:39 is Phe (F).

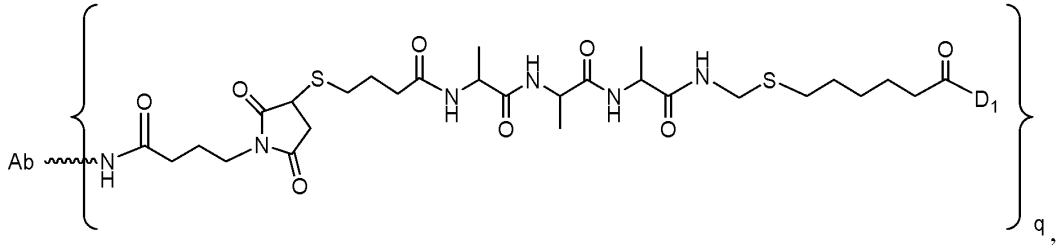
49. The conjugate of claim 47, wherein X (or Xaa), the second residue from the N-terminus of SEQ ID NO:39 is Val (V).

50. The conjugate of claim 45, wherein the anti-CD123 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO:42 and a light chain having the amino acid sequence of SEQ ID NO:43.

51. The conjugate of claim 45, wherein the anti-CD123 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO:44 and a light chain having the amino acid sequence of SEQ ID NO:43.

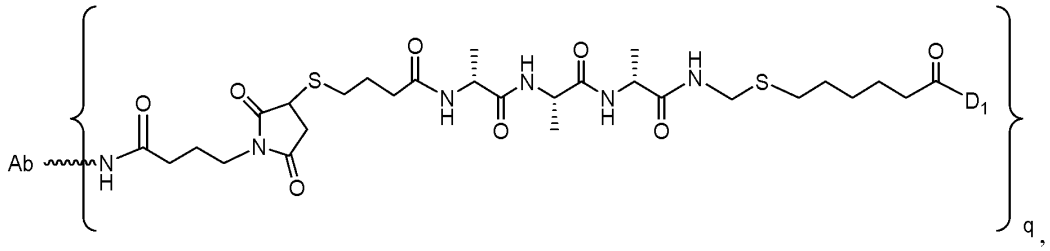
52. The conjugate of claim 50 or 51, wherein X (or Xaa), the second residue from the N-terminus of SEQ ID NO: 42 or SEQ ID NO:44 is Val.

53. The conjugate of claim 1, wherein the conjugate is represented by the following formula:



wherein Ab is an anti-folate receptor antibody; and q is an integer from 1 to 10.

54. The conjugate of claim 1, wherein the conjugate is represented by the following formula:



wherein Ab is an anti-folate receptor antibody; and q is an integer from 1 to 10.

55. The conjugate of claim 53 or 54, wherein the anti-folate receptor antibody comprises (a) a heavy chain CDR1 having the amino acid sequence of SEQ ID NO: 4; a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 5; and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 6; and (b) a light chain CDR1 having the amino acid sequence of SEQ ID NO: 7; a light chain CDR2 having the amino acid sequence of SEQ ID NO: 10; and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 9.

56. The conjugate of claim 53 or 54, wherein the anti-folate receptor antibody comprises a heavy chain variable domain having the amino acid sequence of SEQ ID NO: 14, and a light chain variable domain having the amino acid sequence of SEQ ID NO: 15 or SEQ ID NO: 16.

57. The conjugate of claim 53 or 54, wherein the anti-folate receptor antibody comprises the heavy chain having the amino acid sequence of SEQ ID NO: 11, and the light chain having the amino acid sequence of SEQ ID NO: 12 or SEQ ID NO: 13.

58. The conjugate of claim 53 or 54, wherein the anti-folate receptor antibody comprises the heavy chain having the amino acid sequence of SEQ ID NO: 11 and the light chain having the amino acid sequence of SEQ ID NO: 13.

59. The conjugate of claim 53 or 54, wherein the anti-folate receptor antibody comprises a heavy chain that is encoded by the plasmid DNA having ATCC deposit no. PTA-10772 and a light chain that is encoded by the plasmid DNA having ATCC deposit no. PTA-10774.

60. A compound represented by the following formula:

$$L_2'—A—NH—CR^1R^2—S—L_1—D \quad (II)$$

or a pharmaceutically acceptable salt thereof, wherein:

L_2' is absent or a spacer bearing a reactive moiety that can form a covalent bond with a cell-binding agent;

A is an amino acid or a peptide comprising 2 to 20 amino acids;

R^1 and R^2 are each independently H or a C_{1-3}alkyl;

L_1 is a spacer;

D-L_1-SH is a cytotoxic agent; and

q is an integer from 1 to 20.

61. The compound of claim 60, wherein at least one of R^1 and R^2 is H.

62. The compound of claim 60, wherein R^1 and R^2 are each independently H or Me.

63. The compound of claim 60, wherein one of R^1 and R^2 is H; and the other one is Me.

64. The compound of claim 60, wherein R^1 and R^2 are both H.

65. The compound of any one of claims 60-64, wherein L_1 is –L_1'–C(=O)-; and L_1' is an alkylene or a cycloalkylene.

66. The compound of claim 65, wherein L_1' is C_{1-10}alkylene.

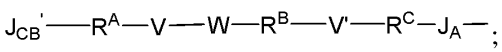
67. The compound of claim 65, wherein L_1 is –CR^3R^4-$(CH_2)_{1-8}$-C(=O)-; R^3 and R^4 are each independently H or Me.

68. The compound of claim 67, wherein L_1 is –CR^3R^4-$(CH_2)_{3-5}$-C(=O)-.

69. The compound of claim 67 or 68, wherein R^3 and R^4 are both Me.

70. The compound of claim 66, wherein L_1 is $-(CH_2)_{4-6}$-C(=O)-.

71. The compound of any one of claims 60-70, wherein L_2' is represented by the following structural formula:



J_{CB}'—R^A—V—W—R^B—V'—R^C—J_A—;

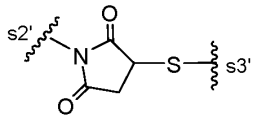
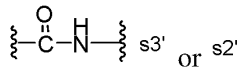
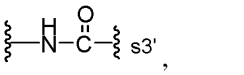
wherein:

R^A is an alkylene, a cycloalkylalkylene or an arylene;

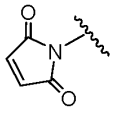
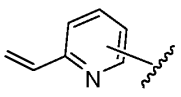
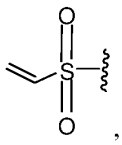
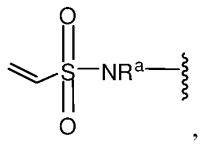
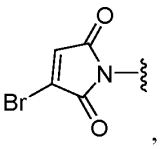
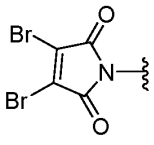
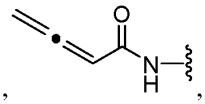
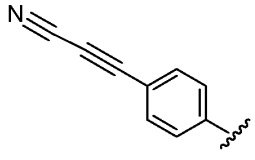
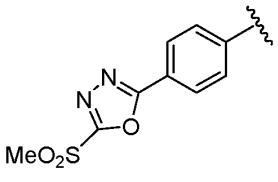
R^B and R^C are each independently absent, an alkylene, a cyclalkylene, or an arylene;

V and V' are each independently -(O-CH_2-CH_2)$_p$-, or -(CH_2-CH_2-O)$_p$-;

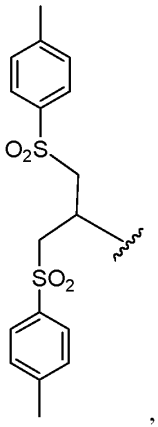
p is 0 or an integer from 1 to 10;

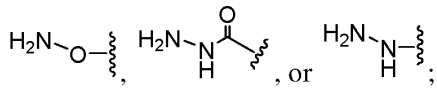
W is absent, ,  or ,

wherein s2' indicates the site connected to V, R^A or J_{CB}' and s3' indicates the site connected to R^B, V', R^C or J_A;

J_{CB}' is -C(=O)OH, -COE, , X^1-CR^bR^c-C(=O)-, X^1-CR^bR^c-C(=O)-NR^e-, , , , , , , , ,

166





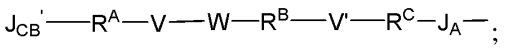
R^a, R^b, R^c, and R^e, for each occurrence, are independently H or an alkyl;

X^1 is –Cl, -Br or –I;

COE is a reactive ester; and

J_A is -C(=O)-.

72. The compound of any one of claims 60-70, wherein L_2' is represented by the following structural formula:



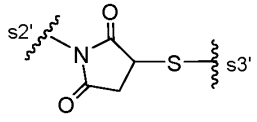
wherein:

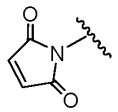
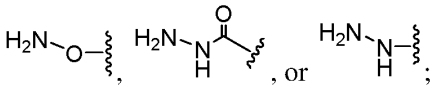
R^A is an alkylene, a cycloalkylalkylene or an arylene;

R^B and R^C are each independently absent, an alkylene, a cyclalkylene, or an arylene;

V and V' are each independently $-(O-CH_2-CH_2)_p-$, or $-(CH_2-CH_2-O)_p-$;

p is 0 or an integer from 1 to 10;

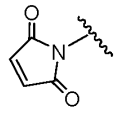
W is absent, or ;

J_{CB}' is -C(=O)OH, -COE, , ;

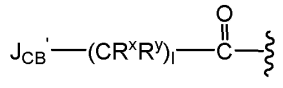
COE is a reactive ester; and

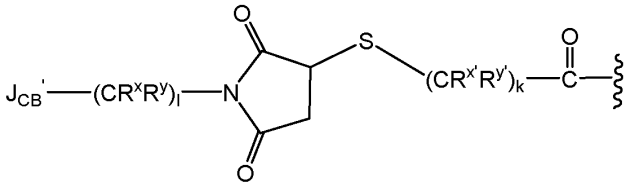
J_A is -C(=O)-.

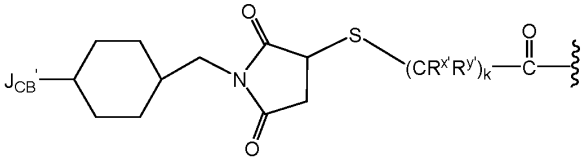
73. The compound of claim 71 or 72, wherein p is 0 and R^C is absent.

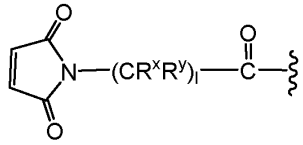
74. The compound of any one of claims 71-73, wherein J_{CB}' is -C(=O)OH, -COE or .

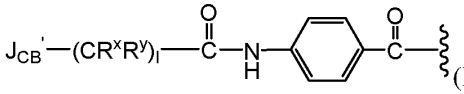
75. The compound of any one of claims 71-74, wherein L_2' is represented by the following structural formulas:

 (L2a');

 (L2b');

 (L2c');

 (L2d'); or

 (L2e');

wherein:

R^x, R^y, $R^{x'}$ and $R^{y'}$, for each occurrence, are independently H, -OH, halogen, -O-(C_{1-4} alkyl), $-SO_3H$, $-NR_{40}R_{41}R_{42}^+$, or a C_{1-4} alkyl optionally substituted with -OH, halogen, $-SO_3H$ or $NR_{40}R_{41}R_{42}^+$, wherein R_{40}, R_{41} and R_{42} are each independently H or a C_{1-4} alkyl;

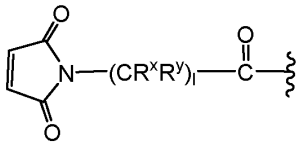
l and k are each independently an integer from 1 to 10;

J_{CB}' is -C(=O)OH or -COE.

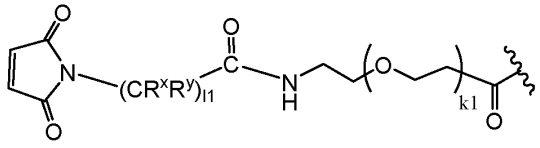
76. The compound of claim 75, wherein R^x, R^y, $R^{x'}$ and $R^{y'}$ are all H.

77. The compound of claim 75 or 76, wherein l and k are each independently an integer an integer from 2 to 6.

78. The compound of any one of claims 71-74, wherein L_2' is represented by the following structural formula:



(L2d'), or



(L2f');

wherein:

R^x and R^y are both H;

l and l1 are each an integer from 2 to 6; and

k1 is an integer from 1 to 12.

79. The compound of any one of claims 60-78, wherein A is a peptide cleavable by a protease.

80. The compound of claim 79, wherein A is a peptide cleavable by a protease expressed in tumor tissue.

81. The compound of any one of claims 60-80, wherein A is a peptide having an amino acid that is covalent linked with –NH-CR^1R^2-S-L_1-D selected from the group consisting of Ala, Arg, Asn, Asp, Cit, Cys, selino-Cys, Gln, Glu, Gly, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, each independently as L or D isomer.

82. The compound of any one of claims 60-81, wherein the amino acid connected to -NH-CR^1R^2-S-L_1-D is an L amino acid.

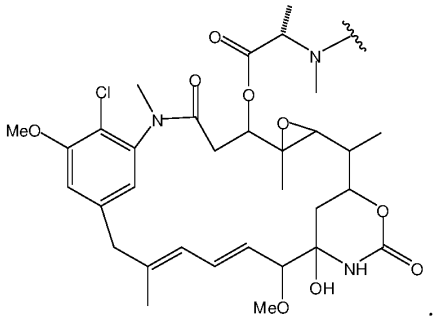
83. The compound of any one of claims 60-78, wherein A is selected from the group consisting of Gly-Gly-Gly, Ala-Val, Val-Ala, D-Val-Ala, Val-Cit, D-Val-Cit, Val-Lys, Phe-Lys, Lys-Lys, Ala-Lys, Phe-Cit, Leu-Cit, Ile-Cit, Phe-Ala, Phe-N^9-tosyl-Arg, Phe-N^9-nitro-Arg, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Leu-Ala-Leu, Ile-Ala-Leu, Val-Ala-Val, Ala-Ala-Ala, D-Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala-D-Ala, Ala-Leu-Ala-Leu (SEQ ID NO: 1), β-Ala-Leu-Ala-Leu (SEQ ID NO: 2), Gly-Phe-Leu-Gly (SEQ ID NO: 3), Val-Arg, Arg-Arg, Val-D-Cit, Val-D-Lys, Val-D-Arg, D-Val-Cit, D-Val-Lys, D-Val-Arg, D-Val-D-Cit, D-Val-D-Lys, D-Val-D-Arg, D-Arg-D-Arg, Ala-Ala, Ala-D-Ala, D-Ala-Ala, D-Ala-

D-Ala, Ala-Met, Gln-Val, Asn-Ala, Gln-Phe, Gln-Ala, D-Ala-Pro, and D-Ala-tBu-Gly, wherein the first amino acid in each peptide is connected to L_2 group and the last amino acid in each peptide is connected to –NH-CR^1R^2-S-L_1-D.

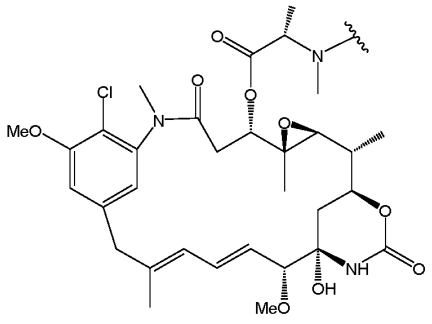
84. The compound of claim 83, wherein A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

85. The compound of any one of claims 60-84, wherein D is a maytansinoid.

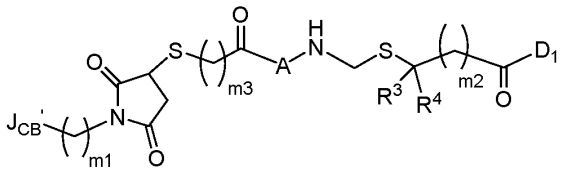
86. The compound of claim 85, wherein D is represented by the following formula:



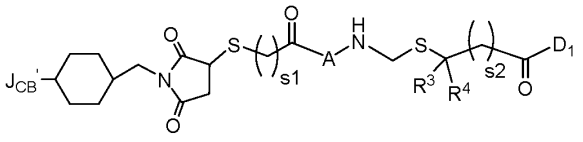
87. The compound of claim 86, wherein D is represented by the following formula:



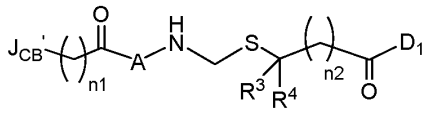
88. The compound of any one of claims 60-84, wherein the compound is represented by the following formula:



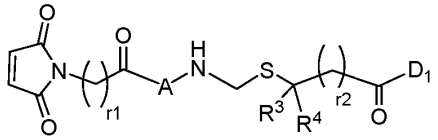
;



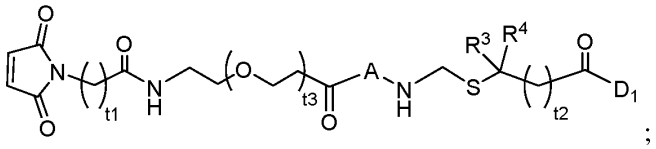
;



;



; or



;

or a pharmaceutically acceptable salt thereof, wherein:

R^3 and R^4 are each independently H or Me;

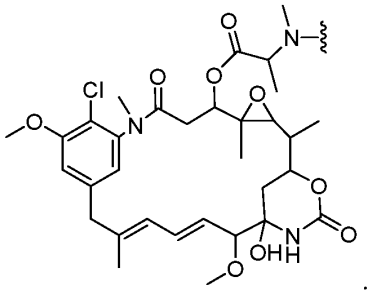
m1, m3, n1, r1, s1, and t1 are each independently an integer from 1 to 6;

m2, n2, r2, s2 and t2 are each independently an integer from 1 to 7;

t3 is an integer from 1 to 12;

J_{CB}' is –C(=O)OH or –COE;

D_1 is represented by the following formula:

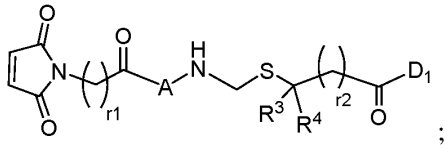


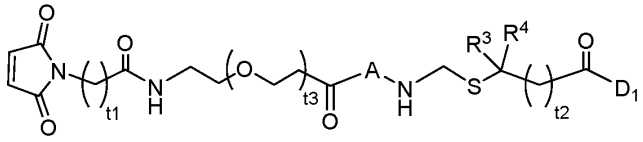
.

89. The compound of claim 88, wherein A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

90. The compound of claim 88 or 89, wherein m1, r1, n1 and m3 are each independently an integer from 2 to 4; and m2, n2 and r2 are each independently an integer from 3 to 5.

91. The compound of claim 88, wherein the compound is represented by the following formula:


; or



wherein:

r1 and t1 are each an integer from 2 to 6;

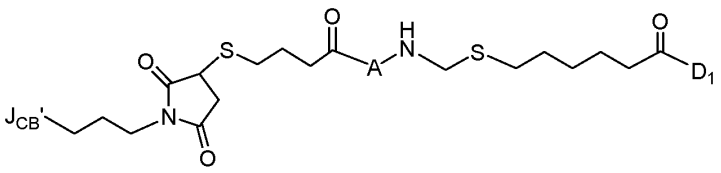
r2 and t2 are each an integer from 2 to 5; and

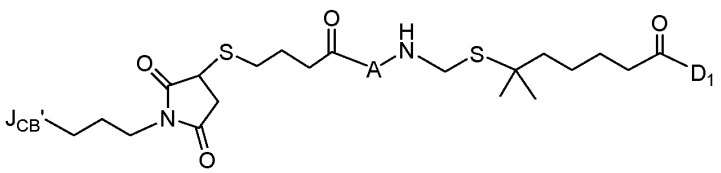
t3 is an integer from 2 to 12.

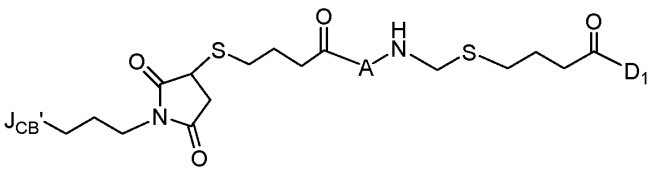
92. The compound of any one of claims 88-91, wherein R^3 and R^4 are both Me.

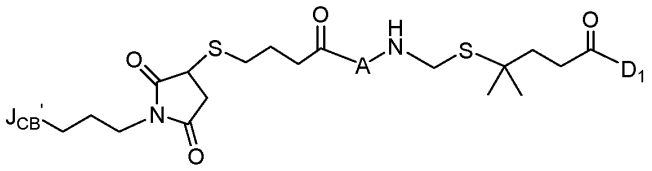
93. The compound of any one of claims 88-91, wherein R^3 and R^4 are both H.

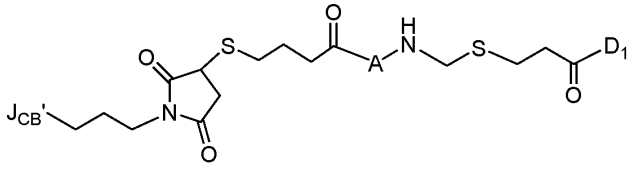
94. The compound of claim 88, wherein the compound is represented by the following formula:

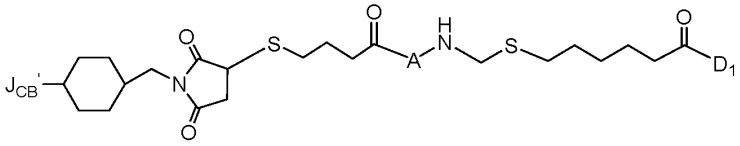

;

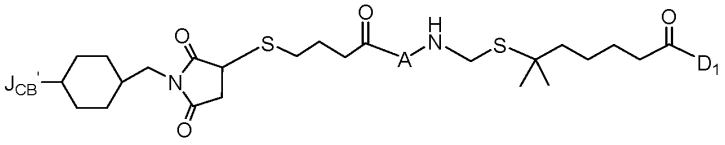

;

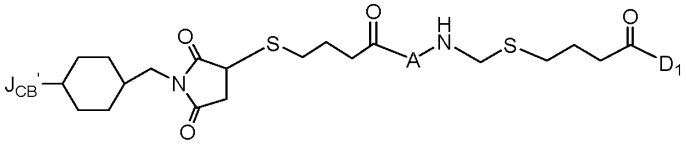

;

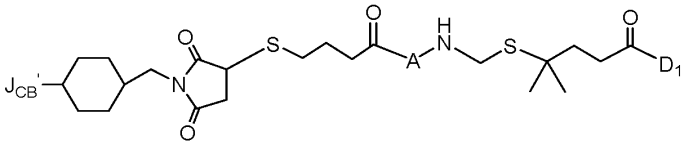

;

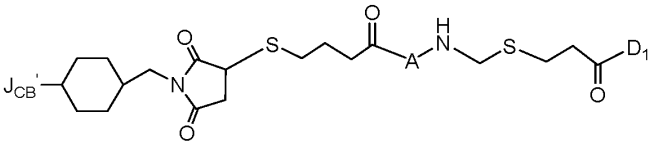

;

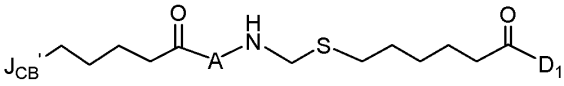

;

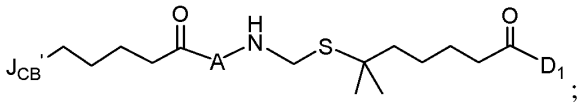

;

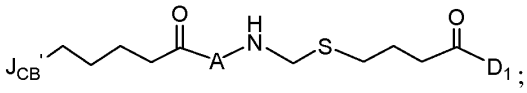

;

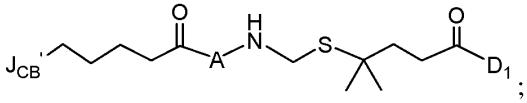

;

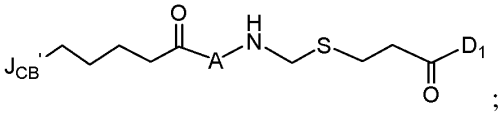

;

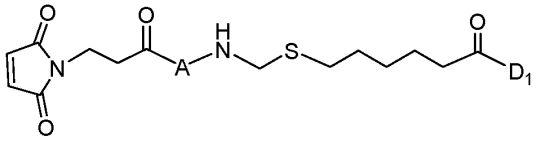

;

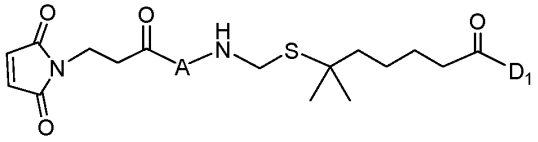

;

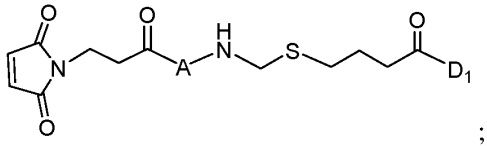

;

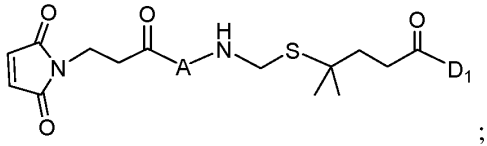

;

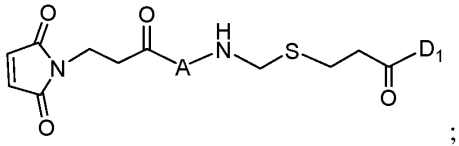

;

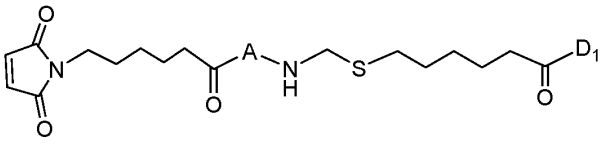

;

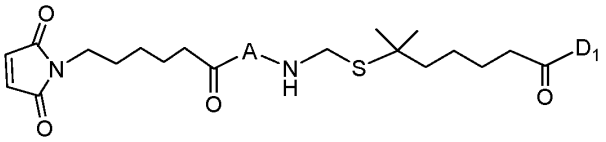

;

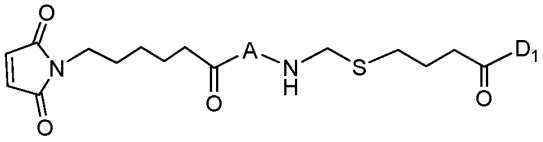

;

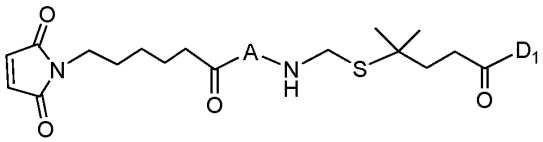

;

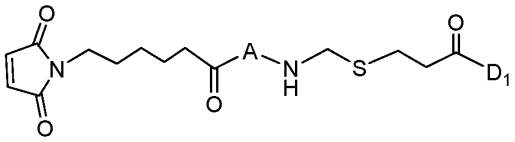

;

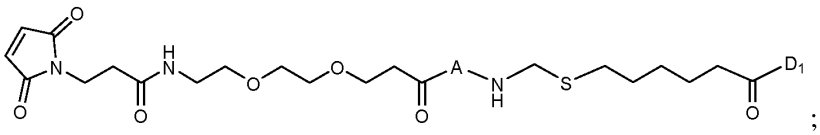

;

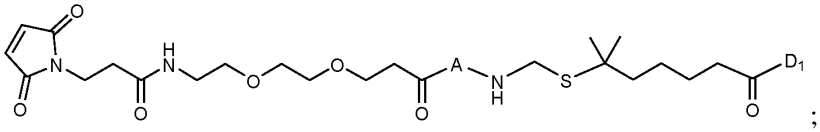

;

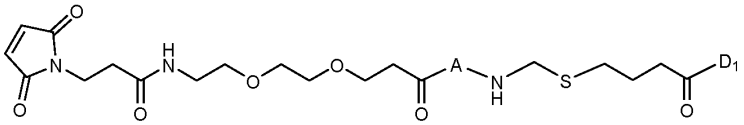

;

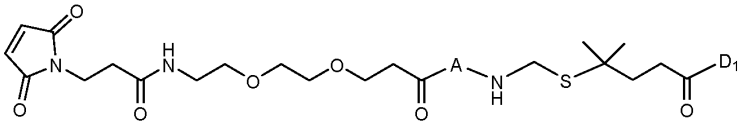

;

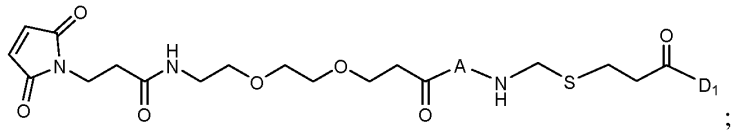

;

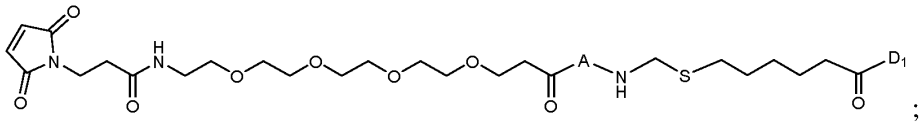

;

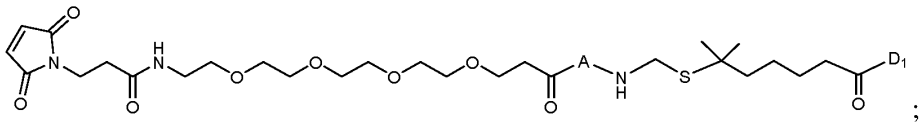

;

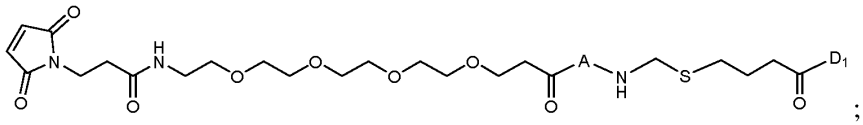

;

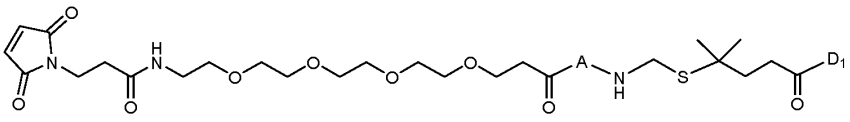

;

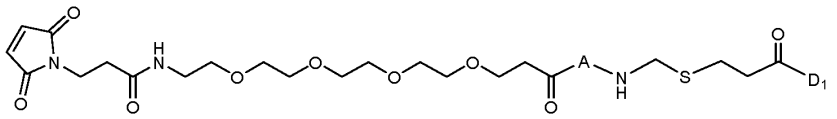

;


;


;


;


; or

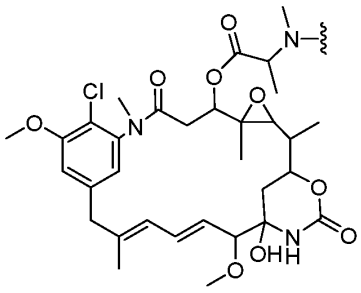


or a pharmaceutically acceptable salt thereof, wherein:

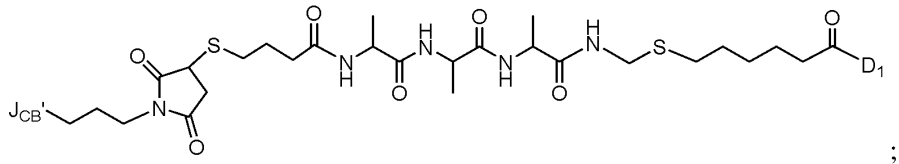
A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly,

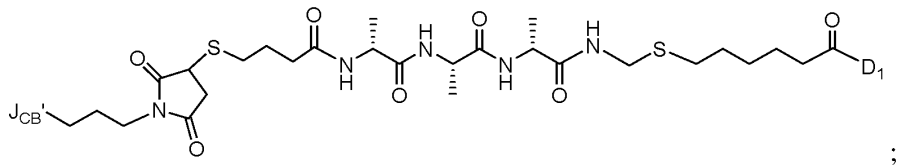
J_{CB}' is –C(=O)OH or –COE; and

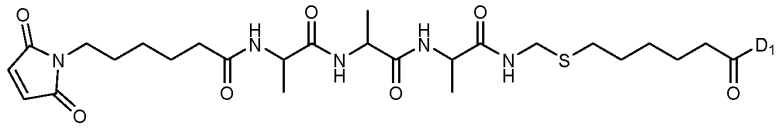
D_1 is represented by the following formula:

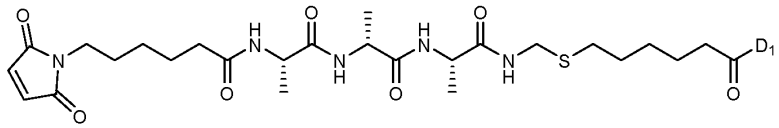

.

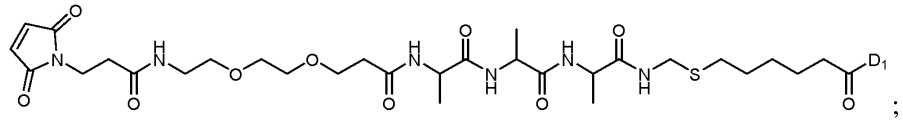
95. The compound of claim 94, wherein the compound is represented by the following formula:

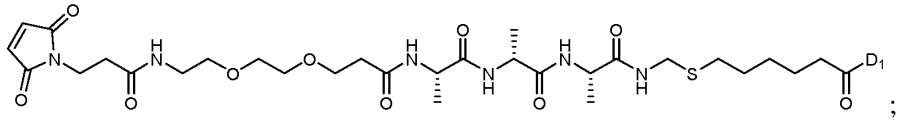

;

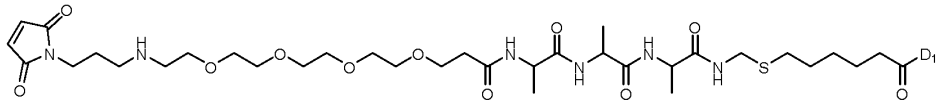

;

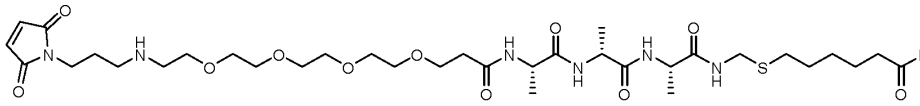

;


;

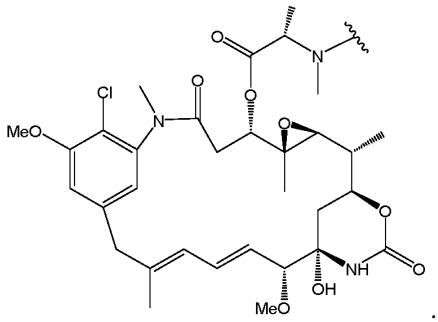

;


;


; or


,

wherein D_1 is represented by the following formula:



96. The compound of any one of claims 60-95, wherein -COE is a reactive ester selected from N-hydroxysuccinimide ester, N-hydroxy sulfosuccinimide ester, nitrophenyl (*e.g.*, 2 or 4-nitrophenyl) ester, dinitrophenyl (*e.g.*, 2,4-dinitrophenyl) ester, sulfo-tetraflurophenyl (*e.g.*, 4-sulfo-2,3,5,6-tetrafluorophenyl) ester, and pentafluorophenyl ester.

97. The compound of any one of claims 60-95, wherein -COE is N-hydroxysuccinimide ester or N-hydroxy sulfosuccinimide ester.

98. A compound represented by the following formula:

$$A'—NH—CR^1R^2—S-L_1—D \quad (III)$$

or a pharmaceutically acceptable salt thereof, wherein:

A' is an amino acid or a peptide comprising 2 to 20 amino acids;

R^1 and R^2 are each independently H or a C_{1-3}alkyl;

L_1 is a spacer;

D-L_1-SH is a cytotoxic agent; and

q is an integer from 1 to 20.

99. The compound of claim 98, wherein at least one of R^1 and R^2 is H.

100. The compound of claim 98, wherein R^1 and R^2 are each independently H or Me.

101. The compound of claim 100, wherein one of R^1 and R^2 is H, and the other one is Me.

102. The compound of claim 98, wherein R^1 and R^2 are both H.

103. The compound of any one of claims 98-102, wherein L_1 is –L_1'–C(=O)-; and L_1' is an alkylene or a cycloalkylene.

104. The compound of claim 103, wherein L_1' is C_{1-10}alkylene.

105. The compound of claim 103, wherein L_1 is $–CR^3R^4-(CH_2)_{1-8}-C(=O)-$; R^3 and R^4 are each independently H or Me.

106. The compound of claim 105, wherein L_1 is $–CR^3R^4-(CH_2)_{3-5}-C(=O)-$.

107. The compound of claim 105 or 106, wherein R^3 and R^4 are both Me.

108. The compound of claim 103, wherein L_1 is $–(CH_2)_{4-6}-C(=O)-$.

109. The compound of any one of claims 98-108, wherein A' is a peptide cleavable by a protease.

110. The compound of claim 109, wherein A' is a peptide cleavable by a protease expressed in tumor tissue.

111. The compound of any one of claims 98-110, wherein A' is a peptide having an amino acid that is covalent linked with $–NH-CR^1R^2-S-L_1-D$ selected from the group consisting of Ala, Arg, Asn, Asp, Cit, Cys, selino-Cys, Gln, Glu, Gly, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, each independently as L or D isomer.

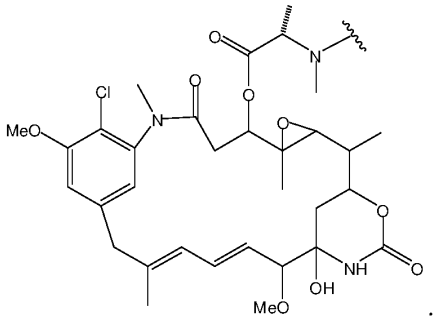
112. The conjugate of any one of claims 98-111, wherein the amino acid connected to $–NH-CR^1R^2-S-L_1-D$ is an L amino acid.

113. The compound of any one of claims 98-108, wherein A' is selected from the group consisting of Gly-Gly-Gly, Ala-Val, Val-Ala, D-Val-Ala, Val-Cit, D-Val-Cit, Val-Lys, Phe-Lys, Lys-Lys, Ala-Lys, Phe-Cit, Leu-Cit, Ile-Cit, Phe-Ala, Phe-N^9-tosyl-Arg, Phe-N^9-nitro-Arg, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Leu-Ala-Leu, Ile-Ala-Leu, Val-Ala-Val, Ala-Ala-Ala, D-Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala-D-Ala, Ala-Leu-Ala-Leu (SEQ ID NO: 1), β-Ala-Leu-Ala-Leu (SEQ ID NO: 2), Gly-Phe-Leu-Gly (SEQ ID NO: 3), Val-Arg, Arg-Arg, Val-D-Cit, Val-D-Lys, Val-D-Arg, D-Val-Cit, D-Val-Lys, D-Val-Arg, D-Val-D-Cit, D-Val-D-Lys, D-Val-D-Arg, D-Arg-D-Arg, Ala-Ala, Ala-D-Ala, D-Ala-Ala, D-Ala-D-Ala, Ala-Met, Gln-Val, Asn-Ala, Gln-Phe, Gln-Ala, D-Ala-Pro, and D-Ala-tBu-Gly, wherein the first amino acid in each peptide is connected to L_2 group and the last amino acid in each peptide is connected to $–NH-CR^1R^2-S-L_1-D$.

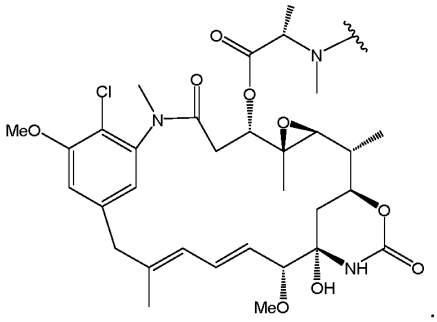
114. The compound of claim 113, wherein A' is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

115. The compound of any one of claims 98-114, wherein D is a maytansinoid.

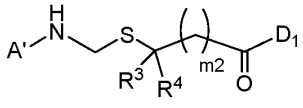
116. The compound of claim 115, wherein D is represented by the following formula:



117. The compound of claim 116, wherein D is represented by the following formula:



118. The compound of any one of claims 98-117, wherein the compound is represented by the following formula:



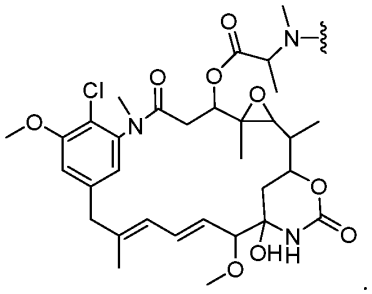
;

or a pharmaceutically acceptable salt thereof, wherein:

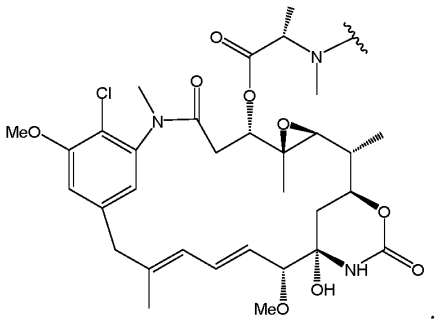
R^3 and R^4 are each independently H or Me;

m2 is an integer from 1 to 7; and

D_1 is represented by the following formula:



119. The compound of claim 118, wherein D_1 is represented by the following formula:



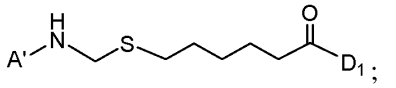
120. The compound of claim 118 or 119, wherein A' is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

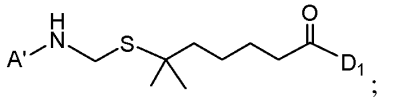
121. The compound of any one of claims 118-120, wherein m2 is an integer from 3 to 5.

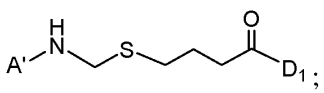
122. The compound of any one of claims 118-121, wherein R^3 and R^4 are both Me.

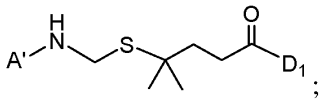
123. The compound of any one of claims 118-121, wherein R^3 and R^4 are both H.

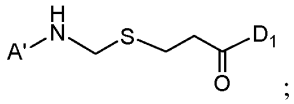
124. The compound of claim 118, wherein the compound is represented by the following formula:







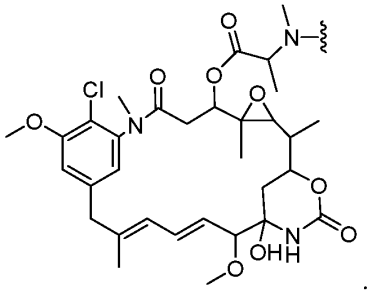




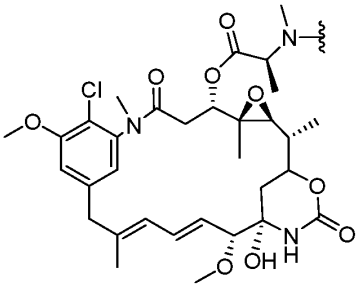
or a pharmaceutically acceptable salt thereof, wherein:

A' is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly,

D_1 is represented by the following formula:



125. The compound of claim 124, wherein D_1 is represented by the following formula:

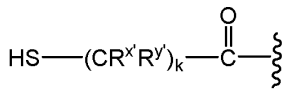


126. A compound represented by the following formula:

$$L_3—A—NH—CR^1R^2—S-L_1—D \quad (IV)$$

or a pharmaceutically acceptable salt thereof, wherein:

L_3 is represented by the following formula:



$R^{x'}$ and $R^{y'}$, for each occurrence, are independently H, -OH, halogen, -O-(C_{1-4}

alkyl), -SO_3H, -$NR_{40}R_{41}R_{42}^+$, or a C_{1-4} alkyl optionally substituted with -OH, halogen, SO_3H or $NR_{40}R_{41}R_{42}^+$, wherein R_{40}, R_{41} and R_{42} are each independently H or a C_{1-4} alkyl;

k is an integer from 1 to 10;

A is an amino acid residue or a peptide comprising 2 to 20 amino acid residues;

R^1 and R^2 are each independently H or a C_{1-3}alkyl;

L_1 is a spacer;

D-L_1-SH is a cytotoxic agent; and

q is an integer from 1 to 20.

127. The compound of claim 126, wherein at least one of R^1 and R^2 is H.

128. The compound of claim 126, wherein R^1 and R^2 are each independently H or Me.

129. The compound of claim 128, wherein one of R^1 and R^2 is H, and the other is Me.

130. The compound of claim 126, wherein R^1 and R^2 are both H.

131. The compound of any one of claims 126-130, wherein L_1 is –L_1'–C(=O)-; and L_1' is an alkylene or a cycloalkylene.

132. The compound of claim 131, wherein L_1' is C_{1-10}alkylene.

133. The compound of claim 131, wherein L_1 is –CR^3R^4-$(CH_2)_{1-8}$-C(=O)-; R^3 and R^4 are each independently H or Me.

134. The compound of claim 133, wherein L_1 is –CR^3R^4-$(CH_2)_{3-5}$-C(=O)-.

135. The compound of claim 133 or 134, wherein R^3 and R^4 are both Me.

136. The compound of claim 131, wherein L_1 is –$(CH_2)_{4-6}$-C(=O)-.

137. The compound of any one of claims 126-136, wherein $R^{x'}$ and $R^{y'}$ are both H.

138. The compound of claim 137, wherein k is an integer an integer from 2 to 6.

139. The compound of claim 137, wherein k is 3.

140. The compound of any one of claims 126-139, wherein A is a peptide cleavable by a protease.

141. The compound of claim 140, wherein A is a peptide cleavable by a protease expressed in tumor tissue.

142. The compound of any one of claims 126-141, wherein A is a peptide having an amino acid that is covalent linked with –NH-CR^1R^2-S-L_1-D selected from the group consisting of Ala, Arg, Asn, Asp, Cit, Cys, selino-Cys, Gln, Glu, Gly, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, each independently as L or D isomer.

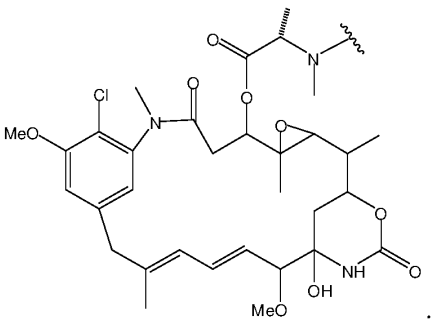
143. The compound of any one of claims 126-142, wherein the amino acid connected to –NH-CR^1R^2-S-L_1-D is an L amino acid.

144. The compound of any one of claims 126-139, wherein A is selected from the group consisting of Gly-Gly-Gly, Ala-Val, Val-Ala, D-Val-Ala, Val-Cit, D-Val-Cit, Val-Lys, Phe-Lys, Lys-Lys, Ala-Lys, Phe-Cit, Leu-Cit, Ile-Cit, Phe-Ala, Phe-N^9-tosyl-Arg, Phe-N^9-nitro-Arg, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Leu-Ala-Leu, Ile-Ala-Leu, Val-Ala-Val, Ala-Ala-Ala, D-Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala-D-Ala, Ala-Leu-Ala-Leu (SEQ ID NO: 1), β-Ala-Leu-Ala-Leu (SEQ ID NO: 2), Gly-Phe-Leu-Gly (SEQ ID NO: 3), Val-Arg, Arg-Arg, Val-D-Cit, Val-D-Lys, Val-D-Arg, D-Val-Cit, D-Val-Lys, D-Val-Arg, D-Val-D-Cit, D-Val-D-Lys, D-Val-D-Arg, D-Arg-D-Arg, Ala-Ala, Ala-D-Ala, D-Ala-Ala, D-Ala-D-Ala, Ala-Met, Gln-Val, Asn-Ala, Gln-Phe, Gln-Ala, D-Ala-Pro, and D-Ala-tBu-Gly, wherein the first amino acid in each peptide is connected to L_2 group and the last amino acid in each peptide is connected to –NH-CR^1R^2-S-L_1-D.

145. The compound of claim 144, wherein A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

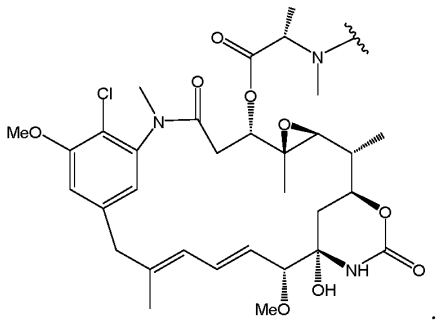
146. The compound of any one of claims 126-145, wherein D is a maytansinoid.

147. The compound of claim 146, wherein D is represented by the following formula:

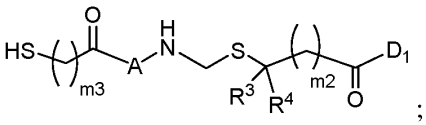


.

148. The compound of claim 147, wherein D is represented by the following formula:



149. The compound of any one of claims 126-148, wherein the compound is represented by the following formula:



;

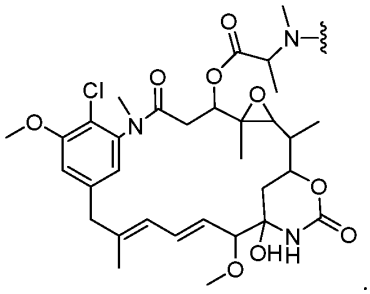
or a pharmaceutically acceptable salt thereof, wherein:

R^3 and R^4 are each independently H or Me;

m3 is an integer from 1 to 6;

m2 is an integer from 1 to 7;

D_1 is represented by the following formula:



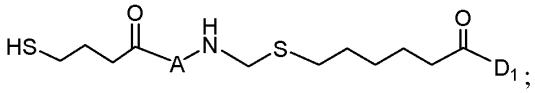
150. The compound of claim 149, wherein A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly.

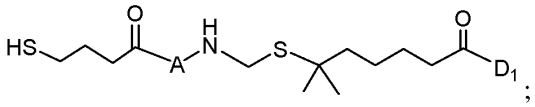
151. The compound of claim 149 or 150, wherein m3 is an integer from 2 to 4; and m2 is an integer from 3 to 5.

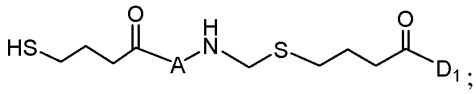
152. The compound of any one of claims 149-151, wherein R^3 and R^4 are both Me.

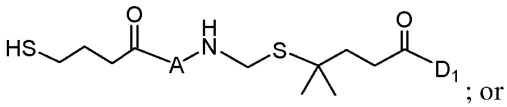
153. The compound of any one of claims 149-151, wherein R^3 and R^4 are both H.

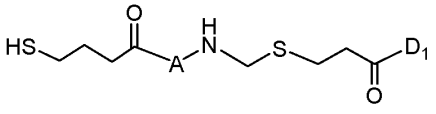
154. The compound of claim 149, wherein the compound is represented by the following formula:


;


;


;

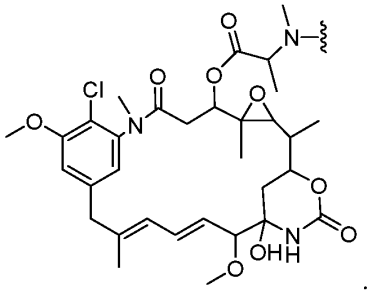

; or


;

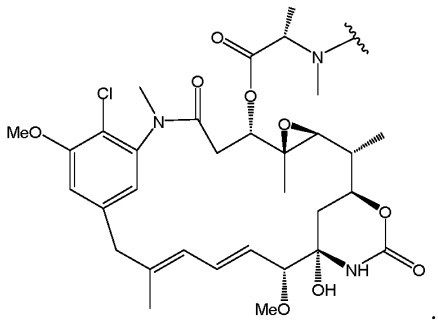
or a pharmaceutically acceptable salt thereof, wherein:

A is Ala-Ala-Ala, Ala-D-Ala-Ala, Ala-Ala, D-Ala-Ala, Val-Ala, D-Val-Ala, D-Ala-Pro, or D-Ala-tBu-Gly, and

D_1 is represented by the following formula:


.

155. The compound of claim 154, wherein D_1 is represented by the following formula:



156. A compound represented by the following formula:

$$D—L_1—SZ^0 \quad (V),$$

wherein:

L_1 is a spacer;

Z^0 is H or Me, provided when Z^0 is H, L_1 is not-C(=O)-$(CH_2)_q$- or –C(=O)-CH_2-CH_2–$C(CH_3)_2$-, wherein q is an integer from 1 to 3; and when Z^0 is Me, L_1 is not -C(=O)-$(CH_2)_2$- or –C(=O)-CH_2-CH_2–$C(CH_3)_2$-; and

D-L_1-SH is a cytotoxic agent.

157. The compound of claim 156, wherein L_1 is –L_1'–C(=O)-; and L_1' is an alkylene or a cycloalkylene, wherein the –C(=O)- moiety in L_1 is attached to D..

158. The compound of claim 157, wherein L_1' is C_{1-10}alkylene.

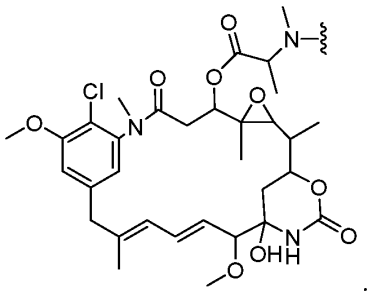
159. The compound of claim 157, wherein L_1 is –CR^3R^4-$(CH_2)_{1-8}$-C(=O)-; and R^3 and R^4 are each independently H or Me.

160. The compound of claim 159, wherein L_1 is –CR^3R^4-$(CH_2)_{3-5}$-C(=O)-.

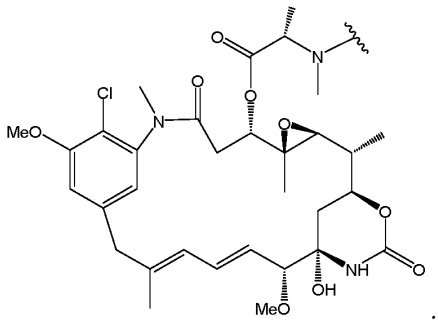
161. The compuond of claim 159 or 160, wherein R^3 and R^4 are both Me.

162. The compound of claim 157, wherein L_1 is –$(CH_2)_{4-6}$-C(=O)-.

163. The compound of any one of claims 156-162, wherein D is represented by the following formula:



164. The compound of claim 163, wherein D is represented by the following formula:



165. A pharmaceutical composition comprising the conjugate of any one of claims 1-59 and a pharmaceutically acceptable carrier.

166. A method of inhibiting abnormal cell growth or treating a proliferative disorder in a mammal comprising administering to said mammal a therapeutically effective amount of the conjugate of any one of claims 1-59.

167. The method of claim 166, wherein the method is for treating a cancer.

168. The method of claim 167, wherein the cancer is selected from renal cancer, breast cancer (e.g., triple-negative breast cancer (TNBC)), colon cancer, brain cancer, prostate cancer, endometrial cancer, cervical cancer, kidney cancer, pancreatic cancer, ovarian cancer (e.g., epithelial ovarian cancer), head and neck cancer, melanoma, colorectal cancer, gastric cancer, squamous cancer, lung cancer (e.g., non small-cell lung cancer and small-cell lung cancer), testicular cancer, choriocarcinoma, Merkel cell carcinoma, sarcoma (e.g., osteosarcoma, chondrosarcoma, liposarcoma, and leiomyosarcoma), glioblastoma, neuroblastoma, lymphoma (e.g., non-Hodgkin lymphoma), myelodysplastic syndrome

(MDS), peritoneal cancer, fallopian tube cancer, uterine cancer or leukemia (e.g., acute myeloid leukemia (AML), acute monocytic leukemia, promyelocytic leukemia, eosinophilic leukemia, acute lymphoblastic leukemia (e.g., B-ALL), chronic lymphocytic leukemia (CLL), or chronic myeloid leukemia (CML)).

169. The method of claim 168, wherein the cancer is breast cancer, ovarian cancer or renal cancer.

170. The method of claim 168, wherein the cancer is cervical cancer, ovarian cancer, uterine cancer, endometrial cancer, or fallopian tube cancer.