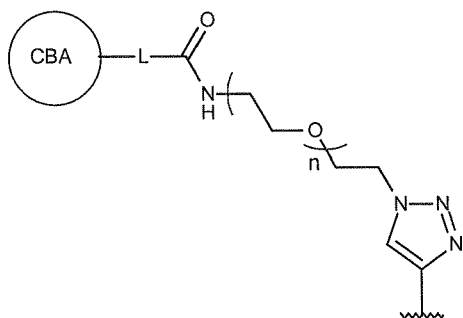
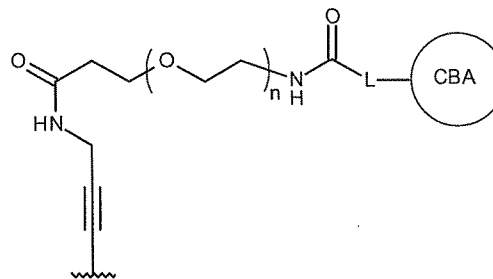


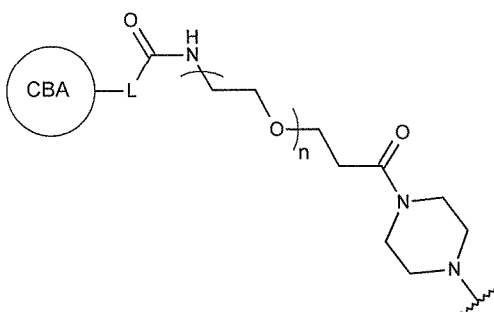
Y is selected from formulae A1, A2, A3, A4, A5 and A6:



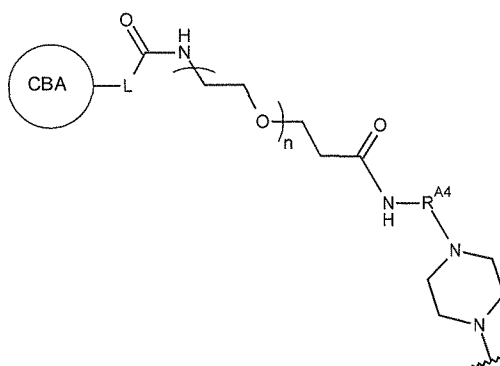
(A1)



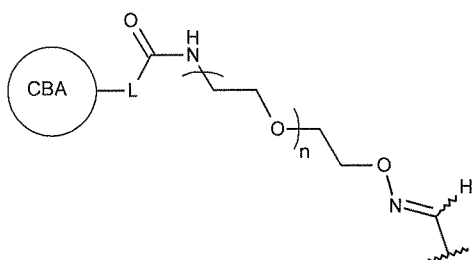
(A2)



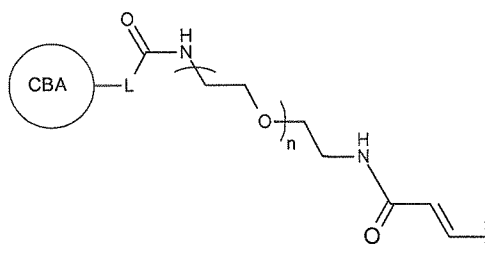
(A3)



(A4)



(A5)



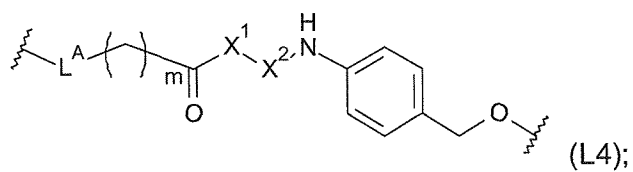
(A6)

L is a linker connected to a cell binding agent and of formula selected from the group:

$-L^A-(CH_2)_m-$ (L1),

$-L^A-(CH_2)_m-O-$ (L2)

, and

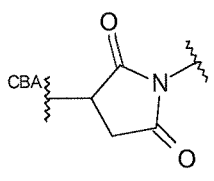
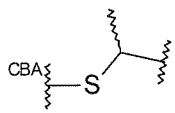


where m is from 0 to 6;

q is from 1 to 3; p is from 1 to 3;

the group $-X^1-X^2-$ is selected from: -Phe-Lys-, Val-Ala-, -Val-Lys-, -Ala-Lys-,
-Val-Cit-; and

- 5 L^A is selected from: L^{A1-1} and L^{A3-2} when L is L1; L^{A3-2} when L is L2; L^{A1-1} when L is L4.

L^{A1-1}	
L^{A3-2}	

where Ar represents a C₅₋₆ arylene group;

CBA is the cell binding agent;

n is an integer selected in the range of 0 to 48;

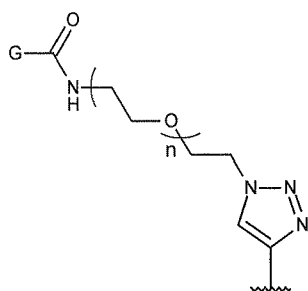
5 R^{A4} is a C₁₋₆ alkylene group;

either

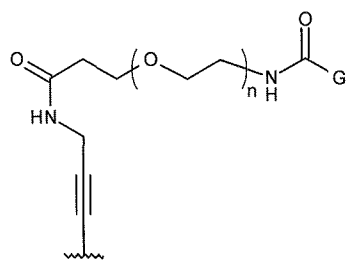
(a) R¹⁰ is H, and R¹¹ is OH, OR^A, where R^A is C₁₋₄ alkyl; or

(b) R¹⁰ and R¹¹ form a nitrogen-carbon double bond between the nitrogen and carbon atoms to which they are bound; or

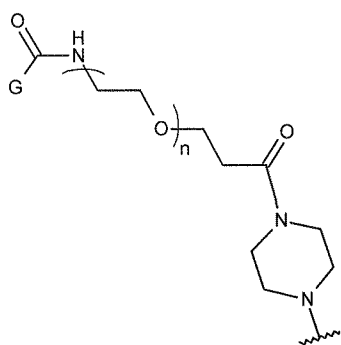
10 (c) R¹⁰ is H and R¹¹ is OSO_zM, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;



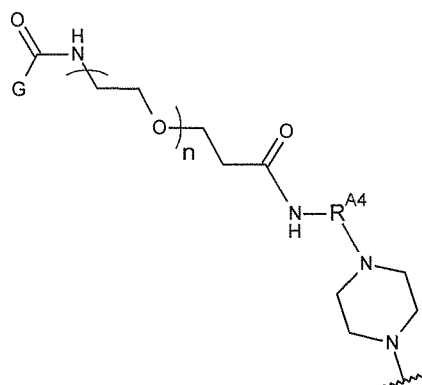
(B1)



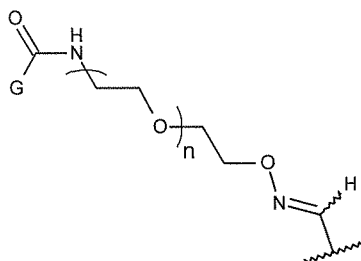
(B2)



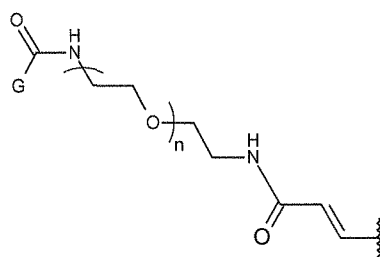
(B3)



(B4)



(B5)

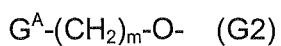
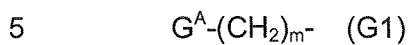


(B6)

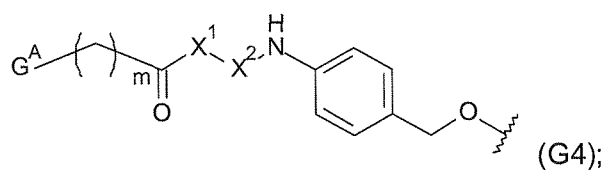
where G is a reactive group for connecting to a cell binding agent

wherein n and R^{A4} are as defined in the first aspect of the present disclosure and

G is of formula selected from the group:



, and



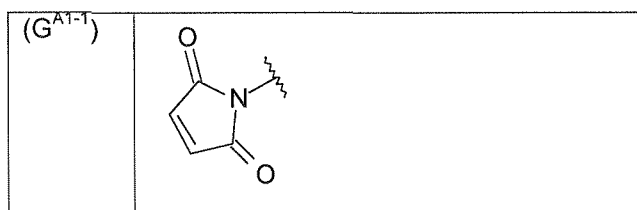
where m is from 0 to 6;

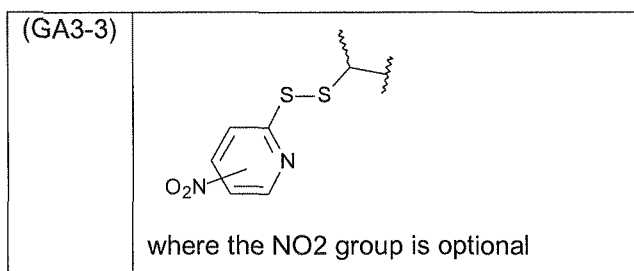
q is from 1 to 3; p is from 1 to 3;

the group $-X^1-X^2-$ is selected from: -Phe-Lys-, -Val-Ala-, -Val-Lys-, -Ala-Lys-,
-Val-Cit-; and

G^A is selected from: G^{A1-1} and G^{A3-3} when L is L1; G^{A3-3} when L is L2; G^{A1-1}

5 when L is L4:

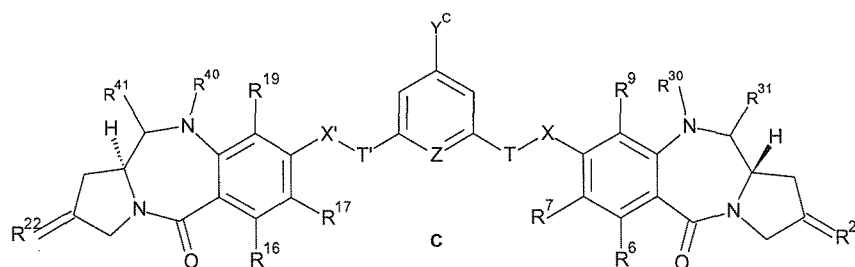


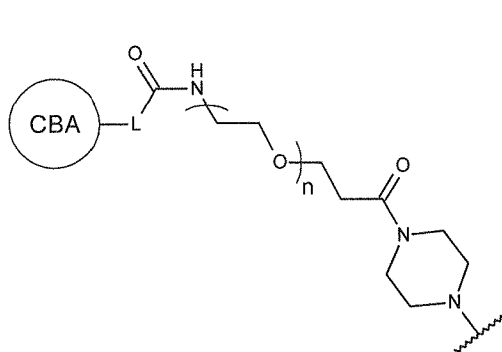


where Ar represents a C₅₋₆ arylene group.

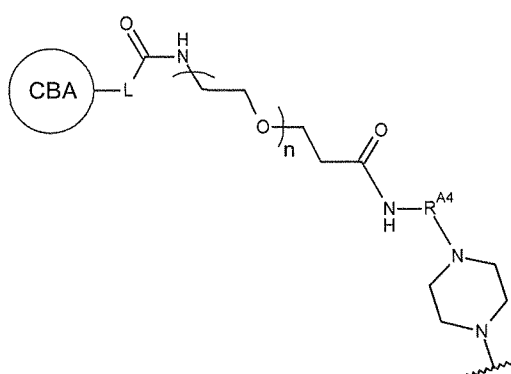
A third aspect of the present disclosure provides compounds of formula (C) which may be used in the preparation of the compounds and conjugate compounds of the present

5 disclosure:

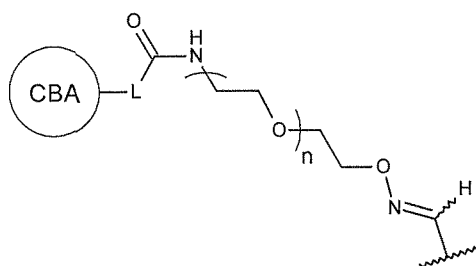




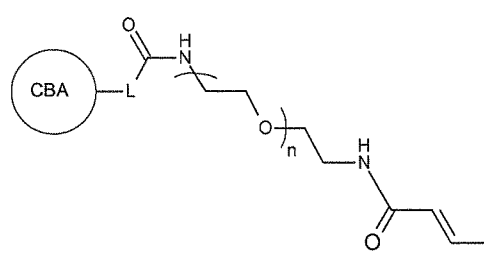
(A3)



(A4)



(A5)



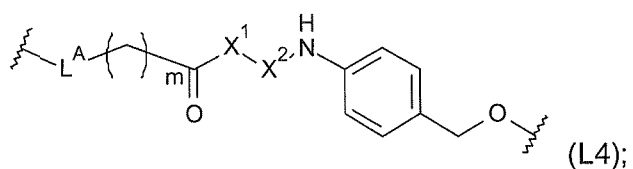
(A6)

L is a linker connected to a cell binding agent and of formula selected from the group:

$-L^A-(CH_2)_m-$ (L1),

$-L^A-(CH_2)_m-O-$ (L2)

, and



(L4);

where m is from 0 to 6; q is from 1 to 3; p is from 1 to 3;

the group $-X^1-X^2-$ is selected from:

$-Phe-Lys-$, $-Val-Ala-$, $-Val-Lys-$, $-Ala-Lys-$, $-Val-Cit-$;

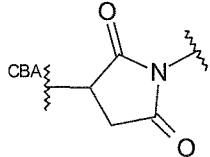
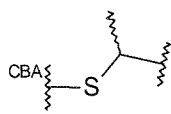
and

L^A is selected from:

L^{A1-1} and L^{A3-2} when L is L1

L^{A3-2} when L is L2

5 L^{A1-1} when L is L4

L^{A1-1}	
L^{A3-2}	

where Ar represents a C_{5-6} arylene group;

CBA is the cell binding agent;

n is an integer selected in the range of 0 to 48;

10 R^{A4} is a C_{1-6} alkylene group; either

16. The conjugate of claim 1, wherein L is of formula L1.
17. The conjugate according to either claim 1 or claim 16, wherein L is of formula L1 and m is 2, 3 or 5.
- 5 18. The conjugate of claim 1, wherein L is of formula L2.
19. The conjugate according to either claim 1 or 18, wherein L is of formula L2 and m is 1.
- 10 20. The conjugate according to claim 1, wherein q is 1.
21. The conjugate according to either claim 1 or 20, wherein p is 2.

22. The conjugate according to claim 1, wherein L is of formula L4.

23. The conjugate according to either claim 1 or claim 22, wherein L is of formula L4 and m is 5.

5

24. The conjugate according to any one of claims 1 to 23, wherein n is an integer between 0 and 16.

10

25. The conjugate according to any one of claims 1 to 24, wherein n is an integer between 0 and 8.

26. The conjugate according to any one of claims 1 to 25, wherein n is 3 or 4.

15

27. The conjugate according to any one of claims 1 to 26, wherein the cell binding agent is an antibody or an active fragment thereof.

28. The conjugate according to claim 27, wherein the antibody or antibody fragment is an antibody or antibody fragment for a tumour-associated antigen.

20

29. The conjugate of claim 28 wherein the antibody or antibody fragment is an antibody which binds to one or more tumor-associated antigens or cell-surface receptors selected from (1)-(38):

- (27) CD22 (B-cell receptor CD22-B isoform);
- (28) CD79a (CD79A, CD79 α , immunoglobulin-associated α);
- (29) CXCR5 (Burkitt's lymphoma receptor 1);
- (30) HLA-DOB (Beta subunit of MHC class II molecule (Ia antigen));
- 5 (31) P2X5 (Purinergic receptor P2X ligand-gated ion channel 5);
- (32) CD72 (B-cell differentiation antigen CD72, Lyb-2);
- (33) LY64 (Lymphocyte antigen 64 (RP105), type I membrane protein of the leucine rich repeat (LRR) family);
- (34) FcRH1 (Fc receptor-like protein 1);
- 10 (35) IRTA2 (Immunoglobulin superfamily receptor translocation associated 2);
- (36) TENB2 (putative transmembrane proteoglycan);
- (37) CD33 (CD33 molecule, SIGLEC-3, SIGLEC3, p67; CD33 antigen (gp67); gp67; myeloid cell surface antigen CD33; sialic acid binding Ig-like lectin 3; sialic acid-binding Ig-like lectin); and
- 15 (38) LGR5/GPR49.

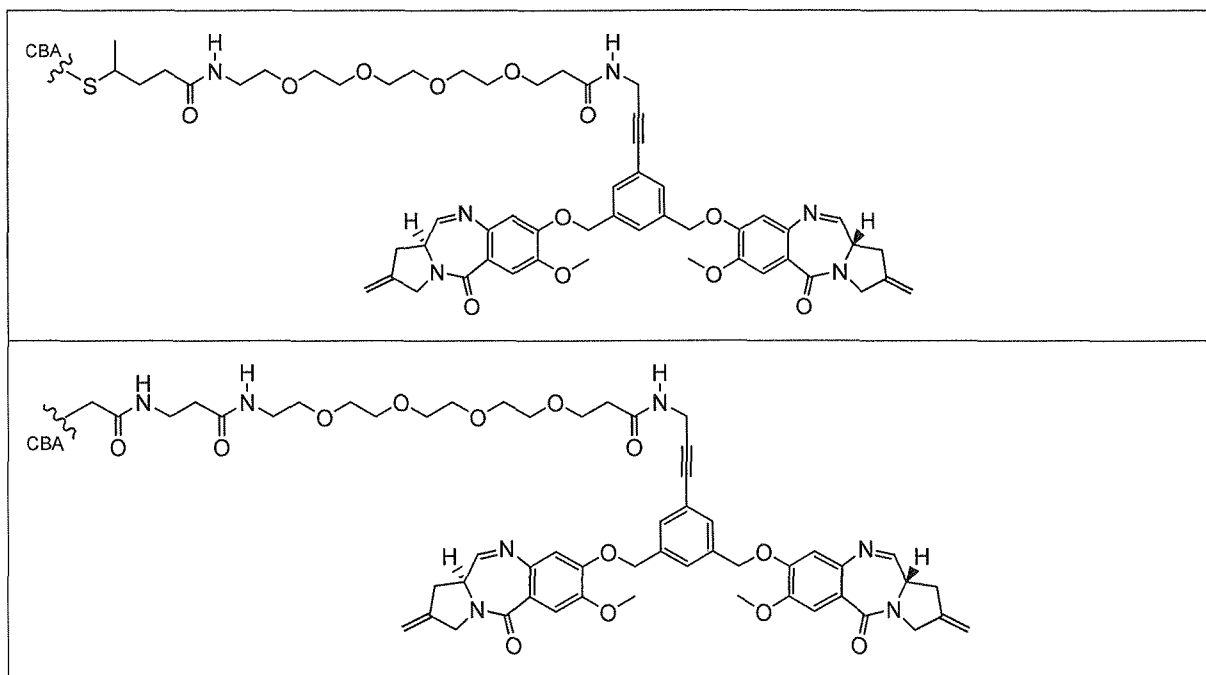
30. The conjugate of claim 27 wherein the antibody or antibody fragment is a cysteine-engineered antibody.

20 31. The conjugate of either claim 27 or claim 30 wherein the antibody or antibody fragment is an antibody which binds to an ErbB receptor.

32. The conjugate of claim 31 wherein the antibody is trastuzumab.

25 33. The conjugate of either claim 27 or claim 30 wherein Ab is an anti-HER2, an anti-Steap1, or an anti-CD22 antibody.

34. The conjugate according to any one of claims 29 to 33, wherein the conjugate is selected from:



where CBA is the cell binding agent.

35. The conjugate according to either claim 27 or claim 34 wherein the drug loading (p)
 5 of drugs (D) to antibody (Ab) is an integer from 1 to about 8.
36. The conjugate according to claim 35, wherein p is 1, 2, 3, or 4.
37. The conjugate according to claim 36 comprising a mixture of the antibody-drug
 10 conjugate compounds, wherein the average drug loading per antibody in the mixture of
 antibody-drug conjugate compounds is about 2 to about 5.

38. The conjugate according to any one of claims 1 to 37, for use in therapy.

39. A pharmaceutical composition comprising the conjugate of any one of claims 1 to 37
5 and a pharmaceutically acceptable diluent, carrier or excipient.

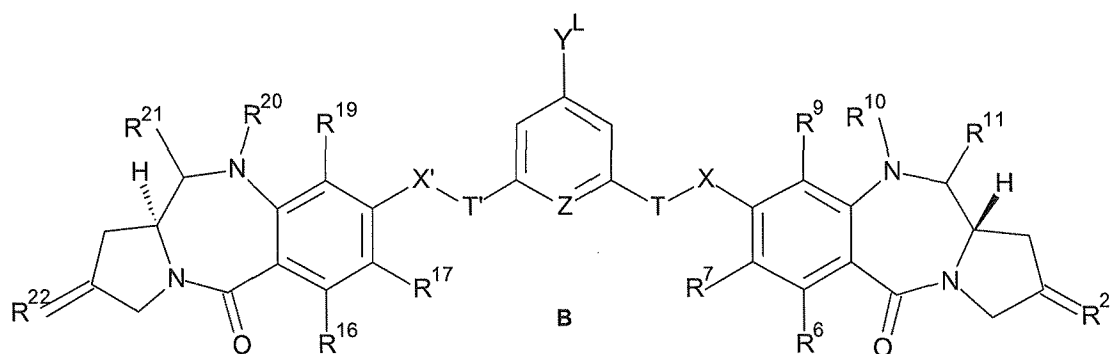
40. The conjugate according to any one of claims 1 to 37 or the pharmaceutical
composition according to claim 39, for use in the treatment of a proliferative disease in a
subject.
10

41. The conjugate according to claim 40, wherein the disease is cancer.

42. Use of a compound according to any one of claims 1 to 37 in a method of
manufacture of a medicament for the treatment of a proliferative disease.
15

43. The use according to claim 42, wherein the disease is cancer.

44. A compound of formula (B):

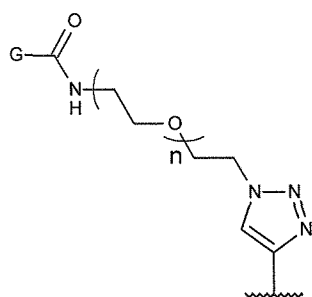


wherein:

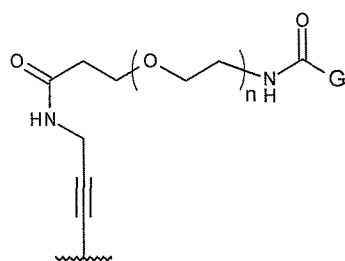
R^2 , R^6 , R^7 , R^9 , R^{10} , R^{11} , R^{22} , R^{16} , R^{17} , R^{19} , R^{20} , R^{21} , Z , T , T' , X and X' are as defined in any

5 one of claims 1 to 15;

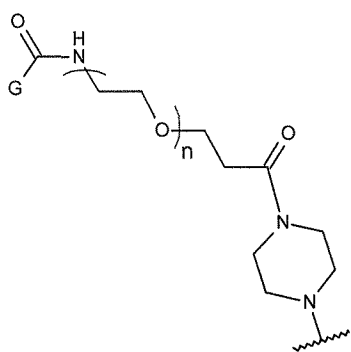
Y^L is selected from a group of formulae B1, B2, B3, B4, B5 and B6:



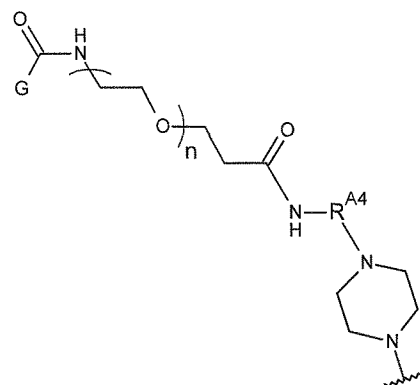
(B1)



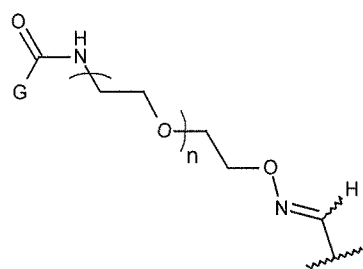
(B2)



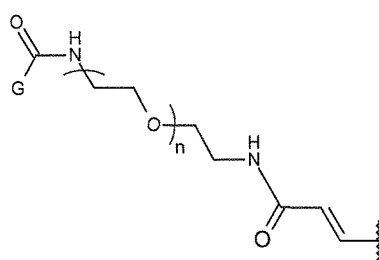
(B3)



(B4)



(B5)

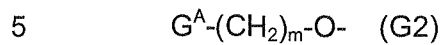
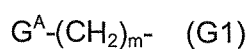


(B6)

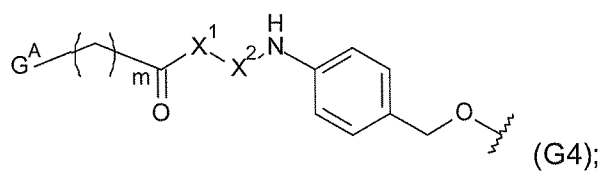
G is a reactive group for connecting to a cell binding agent

wherein n and R^{A4} are as defined in any one of claims 1 to 26 and

G is of formula selected from the group:



, and



where m is from 0 to 6;

q is from 1 to 3;

10 p is from 1 to 3;

the group -X¹-X²- is selected from:

-Phe-Lys-,

-Val-Ala-,

-Val-Lys-,

15 -Ala-Lys-,

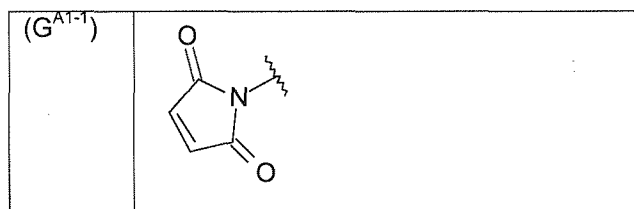
-Val-Cit; and

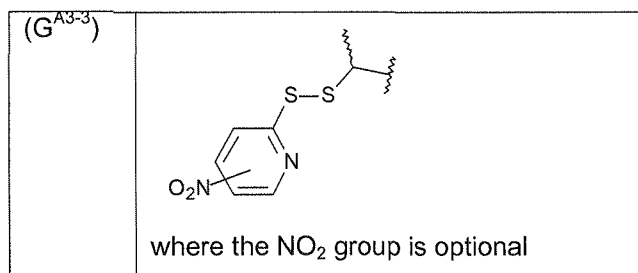
G^A is selected from:

G^{A1-1} and G^{A3-3} when G is G1

G^{A3-3} when G is G2

G^{A1-1} when G is G4





where Ar represents a C₅₋₆ arylene group.

45. The compound of claim 44, wherein G is of formula G1.
- 5 46. The compound according to either claim 44 or claim 45, wherein G is of formula G1 and m is 2, 3 or 5.
47. The compound of claim 44, wherein G is of formula G2.

48. The compound according to either claim 44 or 47, wherein G is of formula G2 and m is 1.

5

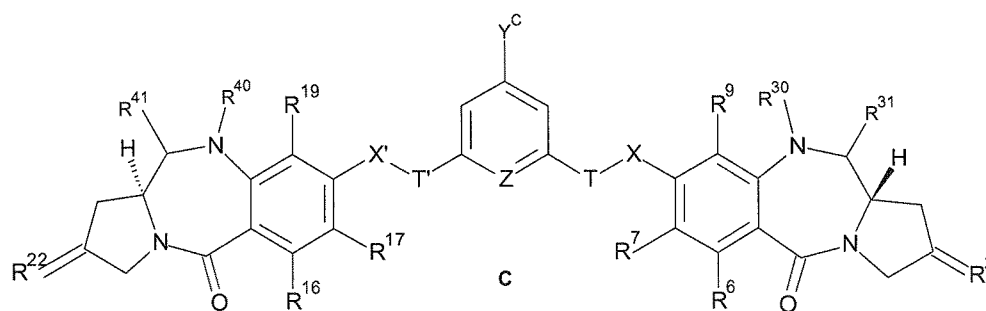
49. The compound according to claim 44, wherein q is 1.

50. The compound according to either claim 44 or 49, wherein p is 2.

10

51. The compound according to claim 44 wherein G is of formula G4 and m is 5.

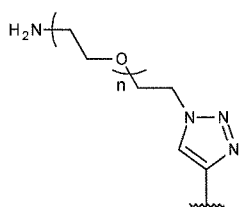
52. A compound of formula (C):



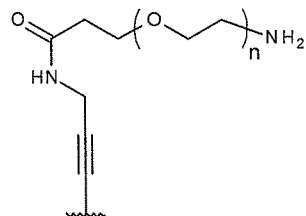
wherein:

15 $R^2, R^6, R^7, R^9, R^{22}, R^{16}, R^{17}, R^{19}, Z, T, T', X$ and X' are as defined in any one of claims 1 to 15;

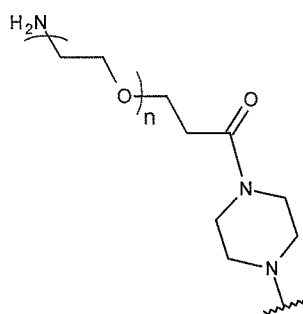
Y^C is selected from a group of formulae C1, C2, C3, C4, C5 and C6:



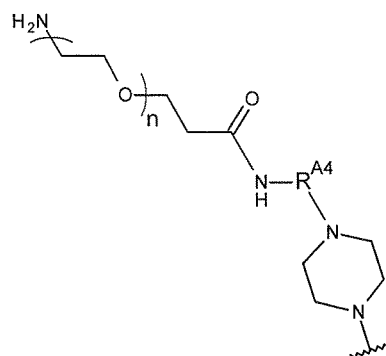
(C1)



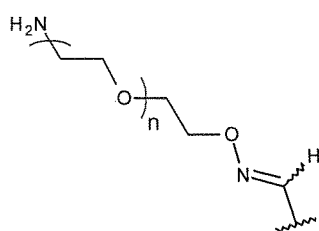
(C2)



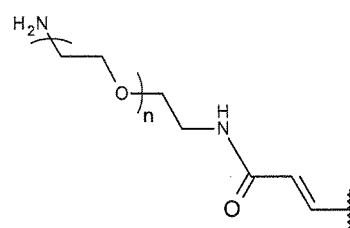
(C3)



(C4)



(C5)



(C6)

wherein n and R^{A4} are as defined in any one of claims 1 to 31;

either

(a) R^{30} is H, and R^{31} is OH, OR^A , where R^A is C_{1-4} alkyl; or

5 (b) R^{30} and R^{31} form a nitrogen-carbon double bond between the nitrogen and carbon atoms to which they are bound; or

(c) R^{30} is H and R^{31} is OSO_zM , where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation; or

10 (d) R^{30} is a nitrogen protecting group and R^{31} is $OProt^O$, where $Prot^O$ is a hydroxy protecting group; and

R^{40} and R^{41} are as defined for R^{30} and R^{31} respectively.

53. The compound according to claim 52, wherein R^{30} is H, and R^{31} is OH.

5 54. The compound according to claim 52, wherein R^{30} and R^{41} form a nitrogen-carbon double bond between the nitrogen and carbon atoms to which they are bound.

55. The compound according to claim 52, wherein R^{30} is a nitrogen protecting group and R^{31} is $OProt^O$, where $Prot^O$ is a hydroxyl protecting group.

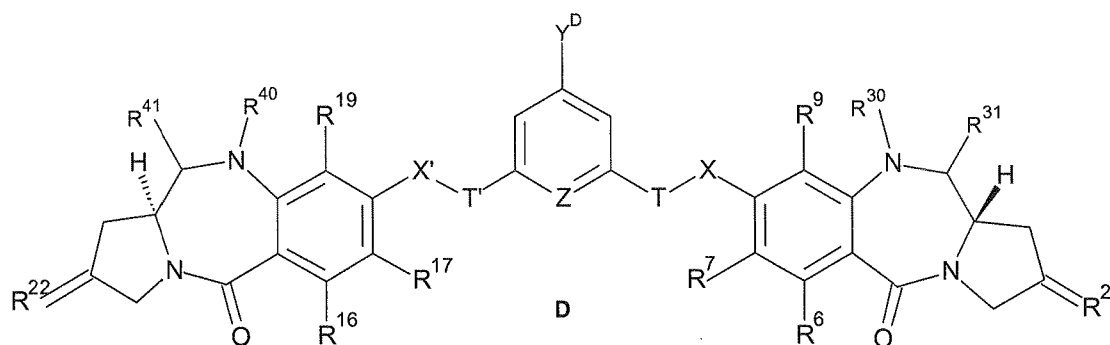
10

56. The compound according to claim 55, wherein the nitrogen protecting group is Boc.

57. The compound according to either claim 55 or claim 56, wherein the hydroxyl protecting group is THP.

15

58. A compound of formula (D):



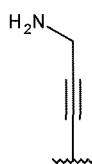
wherein:

R^2 , R^6 , R^7 , R^9 , R^{22} , R^{16} , R^{17} , R^{19} , Z , T , T' , X and X' are as defined in any one of claims 1 to

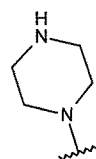
20 15;

R^{30} , R^{31} , R^{40} and R^{41} are as defined in any one of claims 52 to 57;

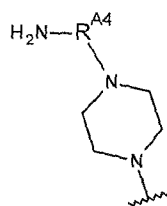
Y^D is selected from a group of formulae D2, D3, D4 and D6:



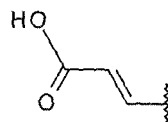
(D2)



(D3)



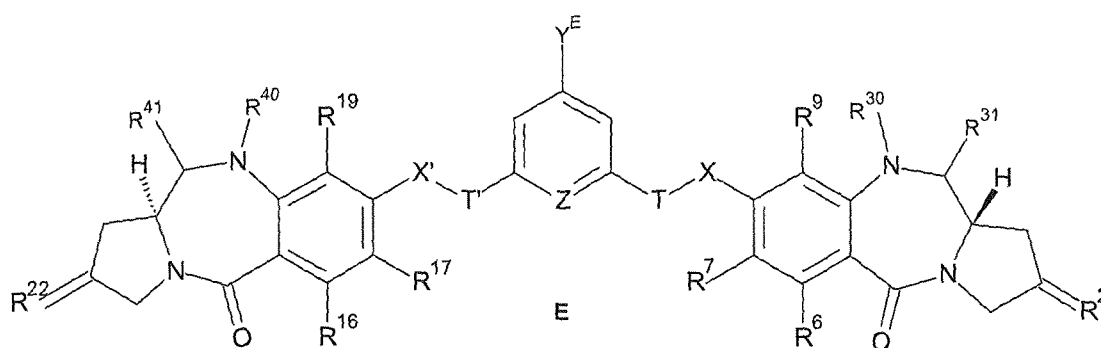
(D4)



(D6)

wherein R^{A4} is as defined in any one of claims 1 to 26.

59. A compound of formula (E):



E

5 wherein:

R^2 , R^6 , R^7 , R^9 , R^{22} , R^{16} , R^{17} , R^{19} , Z , T , T' , X and X' are as defined in any one of claims 1 to 15;

R^{30} , R^{31} , R^{40} and R^{41} are as defined in any one of claims 52 to 57;

Y^E is selected from a group of formulae E1, E2 and E5:



(E1)



(E2)



(E5)

10 where

R^{E1} is selected from H and TMS; and

R^{E2} is selected from Br, Cl and I.

60. A method of synthesis of a compound according to any one of claims 1 to 37,
comprising the step of conjugating a drug-linker according to any one of claims 44 to 51 with
5 a cell-binding agent.