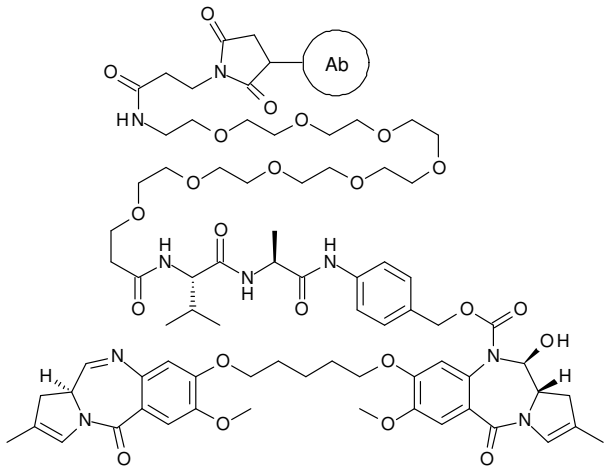
Maximal efficacy with minimal toxicity is sought thereby. Efforts to design and refine ADC have focused on the selectivity of monoclonal antibodies (mAbs) as well as drug mechanism of action, drug-linking, drug/antibody ratio (loading), and drug-releasing properties (Junutula, *et al*., 2008b Nature Biotech., 26(8):925-932; Dornan *et al* (2009) *Blood* 114(13):2721-2729; US 7521541; US 7723485; WO2009/052249; McDonagh (2006) Protein Eng. Design & Sel. 19(7): 299-307; Doronina *et al* (2006) Bioconj. Chem. 17:114-124; Erickson *et al* (2006) *Cancer Res.* 66(8):1-8; Sanderson *et al* (2005) *Clin. Cancer Res.* 11:843-852; Jeffrey *et al* (2005) *J. Med. Chem.* 48:1344-1358; Hamblett *et al* (2004) *Clin. Cancer Res.* 10:7063-7070). Drug moieties may impart their cytotoxic and cytostatic effects by mechanisms including tubulin binding, DNA binding, proteasome and/or topoisomerase inhibition. Some cytotoxic drugs tend to be inactive or less active when conjugated to large antibodies or protein receptor ligands.

The present inventors have developed particular PBD dimer antibody conjugates.

Summary

In one aspect, the present disclosure refers to a conjugate of formula ConjE:



ConjE

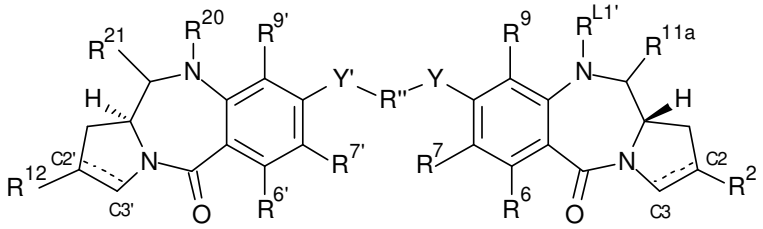
wherein Ab is an antibody that binds to kidney associated antigen 1 (KAAG1), the antibody comprising
a VH domain comprising a VH CDR1 with the amino acid sequence of SEQ ID NO.5, a VH CDR2 with the amino acid sequence of SEQ ID NO.6, and a VH CDR3 with the amino acid sequence of SEQ ID NO.7; and a VL domain comprising a VL CDR1 with the amino acid sequence of SEQ ID NO.8, a VL CDR2 with the amino acid sequence of SEQ ID NO.9, and a VL CDR3 with the amino acid sequence of SEQ ID NO.10,
wherein the drug loading (p) is from 1 to 8.

In another aspect, the present disclosure refers to a pharmaceutical composition comprising the conjugate as disclosed herein and a pharmaceutically acceptable diluent, carrier or excipient.

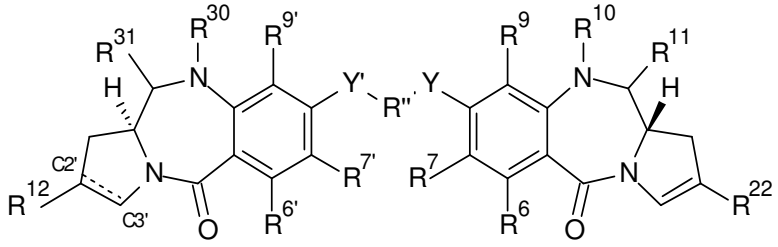
In another aspect, the present disclosure refers to the use of a conjugate as disclosed herein in the preparation of a medicament for the treatment of a kidney associated antigen 1 (KAAG1)-overexpressing cancer in a subject.

In yet another aspect, the present disclosure refers to a conjugate as disclosed herein for use in therapy.

A first ~~aspect~~example of the present disclosure comprises a conjugate of formula L - $(D^L)_p$, where D^L is of formula **I** or **II**:

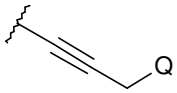


I



II

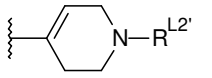
wherein:
L is an antibody (Ab) as defined below;
when there is a double bond present between C2' and C3', R^{12} is selected from the group consisting of:
(ia) C_{5-10} aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C_{1-7} alkyl, C_{3-7} heterocyclyl and bis-oxy-C_{1-3} alkylene;
(ib) C_{1-5} saturated aliphatic alkyl;
(ic) C_{3-6} saturated cycloalkyl;

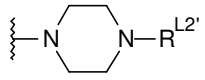


IIIc

(c)

where Q is selected from O-$R^{L2'}$, S-$R^{L2'}$ and NR^N-$R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: O-$R^{L2'}$, S-$R^{L2'}$, CO_2-$R^{L2'}$, CO-$R^{L2'}$, NH-C(=O)-$R^{L2'}$, NHNH-$R^{L2'}$, CONHNH-$R^{L2'}$, 

, 

, $NR^NR^{L2'}$, wherein R^N is selected from the group comprising H and C_{1-4} alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

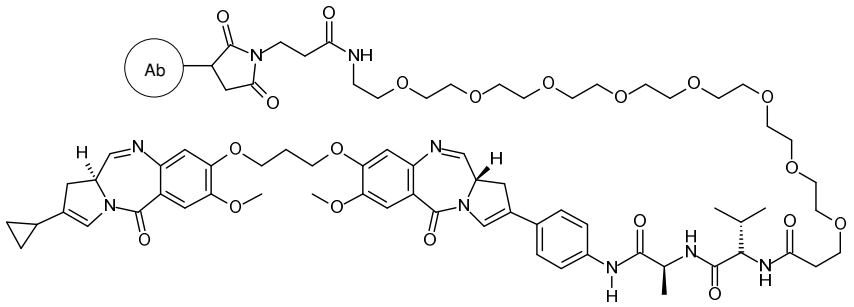
R^{10} is H and R^{11} is selected from OH, OR^A and SO_zM;

R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_zM.

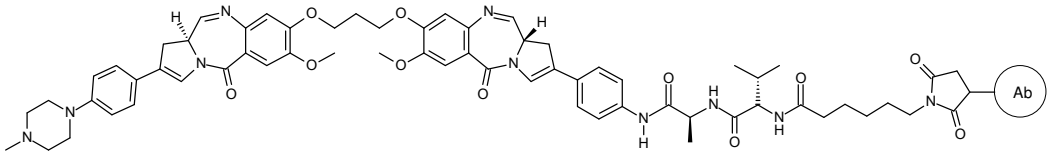
In some ~~embodiments~~examples, the conjugate is not:

ConjA



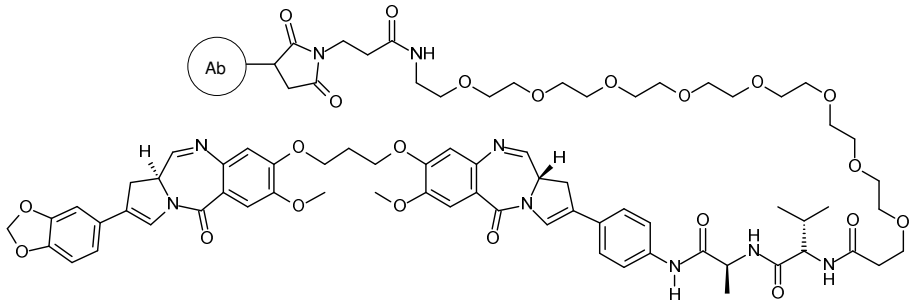
ConjA ;

ConjB



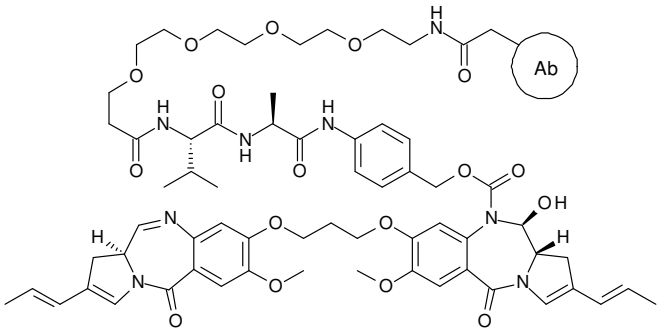
ConjB ;

ConjC:



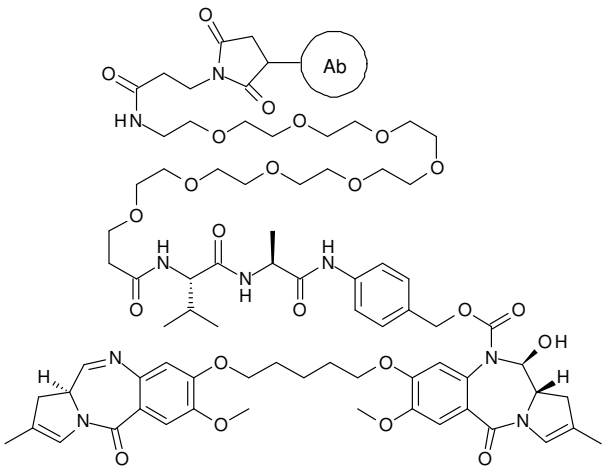
ConjC ;

ConjD



ConjD ; or

ConjE:



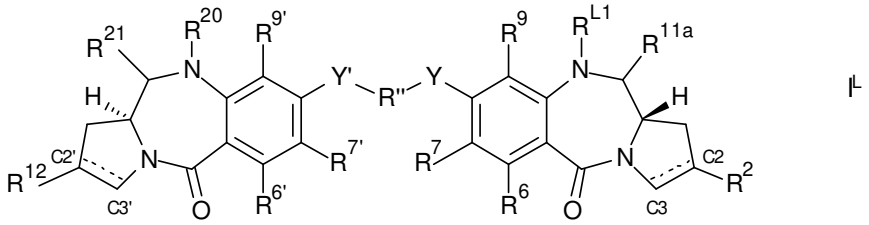
ConjE .

In other ~~embodiments~~examples, it may be preferred that the conjugate is selected from a conjugate of formula ConjA, ConjB, ConjC, ConjD and ConjE.

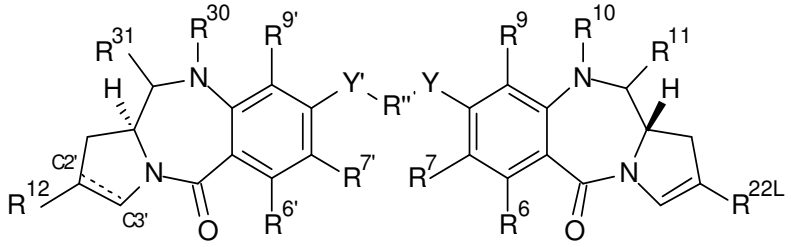
The subscript p in the formula I is an integer of from 1 to 20. Accordingly, the Conjugates comprise an antibody (Ab) as defined below covalently linked to at least one Drug unit by a Linker unit. The Ligand unit, described more fully below, is a targeting agent that binds to a target moiety. Accordingly, the present disclosure also provides methods for the treatment of, for example, various cancers and autoimmune disease. The drug loading is represented

by p, the number of drug molecules per antibody. Drug loading may range from 1 to 20 Drug units (D^L) per antibody. For compositions, p represents the average drug loading of the Conjugates in the composition, and p ranges from 1 to 20.

A second ~~aspect~~example of the disclosure provides a method of making a conjugate according to the first ~~aspect~~example of the disclosure comprising conjugating a compound of formula I^L or II^L:

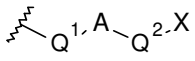


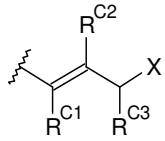
I^L

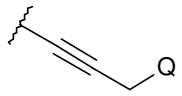


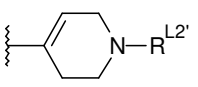
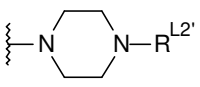
II^L

to the antibody (Ab) as defined below, wherein:
R^{L1} is a linker suitable for conjugation to the antibody (Ab);
R^{22L} is of formula $IIIa^L$, formula $IIIb^L$ or formula $IIIc^L$:

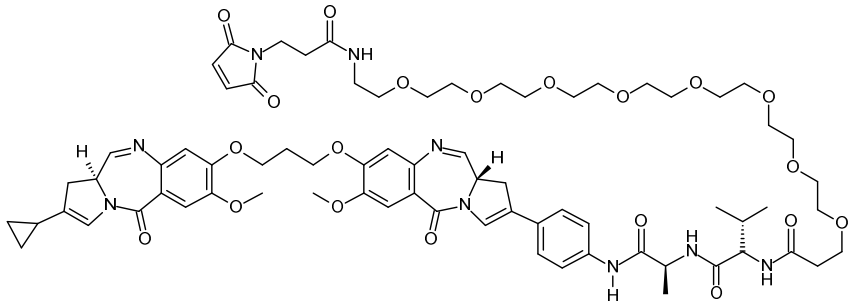
(a)  IIIa ;

(b)  IIIb ;

(c)  IIIc

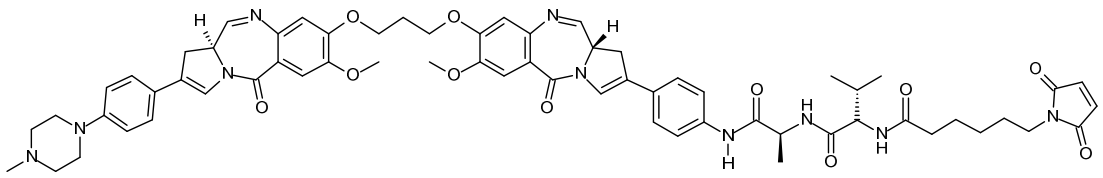
where Q^L is selected from O-R^{L2}, S-R^{L2} and NR^N-R^{L2}, and R^N is selected from H, methyl and ethyl
X^L is selected from the group comprising: O-R^{L2}, S-R^{L2}, CO_2-R^{L2}, CO-R^{L2}, N=C=O-R^{L2}, NHNH-R^{L2}, CONHNH-R^{L2},  ,  , NR^NR^L, wherein R^N is selected from the group comprising H and C_{1-4} alkyl;
R^{L2} is a linker suitable for conjugation to the antibody (Ab);
and all the remaining groups are as defined in the first ~~aspect~~example.

Thus it may be preferred in the second ~~aspect~~example, that the disclosure provides a method of making a conjugate selected from the group consisting of ConjA, ConjB, ConjC, ConjD and ConjE comprising conjugating a compound which is selected respectively from A:



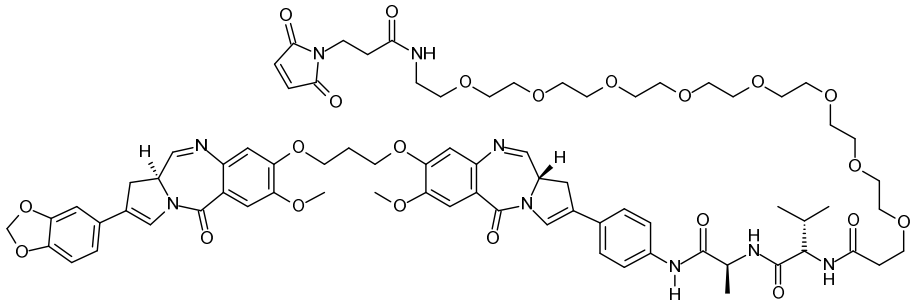
A

B:



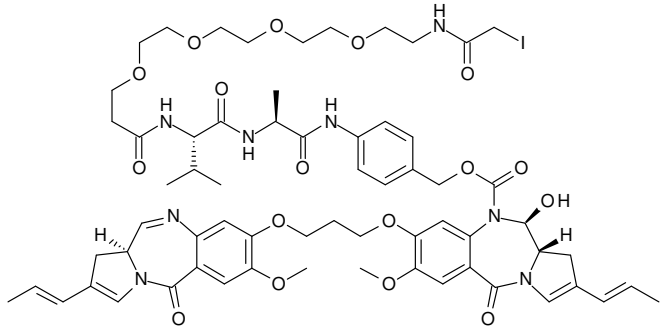
B

C:



C

D:

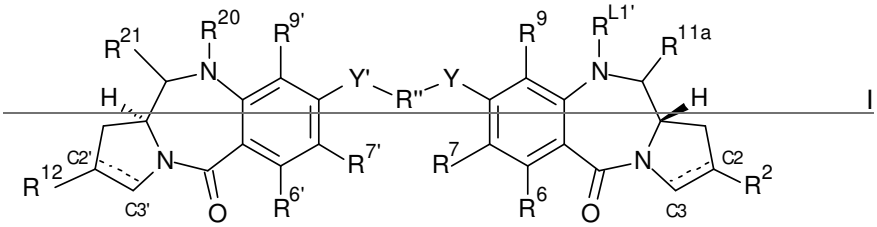


D

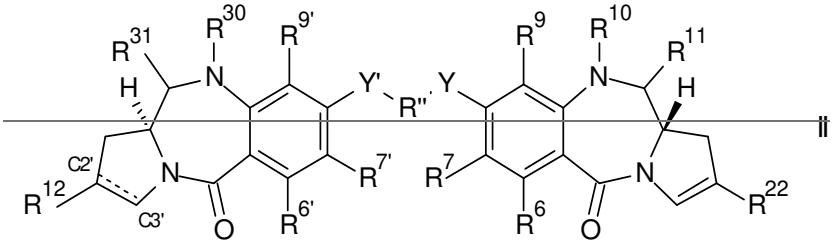
and E:

CLAIMS

1. A conjugate of formula L - $(D^L)_p$, where D^L is of formula I or II:



I



II

wherein:

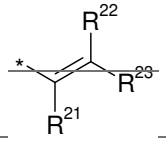
L is an antibody (Ab) which is an antibody that binds to KAAG1;

when there is a double bond present between C2' and C3', R^{12} is selected from the group consisting of:

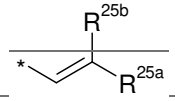
(ia) C_{5-10} aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C_{1-7} alkyl, C_{3-7} heterocyclyl and bis-oxy-C_{1-3} alkylene;

(ib) C_{1-5} saturated aliphatic alkyl;

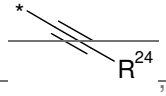
(ic) C_{3-6} saturated cycloalkyl;



(id) , wherein each of R^{21}, R^{22} and R^{23} are independently selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl, where the total number of carbon atoms in the R^{12} group is no more than 5;

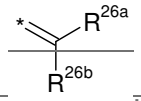


(ie) , wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



(if) , where R^{24} is selected from: H; C_{1-3} saturated alkyl; C_{2-3} alkenyl; C_{2-3} alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;

when there is a single bond present between C2' and C3',



R^{12} is , where R^{26a} and R^{26b} are independently selected from H, F, C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} alkyl amido and C_{1-4} alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C_{1-4} alkyl ester;

R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', nitro, Me_3Sn and halo;

where R and R' are independently selected from optionally substituted C_{1-12} alkyl, C_{3-20} heterocyclyl and C_{5-20} aryl groups;

R^7 is selected from H, R, OH, OR, SH, SR, NH_2, NHR, NHRR', nitro, Me_3Sn and halo;

R″ is a C_{3-12} alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C_{1-4} alkyl), and/or aromatic rings, e.g. benzene or pyridine;

Y and Y' are selected from O, S, or NH;

$R^{6'}$, $R^{7'}$, $R^{9'}$ are selected from the same groups as R^6, R^7 and R^9 respectively;

[Formula I]

$R^{L1'}$ is a linker for connection to the antibody (Ab);

R^{11a} is selected from OH, OR^A, where R^A is C_{1-4} alkyl, and SO_zM, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;

R^{20} and R^{21} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{20} is selected from H and R^C, where R^C is a capping group;

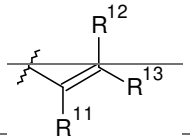
R^{21} is selected from OH, OR^A and SO_zM;

when there is a double bond present between C2 and C3, R^2 is selected from the group consisting of:

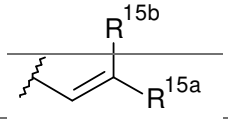
(ia) C_{5-10} aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C_{1-7} alkyl, C_{3-7} heterocyclyl and bis-oxy-C_{1-3} alkylene;

(ib) C_{1-5} saturated aliphatic alkyl;

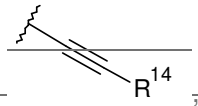
(ic) C_{3-6} saturated cycloalkyl;



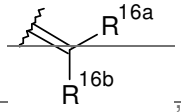
(id) , wherein each of R^{11}, R^{12} and R^{13} are independently selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl, where the total number of carbon atoms in the R^2 group is no more than 5;



(ie) , wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and

(if)  , where R^{14} is selected from: H; C_{1-3} saturated alkyl; C_{2-3} alkenyl; C_{2-3} alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;

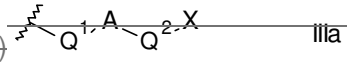
when there is a single bond present between C2 and C3,



R^2 is , where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} alkyl amido and C_{1-4} alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} alkyl ester;

[Formula II]

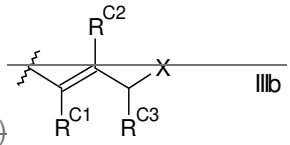
R^{22} is of formula IIIa, formula IIIb or formula IIIc:

(a) 

where A is a C_{5-7} aryl group, and either

(i) Q^1 is a single bond, and Q^2 is selected from a single bond and -Z-$(CH_2)_n$-, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or

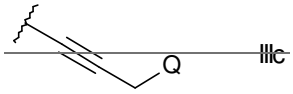
(ii) Q^1 is -CH=CH-, and Q^2 is a single bond;



(b)

where;

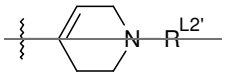
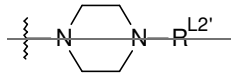
R^{C1}, R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} alkyl;



(c)

where Q is selected from O-$R^{L2'}$, S-$R^{L2'}$ and NR^N-$R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: O-$R^{L2'}$, S-$R^{L2'}$, CO_2-$R^{L2'}$, CO-$R^{L2'}$, NH-C(=O)-$R^{L2'}$,

NHNH-$R^{L2'}$, CONHNH-$R^{L2'}$,  ,  , $NR^NR^{L2'}$, wherein R^N is selected from the group comprising H and C_{1-4} alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

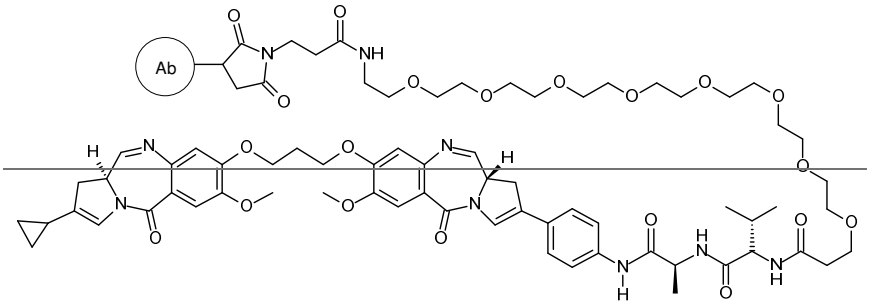
R^{10} is H and R^{11} is selected from OH, OR^A and SO_zM;

R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_zM.

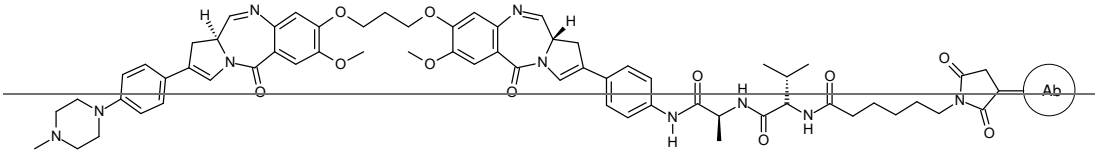
~~2. The conjugate according to claim 1, wherein the conjugate is not:~~

~~ConjA~~



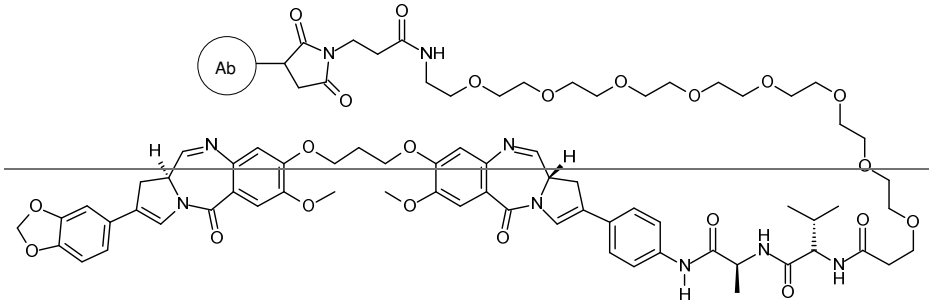
ConjA ~~;~~

~~ConjB~~



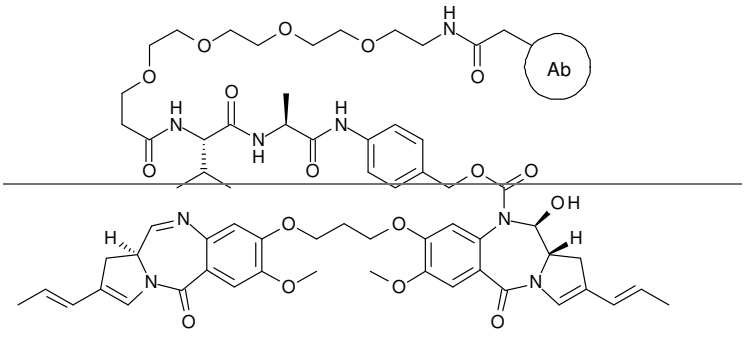
ConjB ~~;~~

~~ConjC:~~



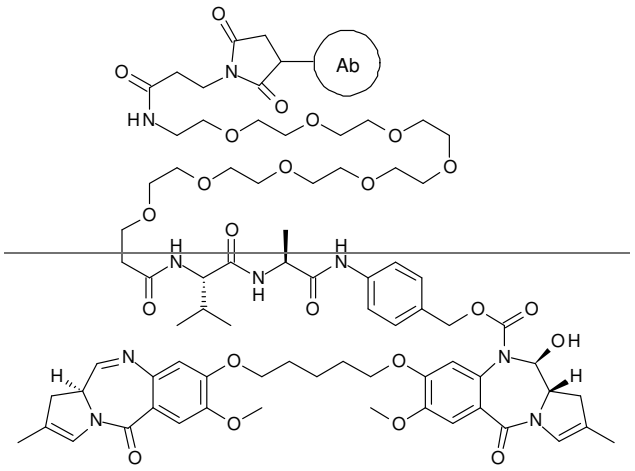
ConjC ~~;~~

~~ConjD~~



ConjD ~~; or~~

~~ConjE:~~



ConjE

3. The conjugate according to either claim 1 or claim 2, wherein R^7 is selected from H, OH and OR.

4. The conjugate according to claim 3, wherein R^7 is a C_{1-4} alkyloxy group.

5. The conjugate according to any one of claims 1 to 4, wherein Y is O.

6. The conjugate according to any one of the preceding claims, wherein R'' is C_{3-7} alkylene.

7. The conjugate according to any one of claims 1 to 6, wherein R^9 is H.

8. The conjugate according to any one of claims 1 to 7, wherein R^6 is selected from H and halo.

9. The conjugate according to any one of claims 1 to 8, wherein there is a double bond between C2' and C3', and R^{12} is a C_{5-7} aryl group.

10. The conjugate according to claim 9, wherein R^{12} is phenyl.

11. The conjugate according to any one of claims 1 to 8, wherein there is a double bond between C2' and C3', and R^{12} is a C_{8-10} aryl group.

12. The conjugate according to any one of claims 9 to 11, wherein R^{12} bears one to three substituent groups.

13. The conjugate according to any one of claims 9 to 12, wherein the substituents are selected from methoxy, ethoxy, fluoro, chloro, cyano, bis-oxy-methylene, methyl-piperazinyl, morpholino and methyl-thiophenyl.

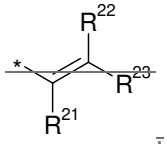
14. The conjugate according to any one of claims 1 to 8, wherein there is a double bond between C2' and C3', and R^{12} is a C_{1-5} saturated aliphatic alkyl group.

15. A compound according to claim 16, wherein R^{12} is methyl, ethyl or propyl.

16. The conjugate according to any one of claims 1 to 8, wherein there is a double bond between C2' and C3', and R^{12} is a C_{3-6} saturated cycloalkyl group.

17. The conjugate according to claim 16, wherein R^{12} is cyclopropyl.

18. The conjugate according to any one of claims 1 to 8, wherein there is a double bond between C2' and C3', and R^{12} is a group of formula:



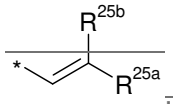
19. The conjugate according to claim 18, wherein the total number of carbon atoms in the R^{12} group is no more than 4.

20. The conjugate according to claim 19, wherein the total number of carbon atoms in the R^{12} group is no more than 3.

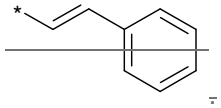
21. The conjugate according to any one of claims 18 to 20, wherein one of R^{21}, R^{22} and R^{23} is H, with the other two groups being selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl.

22. The conjugate according to any one of claims 18 to 20, wherein two of R^{21}, R^{22} and R^{23} are H, with the other group being selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl.

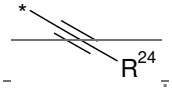
23. The conjugate according to any one of claims 1 to 8, wherein there is a double bond between C2' and C3', and R^{12} is a group of formula:



24. The conjugate according to claim 23, wherein R^{12} is the group:

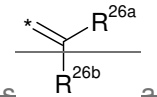


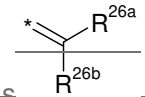
25. The conjugate according to any one of claims 1 to 8, wherein there is a double bond between C2' and C3', and R^{12} is a group of formula:

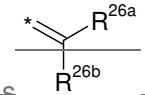


26. The conjugate according to claim 25, wherein R^{24} is selected from H, methyl, ethyl, ethenyl and ethynyl.

27. The conjugate according to claim 26, wherein R^{24} is selected from H and methyl.

28. The conjugate according to any one of claims 1 to 8, wherein there is a single bond between C2' and C3', R^{12} is  and R^{26a} and R^{26b} are both H.

29. The conjugate according to any one of claims 1 to 8, wherein there is a single bond between C2' and C3', R^{12} is  , and R^{26a} and R^{26b} are both methyl.

30. The conjugate according to any one of claims 1 to 8, wherein there is a single bond between C2' and C3', R^{12} is  , one of R^{26a} and R^{26b} is H, and the other is selected from C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted.

[Formula I]

31. The conjugate according to any one of claims 1 to 30, wherein there is a double bond between C2 and C3, and R^2 is a C_{5-7} aryl group.

32. The conjugate according to claim 31, wherein R^2 is phenyl.

33. The conjugate according to any one of claims 1 to 30, wherein there is a double bond between C2 and C3, and R^1 is a C_{8-10} aryl group.

34. A compound according to any one of claims 31 to 33, wherein R^2 bears one to three substituent groups.

35. The conjugate according to any one of claims 31 to 34, wherein the substituents are selected from methoxy, ethoxy, fluoro, chloro, cyano, bis-oxy-methylene, methyl-piperazinyl, morpholino and methyl-thiophenyl.

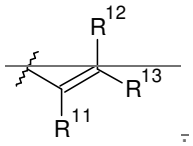
36. The conjugate according to any one of claims 1 to 30, wherein there is a double bond between C2 and C3, and R^2 is a C_{1-5} saturated aliphatic alkyl group.

37. The conjugate according to claim 36, wherein R^2 is methyl, ethyl or propyl.

38. The conjugate according to any one of claims 1 to 30, wherein there is a double bond between C2 and C3, and R^2 is a C_{3-6} saturated cycloalkyl group.

39. The conjugate according to claim 38, wherein R^2 is cyclopropyl.

40. The conjugate according to any one of claims 1 to 30, wherein there is a double bond between C2 and C3, and R^2 is a group of formula:



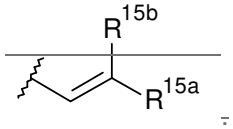
41. The conjugate according to claim 40, wherein the total number of carbon atoms in the R^2 group is no more than 4.

42. The conjugate according to claim 41, wherein the total number of carbon atoms in the R^2 group is no more than 3.

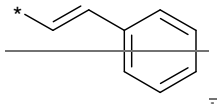
43. The conjugate according to any one of claims 40 to 42, wherein one of R^{11}, R^{12} and R^{13} is H, with the other two groups being selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl.

44. The conjugate according to any one of claims 40 to 42, wherein two of R^{11}, R^{12} and R^{13} are H, with the other group being selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl.

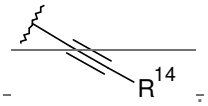
45. The conjugate according to any one of claims 1 to 30, wherein there is a double bond between C2 and C3, and R^2 is a group of formula:



46. The conjugate according to claim 45, wherein R^2 is the group:

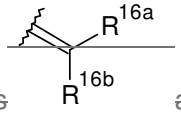


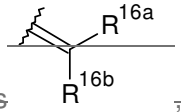
47. The conjugate according to any one of claims 1 to 30, wherein there is a double bond between C2 and C3, and R^2 is a group of formula:

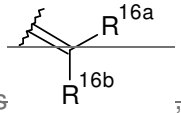


48. The conjugate according to claim 48, wherein R^{14} is selected from H, methyl, ethyl, ethenyl and ethynyl.

49. The conjugate according to claim 48, wherein R^{14} is selected from H and methyl.

50. The conjugate according to any one of claims 1 to 30, wherein there is a single bond between C2 and C3, R^2 is  and R^{16a} and R^{16b} are both H.

51. The conjugate according to any one of claims 1 to 30, wherein there is a single bond between C2 and C3, R^2 is , and R^{16a} and R^{16b} are both methyl.

52. The conjugate according to any one of claims 1 to 30, wherein there is a single bond between C2 and C3, R^2 is , one of R^{16a} and R^{16b} is H, and the other is selected from C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted.

53. The conjugate according to any one of claims 1 to 52, wherein R^{11a} is OH.

54. The conjugate according to any one of claims 1 to 53, wherein R^{21} is OH.

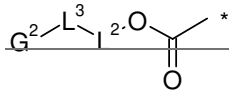
55. The conjugate according to any one of claims 1 to 53, wherein R^{21} is OMe.

56. The conjugate according to any one of claims 1 to 55, wherein R^{20} is H.

57. The conjugate according to any one of claims 1 to 55, wherein R^{20} is R^C.

58. The conjugate according to claim 57, wherein R^C is selected from the group consisting of: Alloc, Fmoc, Boc, Troc, Teoc, Psec, Cbz and PNZ.

60. The conjugate according to claim 57, wherein R^C is a group:



where the asterisk indicates the point of attachment to the N10 position, G^2 is a terminating group, L^3 is a covalent bond or a cleavable linker L^1, L^2 is a covalent bond or together with OC(=O) forms a self-immolative linker.

61. The conjugate according to claim 60, wherein G^2 is Ac or Moc or is selected from the group consisting of: Alloc, Fmoc, Boc, Troc, Teoc, Psec, Cbz and PNZ.

62. The conjugate according to any one of claims 1 to 53, wherein R^{20} and R^{21} together form a double bond between the nitrogen and carbon atoms to which they are bound.

[Formula II]

63. The conjugate according to any one of claims 1 to 30, wherein R^{22} is of formula IIIa, and A is phenyl.

64. The conjugate according to any one of claims 1 to 30 and claim 63, wherein R^{22} is of formula IIa, and Q^1 is a single bond.

65. The conjugate according to claim 63, wherein Q^2 is a single bond.

66. The conjugate according to claim 63, wherein Q^2 is -Z-$(CH_2)_n$-, Z is O or S and n is 1 or 2.

67. The conjugate according any one of claims 1 to 30 and claim 63, wherein R^{22} is of formula IIIa, and Q^1 is -CH=CH-.

68. The conjugate according to any one of claims 1 to 30, wherein R^{22} is of formula IIIb, and R^{C1}, R^{C2} and R^{C3} are independently selected from H and methyl.

69. The conjugate according to claim 68, wherein R^{C1}, R^{C2} and R^{C3} are all H.

70. The conjugate according to claim 68, wherein R^{C1}, R^{C2} and R^{C3} are all methyl.

71. The conjugate according to any one of claims 1 to 30 and claims 63 to 70, wherein R^{22} is of formula IIIa or formula IIIb and X is selected from O-$R^{L2'}$, S-$R^{L2'}$, CO_2-$R^{L2'}$, -N-C(=O)-$R^{L2'}$ and NH-$R^{L2'}$.

72. The conjugate according to claim 71, wherein X is NH-$R^{L2'}$.

73. The conjugate according to any one of claims 1 to 30, wherein R^{22} is of formula IIIc, and Q is NR^N-$R^{L2'}$.

74. The conjugate according to claim 73, wherein R^N is H or methyl.

75. The conjugate according to any one of claims 1 to 30, wherein R^{22} is of formula IIIc, and Q is O-$R^{L2'}$ or S-$R^{L2'}$.

76. The conjugate according to any one of claims 1 to 30 and claims 63 to 75, wherein R^{11} is OH.

77. The conjugate according to any one of claims 1 to 30 and claims 63 to 75, wherein R^{11} is OMe.

78. The conjugate according to any one of claims 1 to 30 and claims 63 to 77, wherein R^{10} is H.

79. The conjugate according to any one of claims 1 to 30 and claims 63 to 75, wherein R^{10} and R^{11} together form a double bond between the nitrogen and carbon atoms to which they are bound.

80. The conjugate according to any one of claims 1 to 30 and claims 63 to 79, wherein R^{31} is OH.

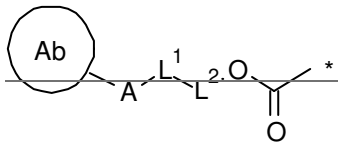
81. The conjugate according to any one of claims 1 to 30 and claims 63 to 79, wherein R^{31} is OMe.

82. The conjugate according to any one of claims 1 to 30 and claims 63 to 81, wherein R^{30} is H.

83. The conjugate according to any one of claims 1 to 30 and claims 63 to 79, wherein R^{30} and R^{31} together form a double bond between the nitrogen and carbon atoms to which they are bound.

84. The conjugate according to any one of claims 1 to 83, wherein $R^{6'}$, $R^{7'}$, $R^{9'}$, and Y' are the same as R^{6}, R^{7}, R^{9}, and Y.

85. The conjugate according to any one of claims 1 to 84 wherein, wherein L-$R^{L1'}$ or L-$R^{L2'}$ is a group:



where the asterisk indicates the point of attachment to the PBD, Ab is the antibody, L^1 is a cleavable linker, A is a connecting group connecting L^1 to the antibody, L^2 is a covalent bond or together with -OC(=O)- forms a self-immolative linker.

86. The conjugate of claim 85, wherein L^1 is enzyme cleavable.

87.The conjugate of claim 85 or claim 86, wherein L^1 comprises a contiguous sequence of amino acids.

88. The conjugate of claim 87, wherein L^1 comprises a dipeptide and the group $-X_1-X_2-$ in dipeptide, $-NH-X_1-X_2-CO-$, is selected from:
-Phe-Lys-,
-Val-Ala-,
-Val-Lys-,
-Ala-Lys-,
-Val-Cit-,
-Phe-Cit-,
-Leu-Cit-,
-Ile-Cit-,
-Phe-Arg-,
-Trp-Cit-.

89. The conjugate according to claim 88, wherein the group $-X_1-X_2-$ in dipeptide, $-NH-X_1-X_2-CO-$, is selected from:
-Phe-Lys-,
-Val-Ala-,
-Val-Lys-,
-Ala-Lys-,
-Val-Cit-.

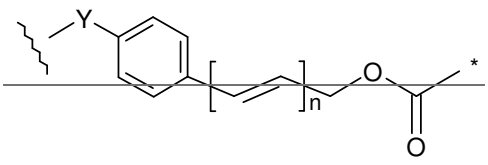
90. The conjugate according to claim 89, wherein the group $-X_1-X_2-$ in dipeptide, $-NH-X_1-X_2-CO-$, is -Phe-Lys-, -Val-Ala- or -Val-Cit-.

91. The conjugate according to any one of claims 88 to 90, wherein the group X_2-CO- is connected to L^2.

92. The conjugate according to any one of claims 88 to 91, wherein the group $NH-X_1-$ is connected to A.

93.The conjugate according to any one of claims 88 to 92, wherein L^2 together with OC(=O) forms a self-immolative linker.

94. The conjugate according to claim 93, wherein C(=O)O and L^2 together form the group:

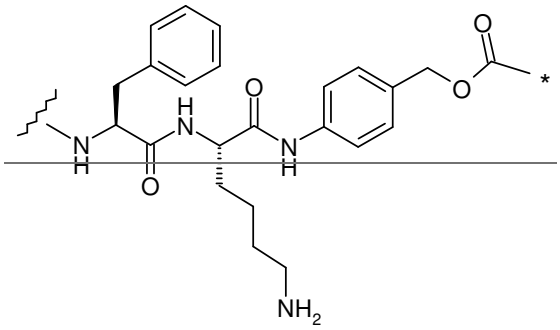


where the asterisk indicates the point of attachment to the PBD, the wavy line indicates the point of attachment to the linker L^1, Y is NH, O, C(=O)NH or C(=O)O, and n is 0 to 3.

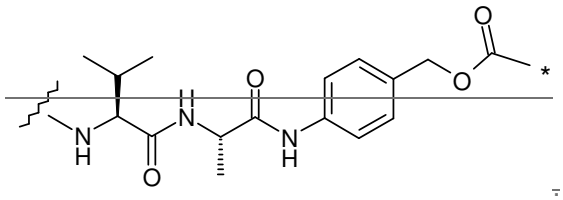
95. The conjugate according to claim 94, wherein Y is NH.

96. The conjugate according to claim 94 or claim 95, wherein n is 0.

97. The conjugate according to claim 95, wherein L^1 and L^2 together with -OC(=O)- comprise a group selected from:



or

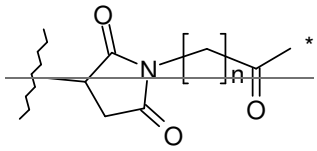


where the asterisk indicates the point of attachment to the PBD, and the wavy line indicates the point of attachment to the remaining portion of the linker L^1 or the point of attachment to A.

98. The conjugate according to claim 97, wherein the wavy line indicates the point of attachment to A.

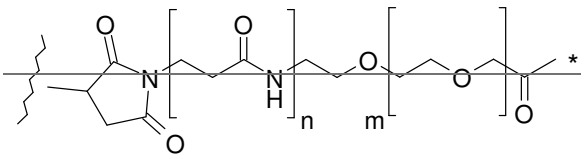
99. The conjugate according to any one of claims 85 to 98, wherein A is:

(i)



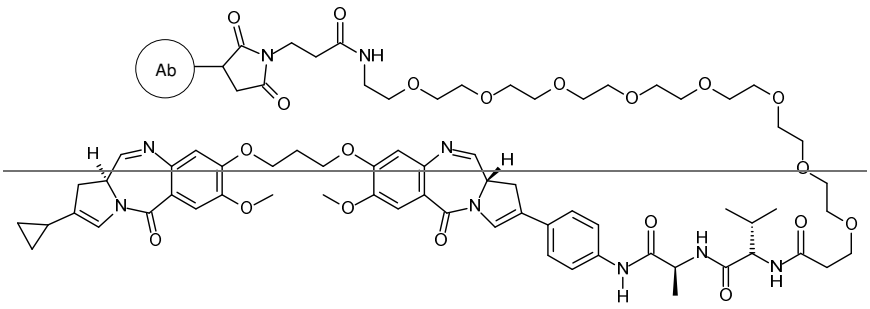
where the asterisk indicates the point of attachment to L^1, the wavy line indicates the point of attachment to the antibody, and n is 0 to 6; or

(ii)



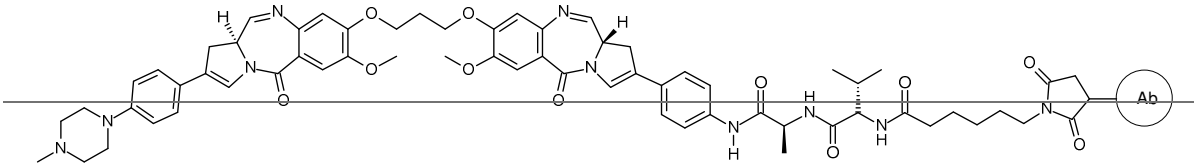
~~where the asterisk indicates the point of attachment to L^1, the wavy line indicates the point of attachment to the antibody, n is 0 or 1, and m is 0 to 30.~~

~~1001~~. A conjugate ~~according to claim 1~~ of formula ~~ConjA:~~



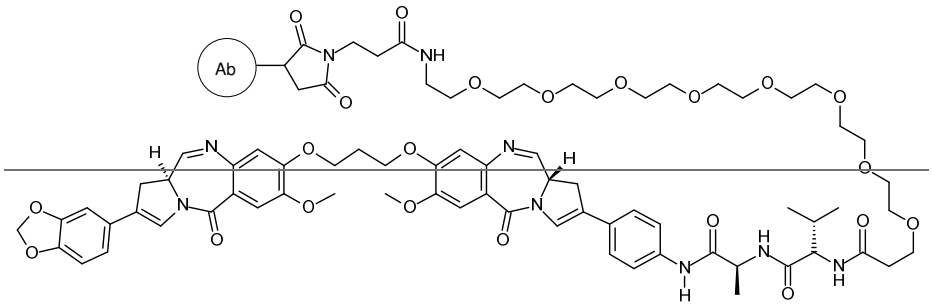
ConjA

~~ConjB:~~



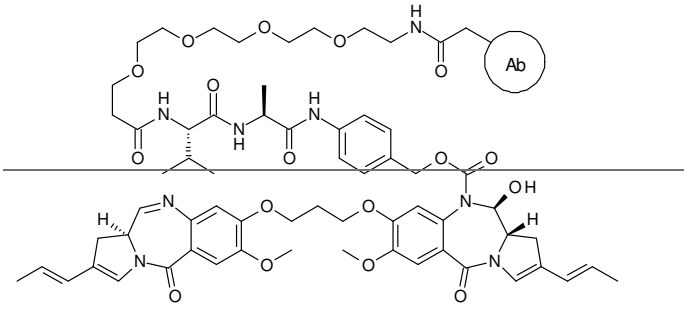
ConjB

~~ConjC:~~



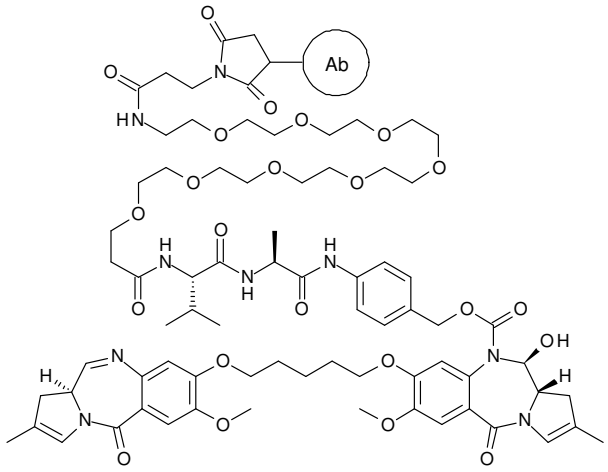
ConjC

~~ConjD:~~



ConjD

~~Or~~ ConjE:



ConjE

wherein Ab is an antibody that binds to kidney associated antigen 1 (KAAG1), the antibody comprising

~~101. The conjugate according to any one of claims 1 to 100 wherein the antibody comprises~~ a VH domain comprising a VH CDR1 with the amino acid sequence of SEQ ID NO.5, a VH CDR2 with the amino acid sequence of SEQ ID NO.6, and a VH CDR3 with the amino acid sequence of SEQ ID NO.7; and

~~optionally wherein the VH domain has the sequence according to SEQ ID NO. 1.~~

~~102. The conjugate according to any one of claims 1 to 101 wherein the antibody comprises:~~

a VL domain comprising a VL CDR1 with the amino acid sequence of SEQ ID NO.8, a VL CDR2 with the amino acid sequence of SEQ ID NO.9, and a VL CDR3 with the amino acid sequence of SEQ ID NO.10,

wherein the drug loading (p) is from 1 to 8.

2. The conjugate according to claim 1, wherein the VH domain has the sequence according to SEQ ID NO. 1.

~~103. The conjugate according to any one of claims 1 to 102 wherein the antibody comprises a VL domain having the sequence according to SEQ ID NO. 2, SEQ ID NO.13, or SEQ ID NO.15.~~

~~104~~3. The conjugate according to ~~any one of claims 1 to 102~~claim 1 or 2, wherein the ~~antibody comprises a~~ VL domain ~~having~~ has the sequence according to SEQ ID NO. 2.

~~105~~4. The conjugate according to any one of claims 1 to ~~104~~ 3 wherein the antibody comprises a heavy chain having the sequence of SEQ ID NO. 3~~,~~ or

~~106. The conjugate according to any one of claims 1 to 104 wherein the antibody comprises a heavy chain having the sequence of~~ SEQ ID NO. 11.

~~107~~5. The conjugate according to any one of the preceding claims~~ 1 to 106,~~ wherein the antibody comprises a light chain having the sequence of SEQ ID NO.4, SEQ ID NO.14, or SEQ ID NO.16.

~~108~~6. The conjugate according to claim 5~~any one of claims 1 to 106,~~ wherein the antibody comprises a light chain having the amino acid sequence of SEQ ID NO.4.

~~109~~7. The conjugate according to any one of the preceding claims~~ 1 to 108,~~ wherein the antibody is~~in~~ an intact antibody.

~~110. The conjugate according to any one of claims 1 to 109 wherein the antibody is humanised, deimmunised or resurfaced.~~

~~111~~8. The conjugate according to any one of the preceding claims~~ 1 to 108,~~ wherein the antibody is a fully human monoclonal IgG1 antibody~~.~~.

9. The conjugate according to claim 8, wherein the antibody is a fully human monoclonal ~~preferably~~ IgG1,κ antibody.

~~112. The conjugate according to any one of claims 1 to 111 wherein the drug loading (p) of drugs (D) to antibody (Ab) is an integer from 1 to about 8.~~

~~113~~10. The conjugate according to any one of the preceding claims, wherein the drug loading (p)~~claim 112, wherein p~~ is 1, 2, 3, or 4.

~~114. The conjugate according to claim 112 comprising a mixture of the antibody-drug conjugate compounds, wherein the average drug loading per antibody in the mixture of antibody-drug conjugate compounds is about 2 to about 5.~~

~~115. The conjugate according to any one of claims 1 to 114, for use in therapy.~~

~~116. The conjugate according to any one of claims 1 to 114, for use in the treatment of a proliferative disease in a subject.~~

~~117. The conjugate according to claim 116, wherein the disease is cancer.~~

~~118~~11. A pharmaceutical composition comprising the conjugate of any one of the preceding claims ~~1 to 114~~ and a pharmaceutically acceptable diluent, carrier or excipient.

12. The pharmaceutical composition according to claim 11, comprising a mixture of antibody-drug conjugates, wherein the average drug loading per antibody in the mixture of antibody-drug conjugates is about 2 to about 5.

~~119~~13. The pharmaceutical composition ~~of~~according to claim ~~118~~11 or 12, further comprising a therapeutically effective amount of a chemotherapeutic agent.

~~120~~14. Use of a conjugate according to any one of claims 1 to ~~114~~10 in the preparation of a medicament for ~~use in~~ the treatment of a kidney associated antigen 1 (KAAG1)-overexpressing cancer ~~proliferative disease~~ in a subject.

~~121. A method of treating cancer comprising administering to a patient the pharmaceutical composition of claim 118.~~

~~122. The method of claim 121 wherein the patient is administered a chemotherapeutic agent, in combination with the conjugate.~~

15 . The use according to claim 14, wherein a therapeutically effective amount of a chemotherapeutic agent is to be further administered to the subject.

16 . The use according to claim 14 or 15, wherein the cancer is ovarian cancer, breast cancer, prostate cancer, or renal cancer.

17. A conjugate according to any one of claims 1 to 10 for use in therapy.