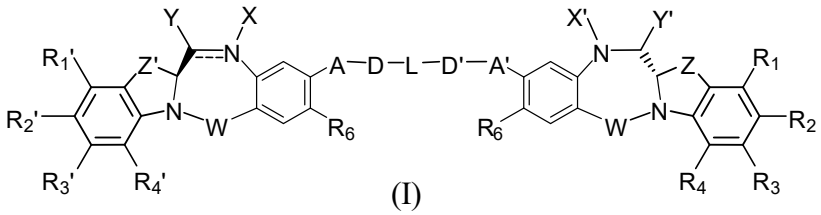
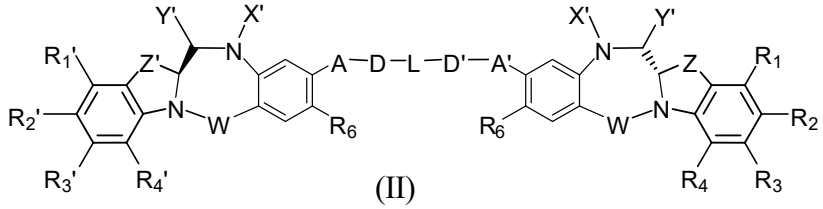
CLAIMS

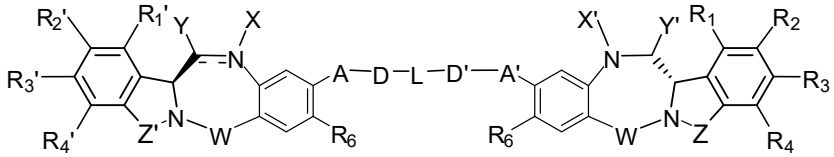
1. A cytotoxic compound comprising a linking group with a reactive group bonded thereto capable of covalently linking the cytotoxic compound to a cell binding agent (CBA), wherein said cytotoxic compound is represented by any one of the following formulas:



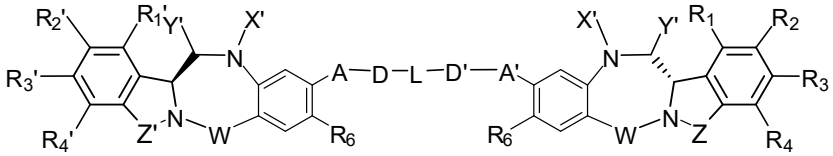
(I)



(II)



(III)



(IV)

or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is -H, or a linear or branched alkyl having 1 to 4 carbon atoms, and when it is a single bond, X is -H, the linking group with the reactive group bonded thereto, or an amine protecting moiety;

Y is -H or a leaving group selected from -OR, -OCOR', -OCOOR', -OCONR'R'',

-NR'R'', -NR'COR'', -NR'NR'R'', an optionally substituted 5- or 6-membered nitrogen-containing heterocycle (*e.g.*, piperidine, tetrahydropyrrole, pyrazole, morpholine, *etc.*), a guanidinum represented by -NR'(C=NH)NR'R'', an amino acid, or a peptide represented by -NRCOP', wherein P' is an amino acid or a polypeptide containing between 2 to 20 amino acid units, -SR, -SOR', $-SO_2M$, $-SO_3M$, $-OSO_3M$, halogen, cyano and an azido; or,

Y is a sulfite (HSO_3, HSO_2 or a salt of HSO_3^-, SO_3^{2-} or HSO_2^- formed with a cation), metabisulfite ($H_2S_2O_5$ or a salt of $S_2O_5^{2-}$ formed with a cation), mono-, di-, tri-, and tetra- thiophosphate (PO_3SH_3, $PO_2S_2H_2$, POS_3H_2, PS_4H_2 or a salt of PO_3S^{3-}, $PO_2S_2^{3-}$, POS_3^{3-} or PS_4^{3-} formed with a cation), thio phosphate ester $(R^iO)_2PS(OR^i)$, R^iS-, R^iSO, R^iSO_2, R^iSO_3, thiosulfate (HS_2O_3 or a salt of $S_2O_3^{2-}$ formed with a cation), dithionite (HS_2O_4 or a salt of $S_2O_4^{2-}$ formed with a cation), phosphorodithioate ($P(=S)(OR^{k'})(S)(OH)$ or a salt thereof formed with a cation), hydroxamic acid ($R^{k'}C(=O)NOH$ or a salt formed with a cation), formaldehyde sulfoxylate ($HOCH_2SO_2^-$ or a salt of $HOCH_2SO_2^-$ formed with a cation, such as $HOCH_2SO_2^-Na^+$) or a mixture thereof, wherein R^i is a linear or branched alkyl having 1 to 10 carbon atoms and is substituted with at least one substituent selected from $-N(R^j)_2$, $-CO_2H$, $-SO_3H$, and $-PO_3H$; R^i can be further optionally substituted with a substituent for an alkyl described herein; R^j is a linear or branched alkyl having 1 to 6 carbon atoms; $R^{k'}$ is a linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, aryl, heterocyclyl or heteroaryl;

M is -H or a cation;

R, for each occurrence, is independently selected from the group consisting of -H, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $-(CH_2CH_2O)_n-R^c$, an optionally substituted aryl having 6 to 18 carbon atoms, an optionally substituted 5- to 18-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an optionally substituted 3- to 18-membered heterocyclic ring containing 1 to 6 heteroatoms independently selected from O, S, N and P;

R' and R'' are each independently selected from -H, -OH, -OR, -NHR, $-NR_2$, -COR, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $-(CH_2CH_2O)_n-R^c$, and an optionally

substituted 3- to 18-membered heterocyclic ring having 1 to 6 heteroatoms independently selected from O, S, N and P;

R^c is -H or a substituted or unsubstituted linear or branched alkyl having 1 to 4 carbon atoms, or the linking group with the reactive group bonded thereto;

n is an integer from 1 to 24;

W is selected from C=O, C=S, CH_2, BH, SO and SO_2;

X' is selected from -H, an amine-protecting group, the linking group with the reactive group bonded thereto, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit -$(CH_2CH_2O)_n$-R^c, an optionally substituted aryl having 6 to 18 carbon atoms, an optionally substituted 5- to 18-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an optionally substituted 3- to 18-membered heterocyclic ring containing 1 to 6 heteroatoms independently selected from O, S, N and P;

Y' is selected from -H, an oxo group, the linking group with the reactive group bonded thereto, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, an optionally substituted 6- to 18-membered aryl, an optionally substituted 5- to 18-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, an optionally substituted 3- to 18-membered heterocyclic ring having 1 to 6 heteroatoms;

R_1, R_2, R_3, R_4, R_1', R_2', R_3' and R_4' are each independently selected from the group consisting of -H, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit -$(OCH_2CH_2)_n$-R^c, halogen, guanidinium [-NH(C=NH)NH_2], -OR, -NR'R'', -NO_2, -NCO, -NR'COR'', -SR, a sulfoxide represented by -SOR', a sulfone represented by -SO_2R', a sulfonate -$SO_3^-M^+$, a sulfate -$OSO_3^-M^+$, a sulfonamide represented by -SO_2NR'R'', cyano, an azido, -COR', -OCOR', -OCONR'R'', and the linking group with the reactive group bonded thereto;

R_6 is -H, -R, -OR, -SR, -NR'R'', -NO_2, halogen or the linking group with the reactive group bonded thereto;

Z and Z' are independently selected from -$(CH_2)_{n'}$-, -$(CH_2)_{n'}$-CR_7R_8-$(CH_2)_{na'}$-, -

$(CH_2)_{n'}$-NR_9-$(CH_2)_{na'}$-, -$(CH_2)_{n'}$-O-$(CH_2)_{na'}$- and -$(CH_2)_{n'}$–S-$(CH_2)_{na'}$-;

n' and na' are the same or different, and are selected from 0, 1, 2 and 3;

R_7 and R_8 are the same or different, and are each independently selected from -H, -OH, -SH, -COOH, -NHR', a polyethylene glycol unit -$(OCH_2CH_2)_n$-, an amino acid, a peptide unit bearing 2 to 6 amino acids, an optionally substituted linear, branched or cyclic alkyl having from 1 to 10 carbon atoms;

R_9 is independently selected from -H, an optionally substituted linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit -$(OCH_2CH_2)_n$-;

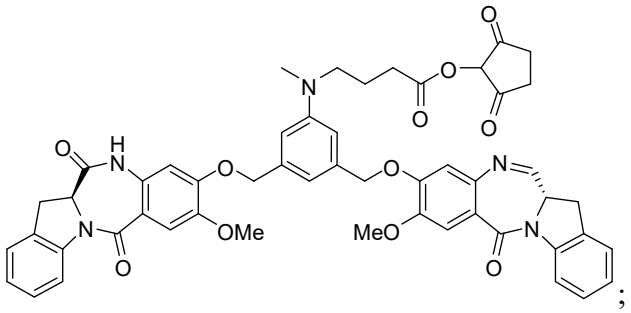
A and A' are the same or different, and are independently selected from -O-, oxo (-C(=O)-), -CRR'O-, -CRR'-, -S-, -CRR'S-, -NR_5 and -CRR'N(R_5)-,

R_5 for each occurrence is independently -H or an optionally substituted linear or branched alkyl having 1 to 10 carbon atoms;

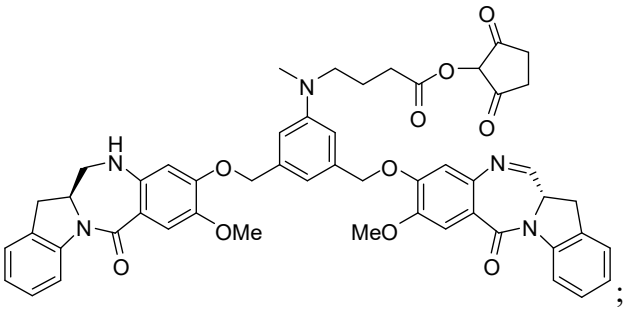
D and D' are the same or different, and are independently absent or selected from the group consisting of an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, an amino acid, a peptide bearing 2 to 6 amino acids, and a polyethylene glycol unit (-$OCH_2CH_2)_n$-;

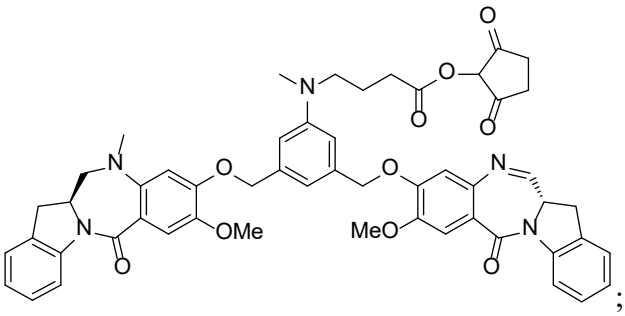
L is absent, the linking group with the reactive group bonded thereto, a polyethylene glycol unit (-$OCH_2CH_2)_n$-, a linear, branched or cyclic alkyl or alkenyl having 1 to 10 carbon atoms, a phenyl group, a 3 to 18-membered heterocyclic ring or a 5- to 18-membered heteroaryl ring having 1 to 6 heteroatoms independently selected from O, S, N and P, wherein the alkyl or alkenyl is optionally substituted with the linking group with the reactive group bonded thereto; phenyl or heterocyclic or heteroaryl ring can be optionally substituted, wherein the substituent can be the linking group with the reactive group bonded thereto;

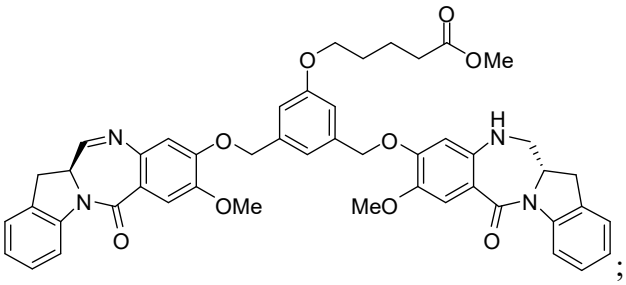
provided that the compound is not any one of the following compounds:

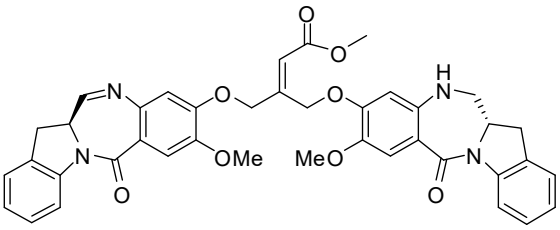


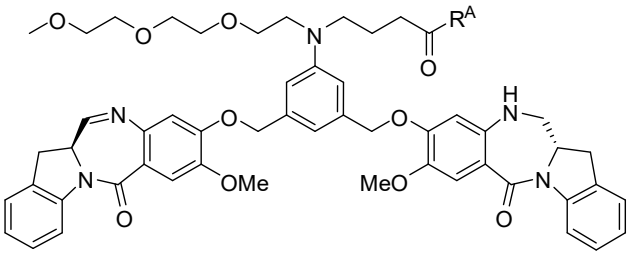
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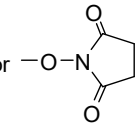

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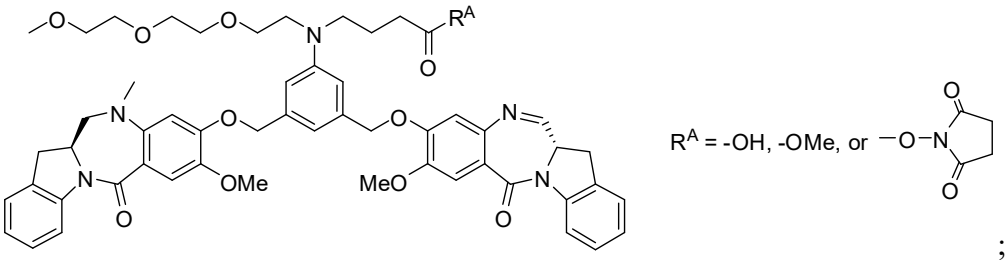

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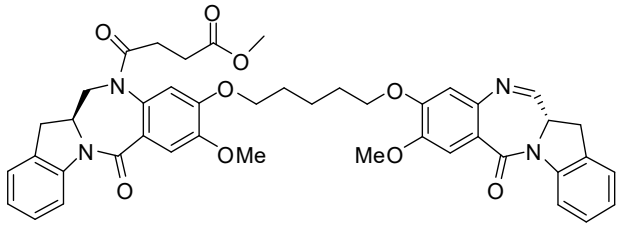


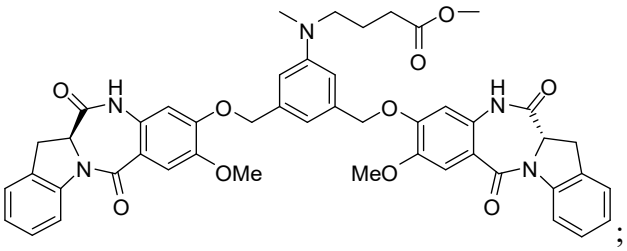
R^A = -OH, -OMe, or 

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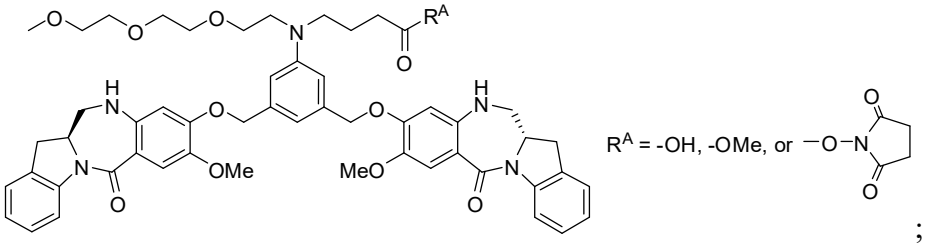


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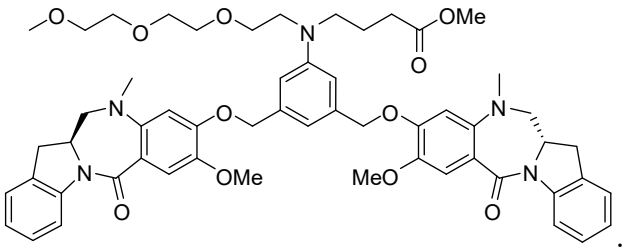




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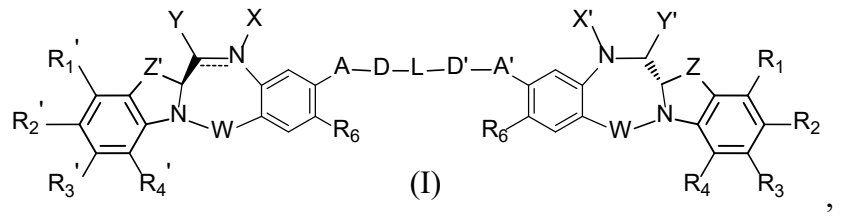


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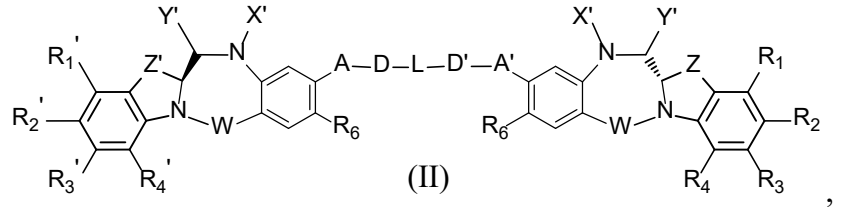


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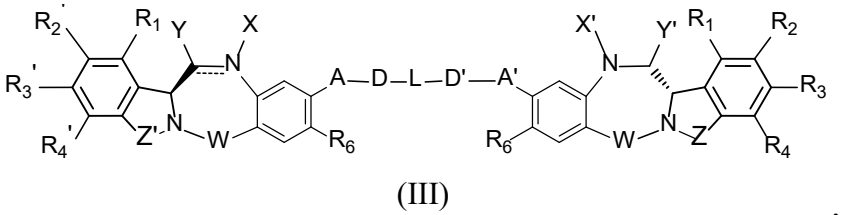
2. A conjugate comprising: a cytotoxic compound and a cell binding agent (CBA), wherein the cytotoxic compound comprises a linking group which covalently links the cytotoxic compound to the CBA, and wherein said cytotoxic compound is represented by any one of the following formulas:



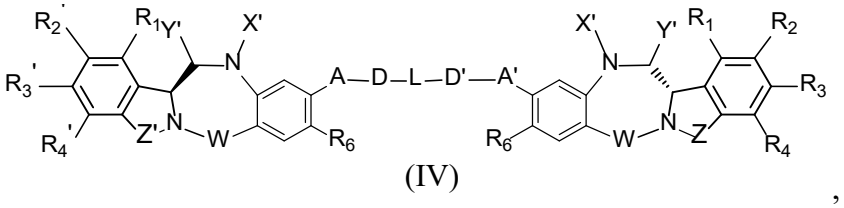
(I) ,



(II) ,



(III) ,



(IV) ,

or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is -H, or a linear or branched alkyl having 1 to 4 carbon atoms, and when it is a single bond, X is -H, the linking group, or an amine protecting moiety;

Y is -H or a leaving group selected from -OR, -OCOR', -OCOOR', -OCONR'R'', -NR'R'', -NR'COR'', -NR'NR'R'', an optionally substituted 5- or 6-membered nitrogen-containing heterocycle (*e.g.*, piperidine, tetrahydropyrrole, pyrazole, morpholine), a guanidinum represented by -NR'(C=NH)NR'R'', an amino acid, or a peptide represented by -NRCOP', wherein P' is an amino acid or a polypeptide containing between 2 to 20 amino acid units, -SR, -SOR', -SO_2M, -SO_3M, -OSO_3M, halogen, cyano and an azido; or,

Y is a sulfite (HSO_3, HSO_2 or a salt of HSO_3^-, SO_3^{2-} or HSO_2^- formed with a cation), metabisulfite ($H_2S_2O_5$ or a salt of $S_2O_5^{2-}$ formed with a cation), mono-, di-, tri-, and tetra- thiophosphate (PO_3SH_3, $PO_2S_2H_2$, POS_3H_2, PS_4H_2 or a salt of PO_3S^{3-}, $PO_2S_2^{3-}$,

POS_3^{3-} or PS_4^{3-} formed with a cation), thio phosphate ester $(R^iO)_2PS(OR^i)$, R^iS-, R^iSO, R^iSO_2, R^iSO_3, thiosulfate (HS_2O_3 or a salt of $S_2O_3^{2-}$ formed with a cation), dithionite (HS_2O_4 or a salt of $S_2O_4^{2-}$ formed with a cation), phosphorodithioate ($P(=S)(OR^{k'})(S)(OH)$ or a salt thereof formed with a cation), hydroxamic acid ($R^{k'}C(=O)NOH$ or a salt formed with a cation), formaldehyde sulfoxylate ($HOCH_2SO_2^-$ or a salt of $HOCH_2SO_2^-$ formed with a cation, such as $HOCH_2SO_2^-Na^+$) or a mixture thereof, wherein R^i is a linear or branched alkyl having 1 to 10 carbon atoms and is substituted with at least one substituent selected from $-N(R^j)_2$, $-CO_2H$, $-SO_3H$, and $-PO_3H$; R^i can be further optionally substituted with a substituent for an alkyl described herein; R^j is a linear or branched alkyl having 1 to 6 carbon atoms; $R^{k'}$ is a linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, aryl, heterocyclyl or heteroaryl;

M is -H or a cation;

R, for each occurrence, is independently selected from the group consisting of -H, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $-(CH_2CH_2O)_n-R^c$, an optionally substituted aryl having 6 to 18 carbon atoms, an optionally substituted 5- to 18-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an optionally substituted 3- to 18-membered heterocyclic ring containing 1 to 6 heteroatoms independently selected from O, S, N and P;

R' and R'' are each independently selected from -H, -OH, -OR, -NHR, $-NR_2$, -COR, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $-(CH_2CH_2O)_n-R^c$, and an optionally substituted 3-18-membered heterocyclic ring having 1 to 6 heteroatoms independently selected from O, S, N and P;

R^c is -H or a substituted or unsubstituted linear or branched alkyl having 1 to 4 carbon atoms, or the linking group;

n is an integer from 1 to 24;

W is selected from C=O, C=S, CH_2, BH, SO and SO_2;

X' is selected from -H, an amine-protecting group, the linking group, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1

to 10 carbon atoms, a polyethylene glycol unit -$(CH_2CH_2O)_n$-R^c, an optionally substituted aryl having 6 to 18 carbon atoms, an optionally substituted 5- to 18-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an optionally substituted 3- to 18-membered heterocyclic ring containing 1 to 6 heteroatoms independently selected from O, S, N and P;

Y' is selected from -H, an oxo group, the linking group, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, an optionally substituted 6- to 18-membered aryl, an optionally substituted 5- to 18-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, an optionally substituted 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms;

R_1, R_2, R_3, R_4, R_1', R_2', R_3' and R_4' are each independently selected from the group consisting of -H, an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit -$(OCH_2CH_2)_n$-R^c, halogen, guanidinium [-$NH(C=NH)NH_2$], -OR, -NR'R'', -NO_2, -NCO, -NR'COR'', -SR, a sulfoxide represented by -SOR', a sulfone represented by -SO_2R', a sulfonate -$SO_3^-M^+$, a sulfate -$OSO_3^-M^+$, a sulfonamide represented by -SO_2NR'R'', cyano, an azido, -COR', -OCOR', -OCONR'R'' and the linking group;

R_6 is -H, -R, -OR, -SR, -NR'R'', -NO_2, halogen or the linking group;

Z and Z' are independently selected from -$(CH_2)_{n'}$-, -$(CH_2)_{n'}$-CR_7R_8-$(CH_2)_{na'}$-, -$(CH_2)_{n'}$-NR_9-$(CH_2)_{na'}$-, -$(CH_2)_{n'}$-O-$(CH_2)_{na'}$- and -$(CH_2)_{n'}$–S-$(CH_2)_{na'}$-;

n' and na' are the same or different, and are selected from 0, 1, 2 and 3;

R_7 and R_8 are the same or different, and are each independently selected from -H, -OH, -SH, -COOH, -NHR', a polyethylene glycol unit -$(OCH_2CH_2)_n$-, an amino acid, a peptide unit bearing 2 to 6 amino acids, an optionally substituted linear, branched or cyclic alkyl having from 1 to 10 carbon atoms;

R_9 is independently selected from -H, an optionally substituted linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit -$(OCH_2CH_2)_n$-;

A and A' are the same or different, and are independently selected from -O-, oxo (-C(=O)-), -CRR'O-, -CRR'-, -S-, -CRR'S-, -N(R_5)- and -CRR'N(R_5)-,

R_5 for each occurrence is independently -H or an optionally substituted linear or

branched alkyl having 1 to 10 carbon atoms;

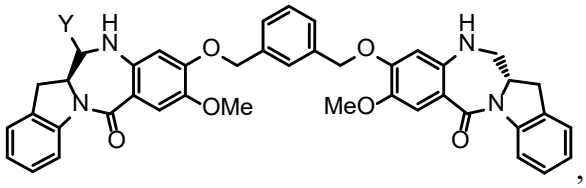
D and D' are the same or different, and are independently absent or selected from the group consisting of an optionally substituted linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, an amino acid, a peptide bearing 2 to 6 amino acids, and a polyethylene glycol unit $(-OCH_2CH_2)_n-$;

L is absent, the linking group, a polyethylene glycol unit $(-OCH_2CH_2)_n-$, a linear, branched or cyclic alkyl or alkenyl having 1 to 10 carbon atoms, a phenyl group, a 3- to 18-membered heterocyclic ring or a 5- to 18-membered heteroaryl ring having 1 to 6 heteroatoms independently selected from O, S, N and P, wherein the alkyl or alkenyl is optionally substituted with the linking group; phenyl or heterocyclic or heteroaryl ring can be optionally substituted, wherein the substituent can be the linking group.

3. A pharmaceutical composition comprising the conjugate of claim 2 and a pharmaceutically acceptable carrier.

4. Use of a compound of claim 1 or a conjugate of claim 2 in the manufacture of a medicament for inhibiting abnormal cell growth or treating a proliferative disorder, an autoimmune disorder, destructive bone disorder, infectious disease, viral disease, fibrotic disease, neurodegenerative disorder, pancreatitis or kidney disease in a mammal, wherein the compound of claim 1 or the conjugate of claim 2 and, optionally, a chemotherapeutic agent is to be administered to said mammal.

5. Use of a compound of the following formula:



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wherein Y is -H or $-SO_3M$ (*e.g.*, Y is $-SO_3M$), and M is -H or a pharmaceutically acceptable cation, in the manufacture of a medicament for inhibiting abnormal cell growth or treating a proliferative disorder, an autoimmune disorder, destructive bone disorder, infectious disease, viral disease, fibrotic disease, neurodegenerative disorder, pancreatitis or kidney disease in a mammal, wherein the compound and optionally, a chemotherapeutic agent, is to be administered to said mammal.