[0006] Therefore, a need exists for new linker technologies and conjugates useful for targeted therapy. The present disclosure addresses those and other needs.

BRIEF SUMMARY

[0007] The disclosure provides, inter alia, Camptothecin Conjugates, Camptothecin-Linker Compounds and Camptothecin Compounds, methods of preparing and using them, and intermediates useful in the preparation thereof. The Camptothecin Conjugates of the present disclosure are stable in circulation, yet capable of inflicting cell death once free drug is released from a Conjugate in the vicinity or within tumor cells.

[0007a] In one aspect, the present disclosure provides a Camptothecin Conjugate having a formula:

$$L\text{-}(Q\text{-}D)_p \qquad (I)$$

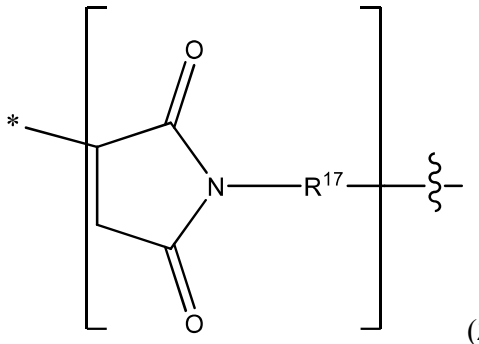
or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Q is a Linker Unit having a formula selected from:

-Z-A-S*-RL-; -Z-A- L^P(S*)-RL-; -Z-A-S*-RL-Y-; or -Z-A- L^P(S*)-RL-Y-,

wherein Z is a Stretcher Unit of Formula Za:



(Za)

wherein the asterisk indicates the position of attachment to the Ligand Unit (L);

the wavy line indicates the position of attachment to the Connector Unit (A); and

R^{17} is -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8

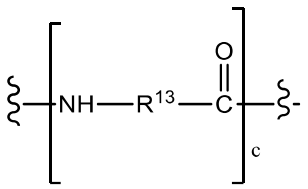
carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

wherein R^{17} is optionally substituted with a Basic Unit (BU) that is $-(CH_2)_x NH_2$, $-(CH_2)_xNHR^a$, or $-(CH_2)_xNR^a{}_2$;

wherein x is an integer of from 1-4; and

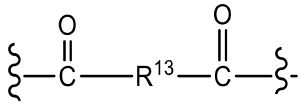
each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form a 4- to 6-membered heterocycloalkyl ring, or an azetidinyl, pyrrolidinyl or piperidinyl group;

A is a bond or a Connector Unit having the formula:



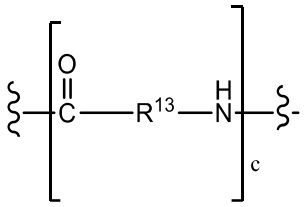
wherein in each instance R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is an integer ranging from 1 to 4; or

A is a Connector Unit having the formula:



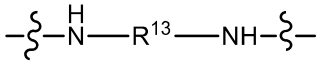
wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-; or

A is a Connector Unit having the formula:



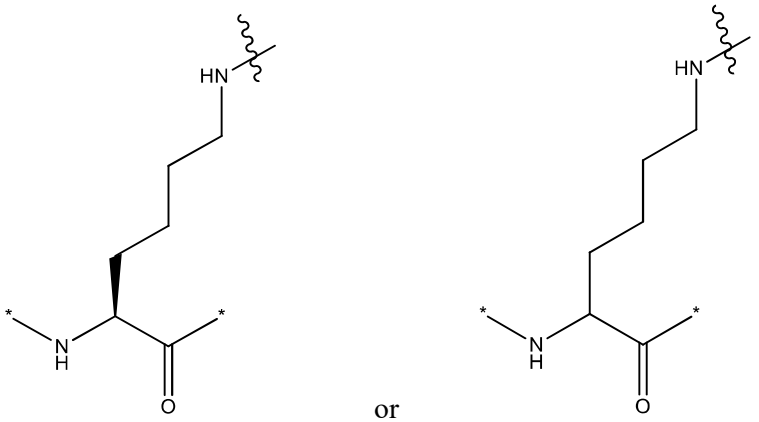
wherein in each instance, R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is from 1 to 14; or

A is a Connector Unit having the formula:



wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, –C(=O)C_1-C_6 alkylene- or -C_1-C_6 alkylene-C(=O)-C_1-C_6 alkylene;

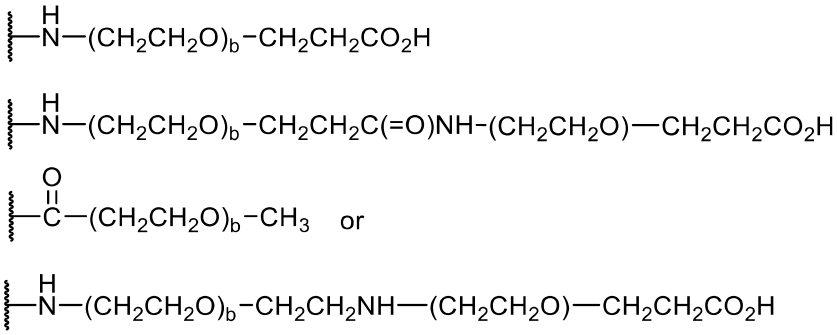
L^P is a Parallel Connector Unit having the formula:



or

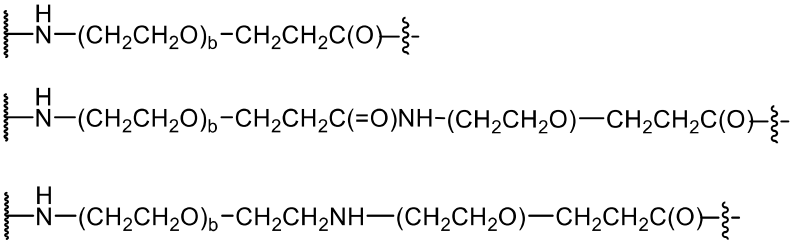
wherein the wavy line indicates the position of attachment to the Partitioning Agent and asterisks indicate positions of attachment to A and RL;

S^* is a bond or a Partitioning Agent having the formula:



wherein the wavy line indicates the site of attachment to the Parallel Connector Unit (L^P), and b is an integer from 2 to 20; or

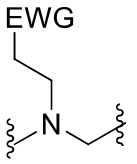
S* is a Partitioning Agent having the formula:

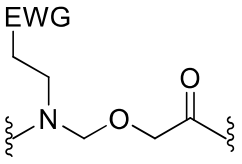


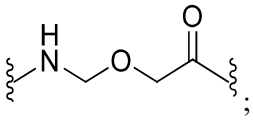
wherein the wavy line on the left indicates the site of attachment to Z-A-, the wavy line on the right indicates the site of attachment to RL, and each b is independently selected from 2 to 24;

RL is a peptide comprising from 2 to 8 amino acids; and

Y is a Spacer Unit having the formula:



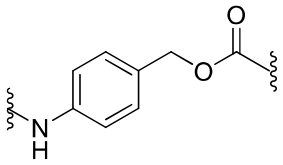
;


; or


;

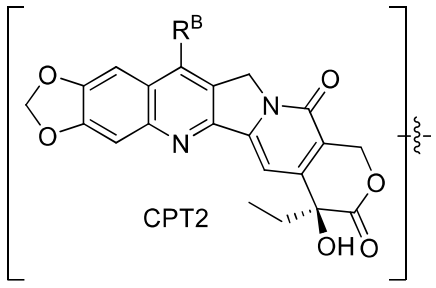
wherein EWG is selected from the group consisting of -CN, -NO_2, -CX_3, -X, -C(=O)$OR^{'}$, -C(=O)$N(R^{'})_2$, -C(=O)$R^{'}$, -C(=O)X, -$S(=O)_2R^{'}$, -$S(=O)_2OR^{'}$, -$S(=O)_2NHR^{'}$, -$S(=O)_2N(R^{'})_2$, -$P(=O)(OR^{'})_2$, -$P(=O)(CH_3)NHR^{'}$, -NO, -$N(R^{'})_3^{+}$, wherein X is -F, -Br, -Cl, or -I, and $R^{'}$ is independently selected from the group consisting of hydrogen and C_{1-6} alkyl; or

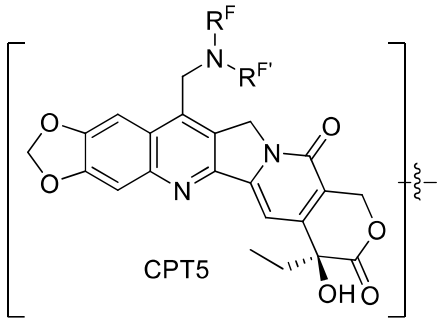
Y is a Spacer Unit having the formula:



;

D is a Drug Unit selected from the group consisting of:



and


;

wherein

R^B is selected from the group consisting of H, -(C_1-C_4)alkyl-OH, -(C_1-C_4)alkyl-O-(C_1-C_4)alkyl-NH_2, -C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, C_3-C_8cycloalkylC_1-C_4 alkyl, phenyl and phenylC_1-C_4 alkyl;

each R^F and $R^{F'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_2-C_6 heteroalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, C_1-C_8 aminoalkylC(O)-, C_3-C_{10} cycloalkyl, C_3-C_{10}cycloalkylC_1-C_4 alkyl, C_3-C_{10} heterocycloalkyl, C_3-C_{10} heterocycloalkylC_1-C_4 alkyl, phenyl, phenylC_1-C_4 alkyl,

diphenylC_1-C_4 alkyl, heteroaryl and heteroarylC_1-C_4 alkyl; or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^B, R^F and $R^{F'}$ are substituted with from 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$; and

p is an integer ranging from 1 to 16;

wherein Q is attached through any one of the hydroxyl or amine groups present on CPT2 or CPT5.

[0007b] In another aspect, the present disclosure provides a Camptothecin-Linker Compound of the formula:

Q'-D,

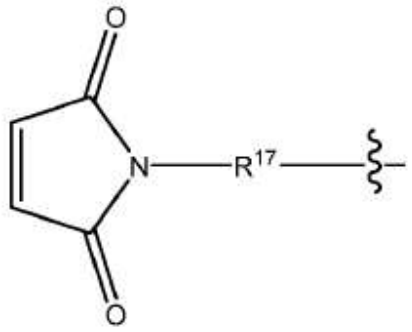
or a pharmaceutically acceptable salt thereof, wherein

Q' is a Linker Unit Precursor having a formula selected from the group consisting of:

Z'-A-S*-RL-; Z'-A-L^P(S*)-RL-; Z'-A-S*-RL-Y-; Z'-A-L^P(S*)-RL-Y-;

wherein

Z' is a Stretcher Unit Precursor of Formula Za:



(Za)

wherein

the wavy line indicates the position of attachment to the Connector Unit (A); and

R^{17} is -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-

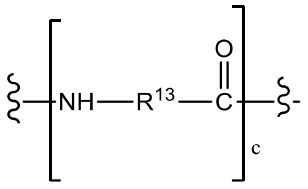
C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

wherein R^{17} is optionally substituted with a Basic Unit (BU) that is –$(CH_2)_x$ NH_2 , –$(CH_2)_x$$NHR^a$, or –$(CH_2)_x$$NR^a_2$;

wherein x is an integer of from 1-4; and

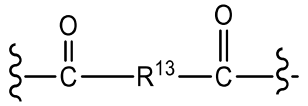
each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form a 4- to 6-membered heterocycloalkyl ring, or an azetidinyl, pyrrolidinyl or piperidinyl group;

A is a bond or a Connector Unit having the formula:



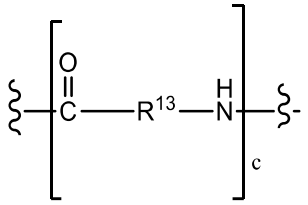
wherein in each instance R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is an integer ranging from 1 to 4; or

A is a Connector Unit having the formula:



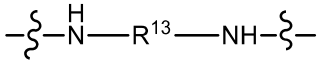
wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-; or

A is a Connector Unit having the formula:



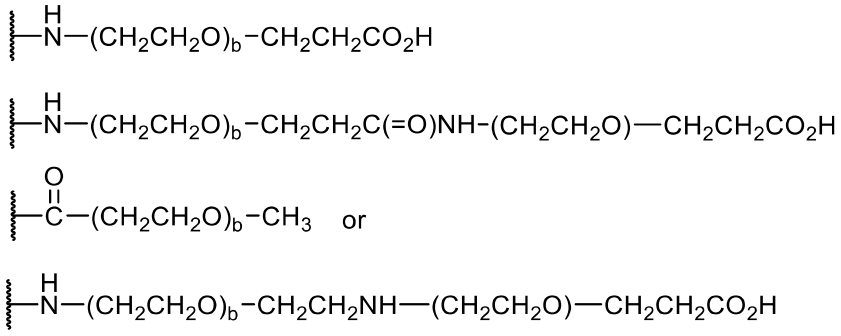
wherein in each instance, R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is from 1 to 14; or

A is a Connector Unit having the formula:



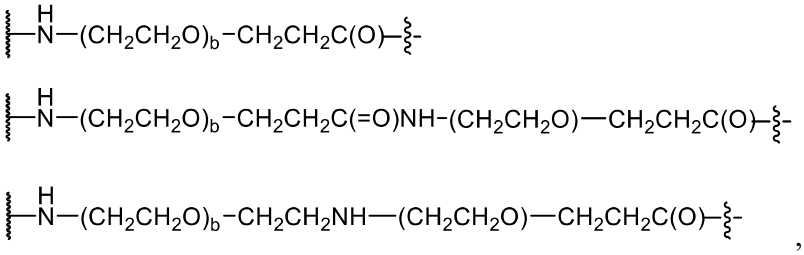
wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, –C(=O)C_1-C_6 alkylene- or -C_1-C_6 alkylene-C(=O)-C_1-C_6 alkylene;

S^* is a bond or a Partitioning Agent having the formula:



wherein the wavy line indicates the site of attachment to the Parallel Connector Unit (L^P), and b is an integer from 2 to 20; or

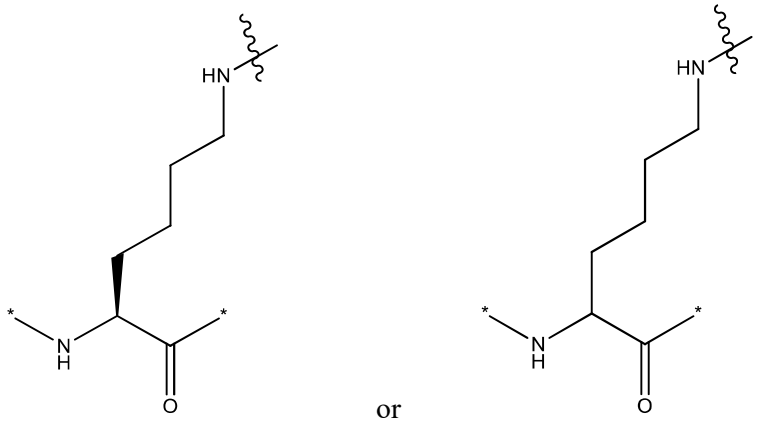
S* is a Partitioning Agent having the formula:



,

wherein the wavy line on the left indicates the site of attachment to Z-A-, the wavy line on the right indicates the site of attachment to RL, and each b is independently selected from 2 to 24;

L^P is a Parallel Connector Unit having the formula:

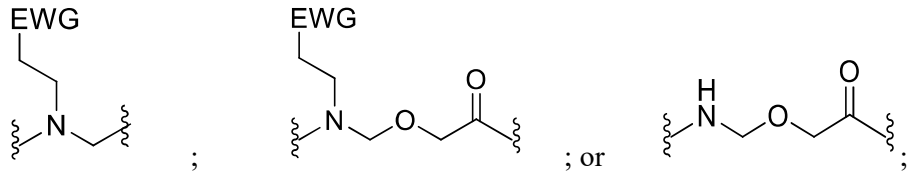


or

wherein the wavy line indicates the position of attachment to the Partitioning Agent and asterisks indicate positions of attachment to A and RL;

RL is a Peptide Releasable Linker comprising a peptide comprising 2 to 8 amino acids; and

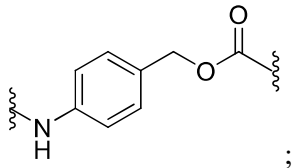
Y is a Spacer Unit having the formula:



; ; or ;

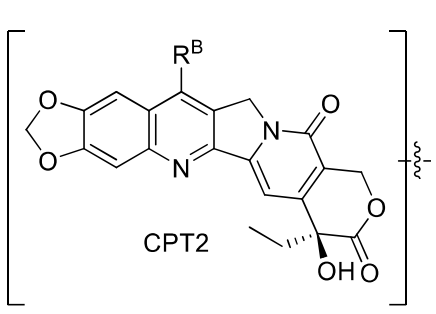
wherein EWG is selected from the group consisting of -CN, $-NO_2$, $-CX_3$, -X, -C(=O)$OR^{'}$, -C(=O)$N(R^{'})_2$, -C(=O)$R^{'}$, -C(=O)X, $-S(=O)_2R^{'}$, $-S(=O)_2OR^{'}$, $-S(=O)_2NHR^{'}$, $-S(=O)_2N(R^{'})_2$, $-P(=O)(OR^{'})_2$, $-P(=O)(CH_3)NHR^{'}$, -NO, $-N(R^{'})_3^{+}$, wherein X is -F, -Br, -Cl, or -I, and $R^{'}$ is independently selected from the group consisting of hydrogen and $C_{1\text{-}6}$ alkyl; or

Y is a Spacer Unit having the formula:

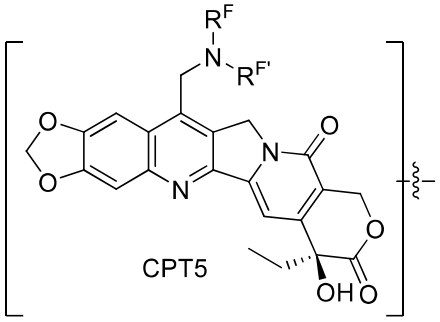


;

D is a Drug Unit selected from the group consisting of:



and



;

wherein

R^B is selected from the group consisting of H, -(C_1-C_4)alkyl-OH, -(C_1-C_4)alkyl-O-(C_1-C_4)alkyl-NH_2, -C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, C_3-C_8cycloalkylC_1-C_4 alkyl, phenyl and phenylC_1-C_4 alkyl;

each R^F and $R^{F'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, C_1-C_8 aminoalkylC(O)-, C_3-C_{10} cycloalkyl, C_3-C_{10}cycloalkylC_1-C_4 alkyl, C_3-C_{10} heterocycloalkyl, C_3-C_{10} heterocycloalkylC_1-C_4 alkyl, phenyl, phenylC_1-C_4 alkyl, diphenylC_1-C_4 alkyl, heteroaryl and heteroarylC_1-C_4 alkyl; or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^B, R^F and $R^{F'}$ are substituted with from 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$,

wherein Q is attached through any one of the hydroxyl or amine groups present on CPT2 or CPT5.

[0008] In one principal example, a Camptothecin Conjugate is provided having a formula:

$$L\text{-}(Q\text{-}D)_p$$

or a pharmaceutically acceptable form thereof, wherein

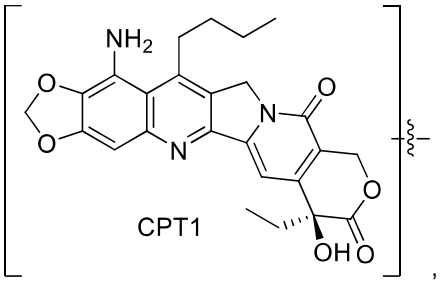
L is a Ligand Unit;

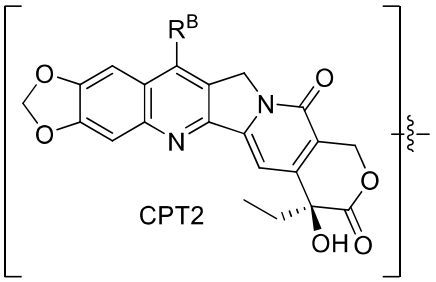
Q is a Linker Unit having a formula selected from the group consisting of:

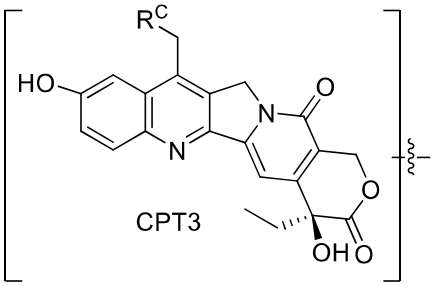
-Z-A-S^*-RL-; -Z-A- $L^P(S^*)$-RL-; -Z-A-S^*-RL-Y-; and -Z-A- $L^P(S^*)$-RL-Y-;

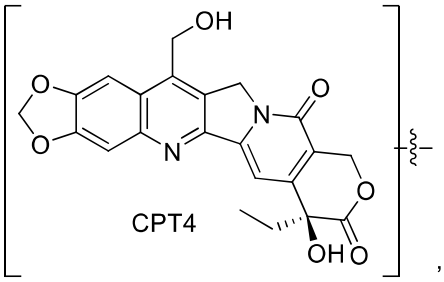
wherein Z is a Stretcher Unit, A is a bond or a Connector Unit; L^P is a Parallel Connector Unit; S^* is a bond or a Partitioning Agent; RL is a peptide comprising from 2 to 8 amino acids; and Y is a Spacer Unit;

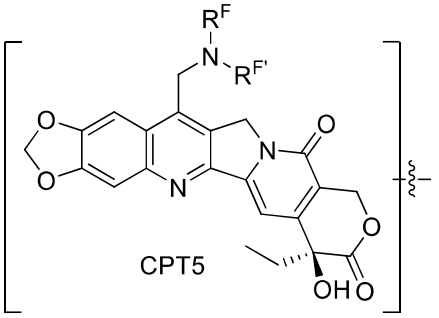
D is a Drug Unit selected from:



,


,


,


, or


; ;

wherein

R^B is a member selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, C_3-C_8cycloalkylC_1-C_4 alkyl, phenyl and phenylC_1-C_4 alkyl;

R^C is a member selected from the group consisting of C_1-C_6 alkyl and C_3-C_6 cycloalkyl;

each R^F and $R^{F'}$ is a member independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_2-C_6 heteroalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, C_1-C_8 aminoalkylC(O)-, C_3-C_{10} cycloalkyl, C_3-C_{10}cycloalkylC_1-C_4 alkyl, C_3-C_{10} heterocycloalkyl, C_3-C_{10} heterocycloalkylC_1-C_4 alkyl, phenyl, phenylC_1-C_4 alkyl, diphenylC_1-C_4 alkyl, heteroaryl and heteroarylC_1-C_4 alkyl; or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-

membered ring having 0 to 3 substituents selected from halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and $N(C_1$-C_4 alkyl$)_2$;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^B, R^C, R^F and $R^{F'}$ are substituted with from 0 to 3 substituents selected from halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and $N(C_1$-C_4 alkyl$)_2$; and

p is from about 1 to about 16;

wherein Q is attached through any one of the hydroxyl or amine groups present on CPT1, CPT2, CPT3, CPT4 or CPT5.

[0009] In another principal example, a Camptothecin Conjugate is provided having a formula:

$$L\text{-}(Q\text{-}D)_p$$

or a pharmaceutically acceptable salt thereof, wherein

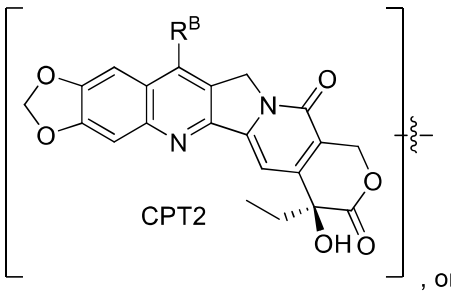
L is a Ligand Unit;

Q is a Linker Unit having a formula selected from the group consisting of:

-Z-A-S*-RL-; -Z-A- L^P(S*)-RL-; -Z-A-S*-RL-Y-; and -Z-A- L^P(S*)-RL-Y-;

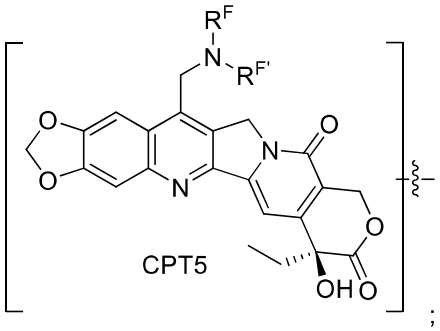
wherein Z is a Stretcher Unit, A is a bond or a Connector Unit; L^P is a Parallel Connector Unit; S* is a bond or a Partitioning Agent; RL is a peptide comprising from 2 to 8 amino acids; and Y is a Spacer Unit;

D is a Drug Unit selected from the group consisting of:



CPT2

, or



CPT5

;

wherein

R^B is a member selected from the group consisting of -H, -(C_1-C_4)alkyl-OH, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, C_3-C_8cycloalkylC_1-C_4 alkyl, phenyl and phenylC_1-C_4 alkyl;

each R^F and $R^{F'}$ is a member independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_2-C_6 heteroalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, C_1-C_8 aminoalkylC(O)-, C_3-C_{10} cycloalkyl, C_3-C_{10}cycloalkylC_1-C_4 alkyl, C_3-C_{10} heterocycloalkyl, C_3-C_{10} heterocycloalkylC_1-C_4 alkyl, phenyl, phenylC_1-C_4 alkyl, diphenylC_1-C_4 alkyl, heteroaryl and heteroarylC_1-C_4 alkyl; or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents selected from halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^B, R^C, R^F and $R^{F'}$ are substituted with from 0 to 3 substituents selected from halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$; and

p is from about 1 to about 16;

wherein Q is attached through any one of the hydroxyl or amine groups present on CPT2 or CPT5.

[0010] In yet another principal example, a Camptothecin Conjugate is provided having a formula:

$$L\text{-}(Q\text{-}D)_p$$

or a pharmaceutically acceptable salt thereof, wherein

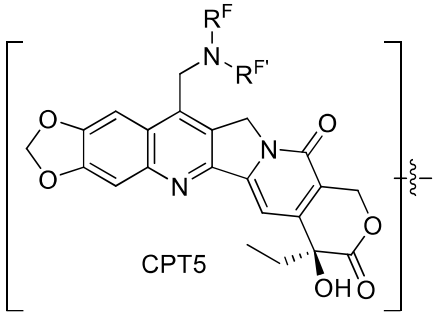
L is a Ligand Unit;

Q is a Linker Unit having a formula selected from the group consisting of:

-Z-A-S^*-RL-; -Z-A- $L^P(S^*)$-RL-; -Z-A-S^*-RL-Y-; and -Z-A- $L^P(S^*)$-RL-Y-;

wherein Z is a Stretcher Unit, A is a bond or a Connector Unit; L^P is a Parallel Connector Unit; S^* is a bond or a Partitioning Agent; RL is a peptide comprising from 2 to 8 amino acids; and Y is a Spacer Unit;

D is a Drug Unit having the following structure formula:



;

wherein

each R^F and $R^{F'}$ is a member independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_2-C_6 heteroalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, C_1-C_8 aminoalkylC(O)-, C_3-C_{10} cycloalkyl, C_3-C_{10}cycloalkylC_1-C_4 alkyl, C_3-C_{10} heterocycloalkyl, C_3-C_{10} heterocycloalkylC_1-C_4 alkyl, phenyl, phenylC_1-C_4 alkyl, diphenylC_1-C_4 alkyl, heteroaryl and heteroarylC_1-C_4 alkyl; or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents selected from halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^B, R^C, R^F and $R^{F'}$ are substituted with from 0 to 3 substituents selected from halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$; and

p is from about 1 to about 16;

wherein Q is attached through any one of the hydroxyl or amine groups present on CPT5.

[0011] Other principal examples as noted above, are Camptothecin-Linker Compounds useful as intermediates for preparing Camptothecin Conjugates, wherein the Camptothecin-Linker Compound is comprised of a Camptothecin (D) and a Linker Unit (Q), wherein the Linker Unit is comprised of a Stretcher Unit precursor (Z') capable of forming a covalent bond to a targeting ligand that provides for a Ligand Unit, and a Releasable Linker (RL) which is a peptide of from 2 to 8 amino acids.

[0012] In another aspect, the present disclosure provides use of a composition comprising the Camptothecin Conjugate as described herein in the manufacture of a medicament for treating cancer or an autoimmune disease in a subject in need thereof. In another example, provided herein are methods of treating cancer comprising administering to a subject in need thereof a Camptothecin Conjugate described herein. In another aspect, the present disclosure provides a method of preparing a Camptothecin Conjugate as described herein, comprising reacting an antibody or antigen-binding fragment thereof with a Camptothecin-Linker Compound as described herein. In another aspect, the present disclosure provides a pharmaceutical composition comprising the Camptothecin Conjugate as described herein and a pharmaceutically acceptable carrier.

[0013] In another example, provided herein are methods of treating cancer using Camptothecin-Linker Compounds or Camptothecins described herein.

[0014] In another example, provided herein are kits comprising a Camptothecin Conjugate described herein.

WHAT IS CLAIMED IS:

1. A Camptothecin Conjugate having a formula:

$$L\text{-}(Q\text{-}D)_p \qquad (I)$$

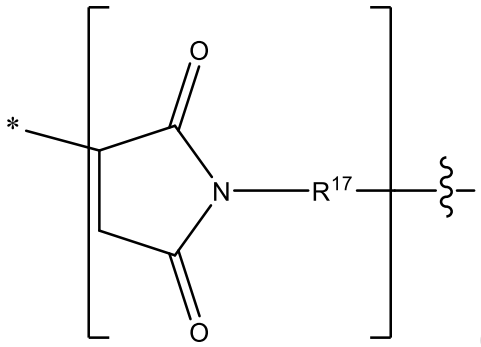
or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Q is a Linker Unit having a formula selected from:

-Z-A-S^*-RL-; -Z-A- $L^P(S^*)$-RL-; -Z-A-S^*-RL-Y-; or -Z-A- $L^P(S^*)$-RL-Y-,

wherein Z is a Stretcher Unit of Formula Za:



(Za)

wherein the asterisk indicates the position of attachment to the Ligand Unit (L);

the wavy line indicates the position of attachment to the Connector Unit (A); and

R^{17} is -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8

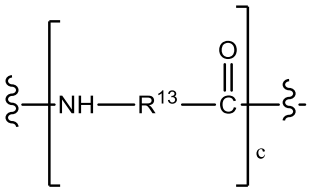
carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

wherein R^{17} is optionally substituted with a Basic Unit (BU) that is $–(CH_2)_x NH_2$, $–(CH_2)_xNHR^a$, or $–(CH_2)_xNR^a{}_2$;

wherein x is an integer of from 1-4; and

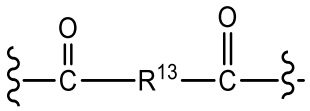
each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form a 4- to 6-membered heterocycloalkyl ring, or an azetidinyl, pyrrolidinyl or piperidinyl group;

A is a bond or a Connector Unit having the formula:



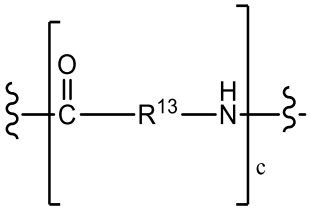
wherein in each instance R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is an integer ranging from 1 to 4; or

A is a Connector Unit having the formula:



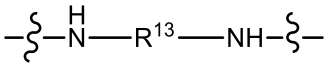
wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-; or

A is a Connector Unit having the formula:



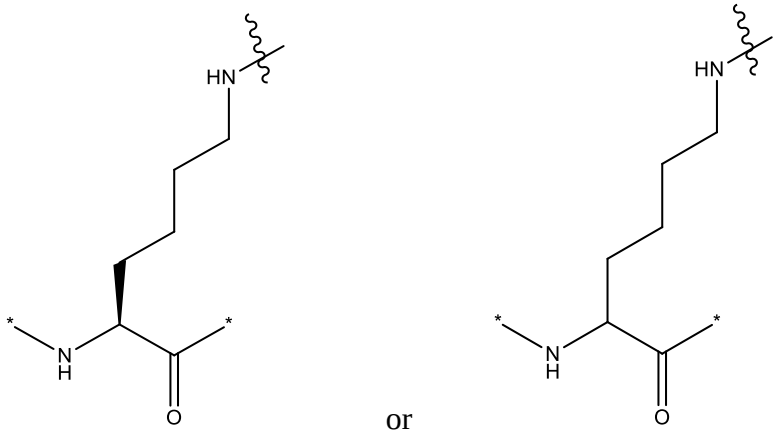
wherein in each instance, R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is from 1 to 14; or

A is a Connector Unit having the formula:



wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, –C(=O)C_1-C_6 alkylene- or -C_1-C_6 alkylene-C(=O)-C_1-C_6 alkylene;

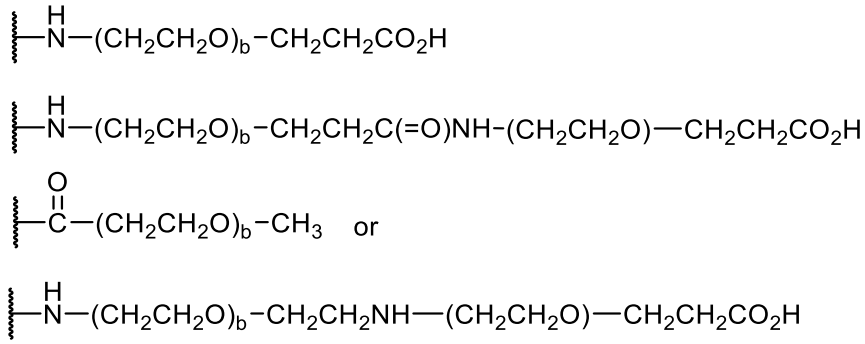
L^P is a Parallel Connector Unit having the formula:



or

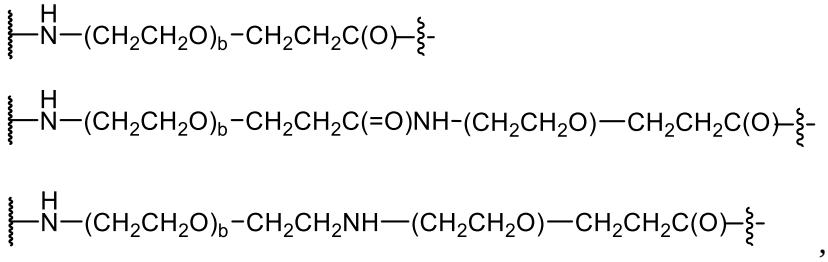
wherein the wavy line indicates the position of attachment to the Partitioning Agent and asterisks indicate positions of attachment to A and RL;

S^* is a bond or a Partitioning Agent having the formula:



wherein the wavy line indicates the site of attachment to the Parallel Connector Unit (L^P), and b is an integer from 2 to 20; or

S* is a Partitioning Agent having the formula:

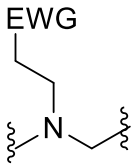


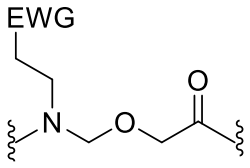
,

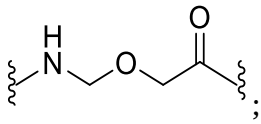
wherein the wavy line on the left indicates the site of attachment to Z-A-, the wavy line on the right indicates the site of attachment to RL, and each b is independently selected from 2 to 24;

RL is a peptide comprising from 2 to 8 amino acids; and

Y is a Spacer Unit having the formula:



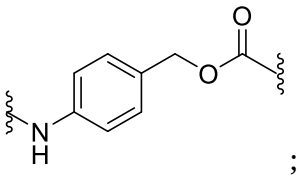
;


; or


;

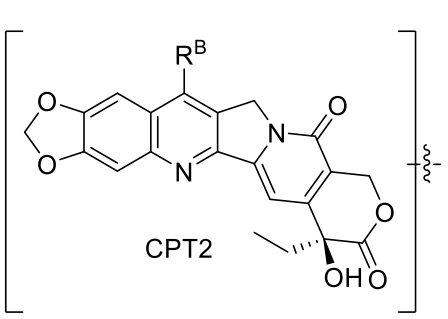
wherein EWG is selected from the group consisting of -CN, $-NO_2$, $-CX_3$, -X, $-C(=O)OR'$, $-C(=O)N(R')_2$, $-C(=O)R'$, -C(=O)X, $-S(=O)_2R'$, $-S(=O)_2OR'$, $-S(=O)_2NHR'$, $-S(=O)_2N(R')_2$, $-P(=O)(OR')_2$, $-P(=O)(CH_3)NHR'$, -NO, $-N(R')_3^+$, wherein X is -F, -Br, -Cl, or -I, and R' is independently selected from the group consisting of hydrogen and C_{1-6} alkyl; or

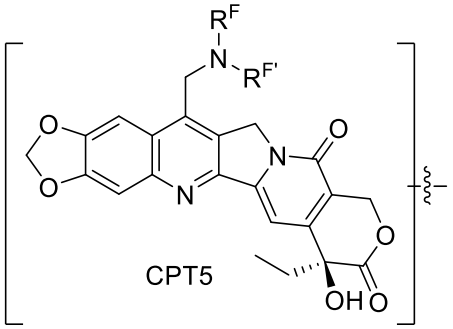
Y is a Spacer Unit having the formula:



;

D is a Drug Unit selected from the group consisting of:



and


;

wherein

R^B is selected from the group consisting of H, -(C_1-C_4)alkyl-OH, -(C_1-C_4)alkyl-O-(C_1-C_4)alkyl-NH_2, -C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, C_3-C_8cycloalkylC_1-C_4 alkyl, phenyl and phenylC_1-C_4 alkyl;

each R^F and $R^{F'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_2-C_6 heteroalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, C_1-C_8 aminoalkylC(O)-, C_3-C_{10} cycloalkyl, C_3-C_{10}cycloalkylC_1-C_4 alkyl, C_3-C_{10} heterocycloalkyl, C_3-C_{10} heterocycloalkylC_1-C_4 alkyl, phenyl, phenylC_1-C_4 alkyl, diphenylC_1-C_4 alkyl, heteroaryl and heteroarylC_1-C_4 alkyl; or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^B, R^F and $R^{F'}$ are substituted with from 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$; and

p is an integer ranging from 1 to 16;

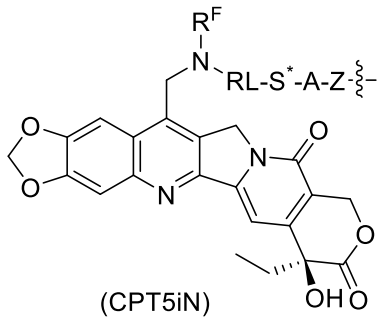
wherein Q is attached through any one of the hydroxyl or amine groups present on CPT2 or CPT5.

2. The Camptothecin Conjugate of claim 1, wherein D has formula CPT2.

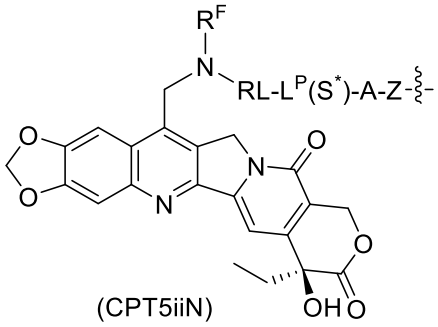
3. The Camptothecin Conjugate of claim 1, wherein D has formula CPT5.

4. The Camptothecin Conjugate of claim 1 or 3, wherein the –Q-D component of the Conjugate has a formula selected from (CPT5iN), (CPT5iiN), (CPT5iiiN),

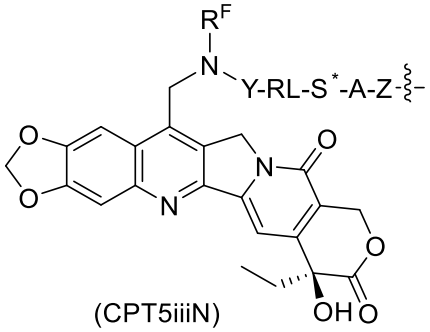
(CPT5ivN), (CPT5vN), (CPT5viN), (CPT5iO), (CPT5iiO), (CPT5iiiO), (CPT5ivO), (CPT5vO), and (CPT5viO):



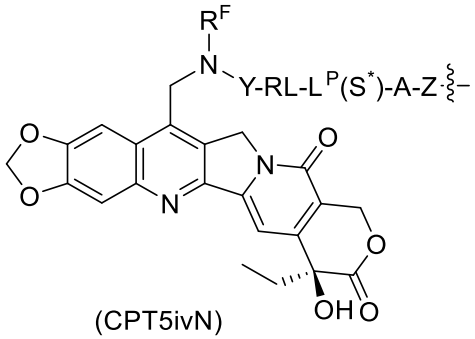
(CPT5iN)



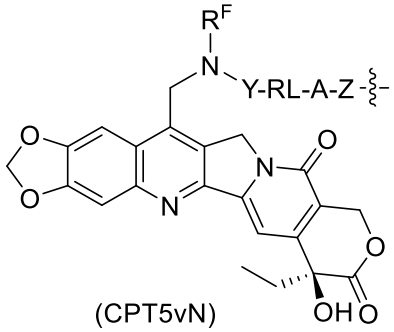
(CPT5iiN)



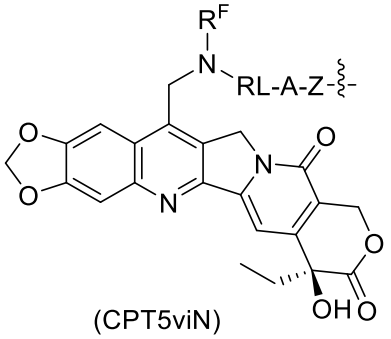
(CPT5iiiN)



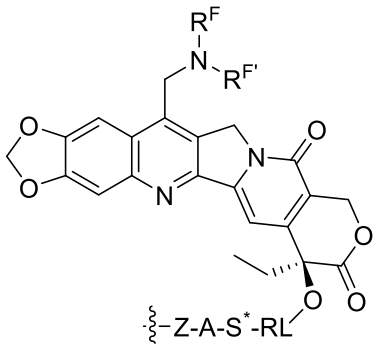
(CPT5ivN)



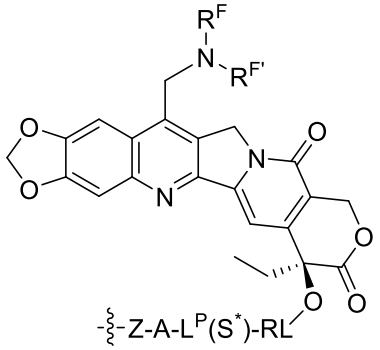
(CPT5vN)



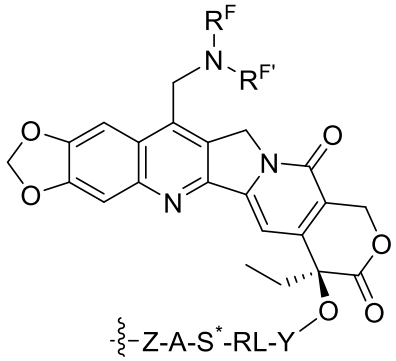
(CPT5viN)



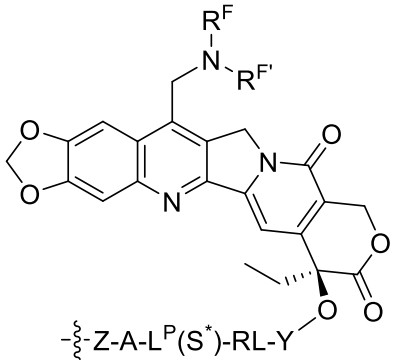
(CPT5iO)



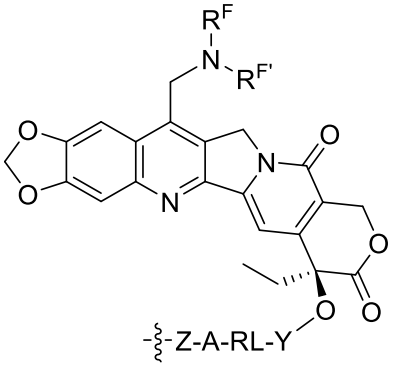
(CPT5iiO)



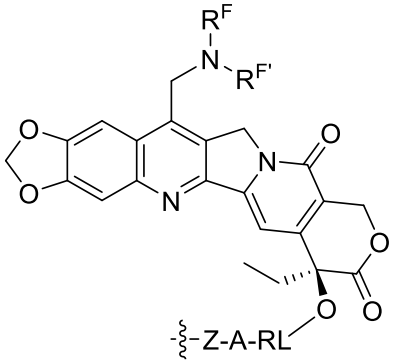
(CPT5iiiO)



(CPT5ivO)



(CPT5vO)



(CPT5viO)

5. The Camptothecin Conjugate of claim 4, wherein the –Q-D component of the Camptothecin Conjugate has a formula selected from (CPT5iN), (CPT5iiN), (CPT5iiiN), (CPT5ivN), (CPT5vN), and (CPT5viN).

6. The Camptothecin Conjugate of claim 5, wherein R^F is selected from the group consisting of -H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, and C_1-C_8 aminoalkylC(O)-;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^F are substituted with from 0 to 3 substituents selected from halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$.

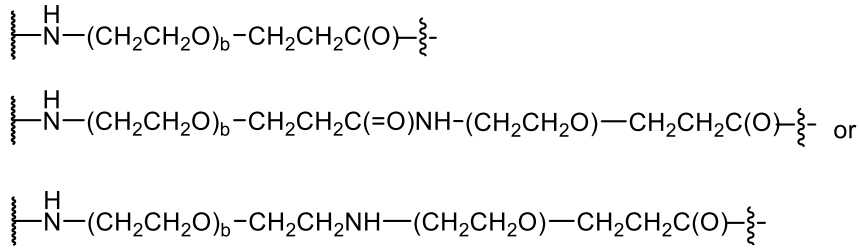
7. The Camptothecin Conjugate of any one of claims 1 to 6, wherein S* is a bond and Q is -Z-A-RL- or -Z-A-RL-Y-.

8. The Camptothecin Conjugate of any one of claims 1 to 6, wherein S^* is a PEG Unit, and Q is

-Z-A-S^*-RL-; -Z-A- $L^P(S^*)$-RL-; -Z-A-S^*-RL-Y-;

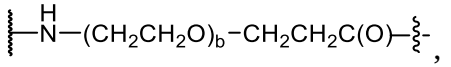
or -Z-A- $L^P(S^*)$-RL-Y-.

9. The Camptothecin Conjugate of claim 8, wherein the PEG Unit has the formula:



wherein the wavy line on the left indicates the site of attachment to A, the wavy line on the right indicates the site of attachment to RL, and b is an integer from 2 to 20, or is 2, 4, 8, or 12.

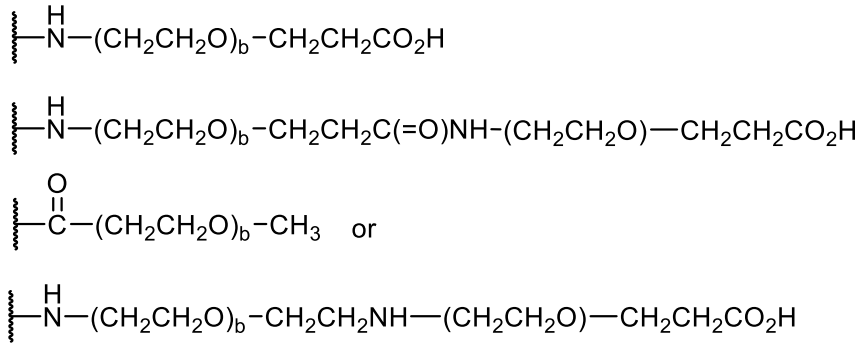
10. The Camptothecin Conjugate of claim 9, wherein the PEG Unit has the formula:



wherein the wavy line on the left indicates the site of attachment to A, the wavy line on the right indicates the site of attachment to RL, and b is an integer from 2 to 20, or is 2, 4, 8, or 12.

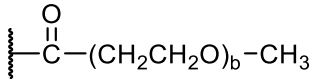
11. The Camptothecin Conjugate of 8, wherein Q is of formula -Z-A-$L^P(S^*)$-RL- or -Z-A-$L^P(S^*)$-RL-Y- and S* is a PEG Unit which comprises 2, 4, 8, or 12 -CH_2CH_2O- subunits and a PEG Unit terminal cap group that is C_{1-4}alkyl or C_{1-4}alkyl-CO_2H.

12. The Camptothecin Conjugate of claim 11, wherein S* is of formula:



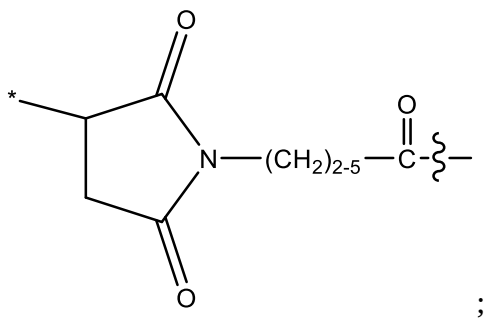
wherein the wavy line indicates the site of attachment to the Parallel Connector Unit (L^P), and b is an integer from 2 to 20, or is 2, 4, 8, or 12.

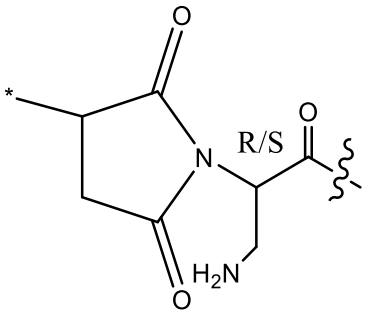
13. The Camptothecin Conjugate of claim 12, wherein S* is of formula:

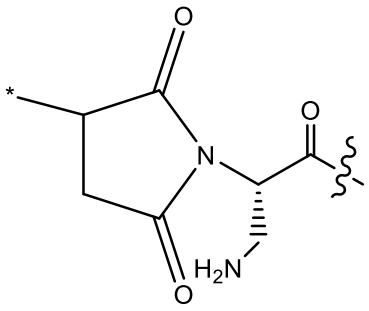


wherein the wavy line indicates the site of attachment to the Parallel Connector Unit (L^P), and b is an integer from 2 to 20, or is 2, 4, 8, or 12.

14. The Camptothecin Conjugate of any one of claims 1 to 13, wherein Z is:

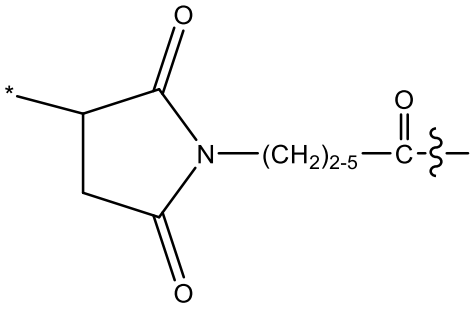


;


; or


.

15. The Camptothecin Conjugate of claim 14, wherein Z is:



.

16. The Camptothecin Conjugate of any one of claims 1 to 15, wherein A is a bond.

17. The Camptothecin Conjugate of any one of claims 1 to 16, wherein RL is a dipeptide, tripeptide, or tetrapeptide.

18. The Camptothecin Conjugate of claim 17, wherein RL is gly-gly, gly-gly-gly, gly-gly-gly-gly, val-gly-gly, val-cit-gly, val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-

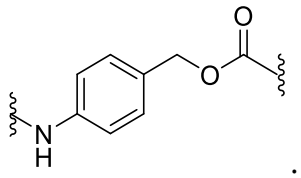
gly, gly-val-lys-gly, val-lys-gly-gly, val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly, gly-gly-phe-gly, gly-gly-phe-gly-gly, val-gly, or val-lys-β-ala.

19. The Camptothecin Conjugate of claim 17, wherein RL is a tripeptide having the formula: AA_1-AA_2- AA_3, wherein AA_1, AA_2 and AA_3 are each independently an amino acid, wherein AA_1 attaches to –NH- and AA_3 attaches to S*.

20. The Camptothecin Conjugate of claim 19, wherein AA_3 is gly or β-ala.

21. The Camptothecin Conjugate of claim 20, wherein RL is val-lys-gly, wherein val attaches to –NH- and gly attaches to S*.

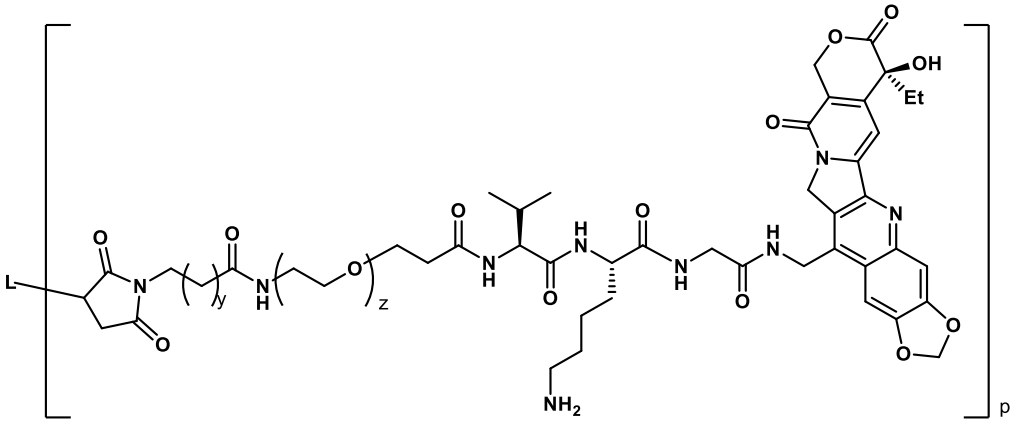
22. The Camptothecin Conjugate of any one of claims 1 to 21, wherein Y is of the formula:



.

23. The Camptothecin Conjugate of any one of claims 1 to 22, wherein p is 1 to 16.

24. The Camptothecin Conjugate of claim 1, having the Formula (IC):



(IC)

or a pharmaceutically acceptable salt thereof;

wherein

y is 1, 2, 3, or 4; and

z is 2, 4, 8, or 12;

and p is 1-16.

25. The Camptothecin Conjugate of claim 24, wherein p is 4 or 8.

26. The Camptothecin Conjugate of any one of claims 1 to 25, wherein the Ligand Unit is an antibody or an antigen-binding fragment thereof.

27. A Camptothecin-Linker Compound of the formula:

Q'-D,

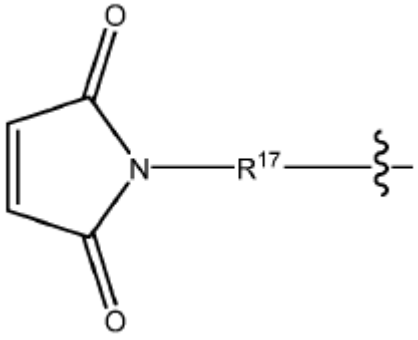
or a pharmaceutically acceptable salt thereof, wherein

Q' is a Linker Unit Precursor having a formula selected from the group consisting of:

Z'-A-S*-RL-; Z'-A-L^P(S*)-RL-; Z'-A-S*-RL-Y-; Z'-A-L^P(S*)-RL-Y-;

wherein

Z' is a Stretcher Unit Precursor of Formula Za:



(Za)

wherein

the wavy line indicates the position of attachment to the Connector Unit (A); and

R^{17} is -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-

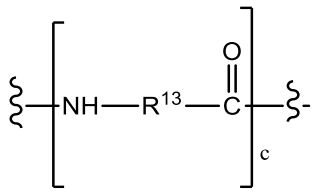
C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

wherein R^{17} is optionally substituted with a Basic Unit (BU) that is $–(CH_2)_x NH_2$, $–(CH_2)_xNHR^a$, or $–(CH_2)_xNR^a{}_2$;

wherein x is an integer of from 1-4; and

each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form a 4- to 6-membered heterocycloalkyl ring, or an azetidinyl, pyrrolidinyl or piperidinyl group;

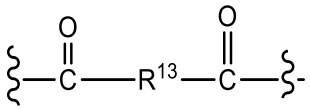
A is a bond or a Connector Unit having the formula:



wherein in each instance R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-

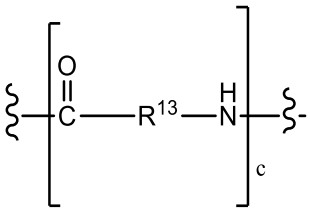
C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is an integer ranging from 1 to 4; or

A is a Connector Unit having the formula:



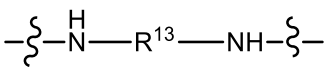
wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-; or

A is a Connector Unit having the formula:



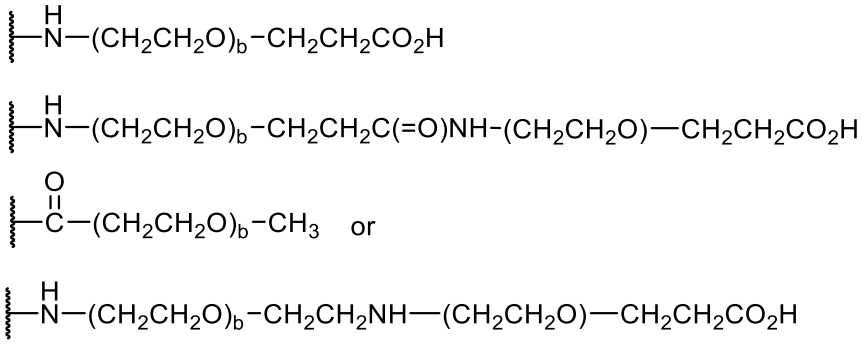
wherein in each instance, R^{13} is independently selected from the group consisting of -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, and the subscript c is from 1 to 14; or

A is a Connector Unit having the formula:



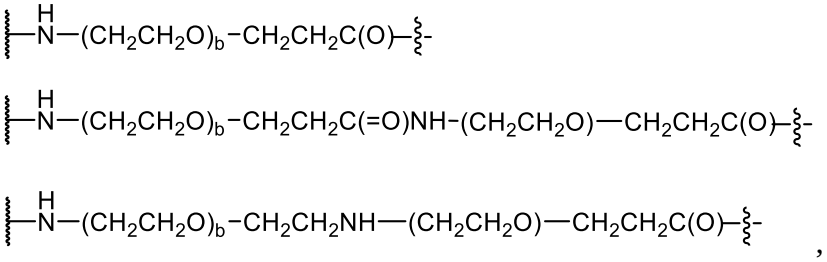
wherein R^{13} is -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -C_6-C_{20} arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-C_6-C_{20} arylene-, -C_6-C_{20} arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, –C(=O)C_1-C_6 alkylene- or -C_1-C_6 alkylene-C(=O)-C_1-C_6 alkylene;

S^* is a bond or a Partitioning Agent having the formula:



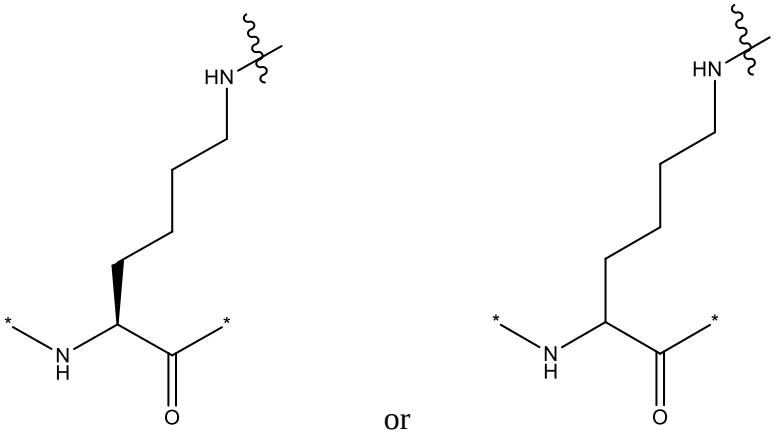
wherein the wavy line indicates the site of attachment to the Parallel Connector Unit (L^P), and b is an integer from 2 to 20; or

S* is a Partitioning Agent having the formula:



wherein the wavy line on the left indicates the site of attachment to Z-A-, the wavy line on the right indicates the site of attachment to RL, and each b is independently selected from 2 to 24;

L^P is a Parallel Connector Unit having the formula:

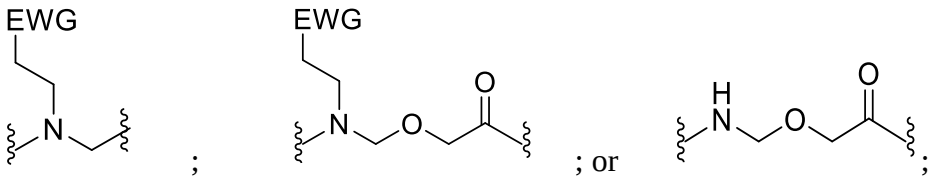


or

wherein the wavy line indicates the position of attachment to the Partitioning Agent and asterisks indicate positions of attachment to A and RL;

RL is a Peptide Releasable Linker comprising a peptide comprising 2 to 8 amino acids; and

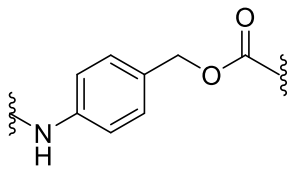
Y is a Spacer Unit having the formula:



; ; or ;

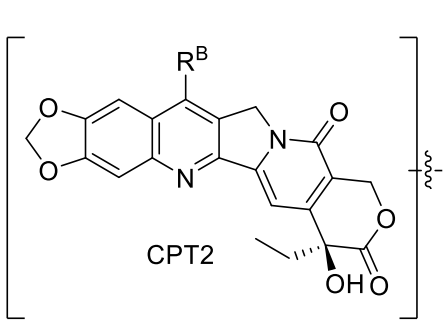
wherein EWG is selected from the group consisting of -CN, -NO_2, -CX_3, -X, -$C(=O)OR^{'}$, -$C(=O)N(R^{'})_2$, -$C(=O)R^{'}$, -C(=O)X, -$S(=O)_2R^{'}$, -$S(=O)_2OR^{'}$, -$S(=O)_2NHR^{'}$, -$S(=O)_2N(R^{'})_2$, -$P(=O)(OR^{'})_2$, -$P(=O)(CH_3)NHR^{'}$, -NO, -$N(R^{'})_3^{+}$, wherein X is -F, -Br, -Cl, or -I, and $R^{'}$ is independently selected from the group consisting of hydrogen and C_{1-6} alkyl; or

Y is a Spacer Unit having the formula:

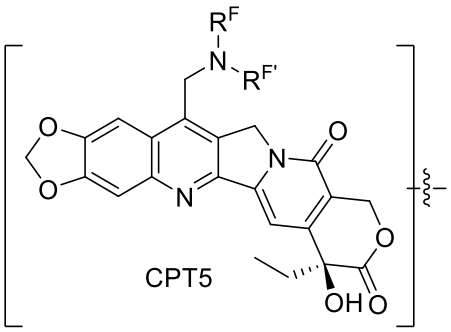


;

D is a Drug Unit selected from the group consisting of:



and



;

wherein

R^B is selected from the group consisting of H, -(C_1-C_4)alkyl-OH, -(C_1-C_4)alkyl-O-(C_1-C_4)alkyl-NH_2, -C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, C_3-C_8cycloalkylC_1-C_4 alkyl, phenyl and phenylC_1-C_4 alkyl;

each R^F and $R^{F'}$ is independently selected from the group consisting of H, C_1-C_8 alkyl, C_1-C_8 hydroxyalkyl, C_1-C_8 aminoalkyl, C_1-C_4 alkylaminoC_1-C_8 alkyl, (C_1-C_4 hydroxyalkyl)(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, di(C_1-C_4 alkyl)aminoC_1-C_8 alkyl, C_1-C_4 hydroxyalkylC_1-C_8 aminoalkyl, C_1-C_8 alkylC(O)-, C_1-C_8 hydroxyalkylC(O)-, C_1-C_8 aminoalkylC(O)-, C_3-C_{10} cycloalkyl, C_3-C_{10}cycloalkylC_1-C_4 alkyl, C_3-C_{10} heterocycloalkyl, C_3-C_{10} heterocycloalkylC_1-C_4 alkyl, phenyl, phenylC_1-C_4 alkyl, diphenylC_1-C_4 alkyl, heteroaryl and heteroarylC_1-C_4 alkyl; or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$;

and wherein cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^B, R^F and $R^{F'}$ are substituted with from 0 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, OH, OC_1-C_4 alkyl, NH_2, NHC_1-C_4 alkyl and N(C_1-C_4 alkyl)$_2$,

wherein Q is attached through any one of the hydroxyl or amine groups present on CPT2 or CPT5.

28. The Camptothecin-Linker Compound of claim 27, wherein D has formula CPT2.

29. The Camptothecin-Linker Compound of claim 27, wherein D has formula CPT5.

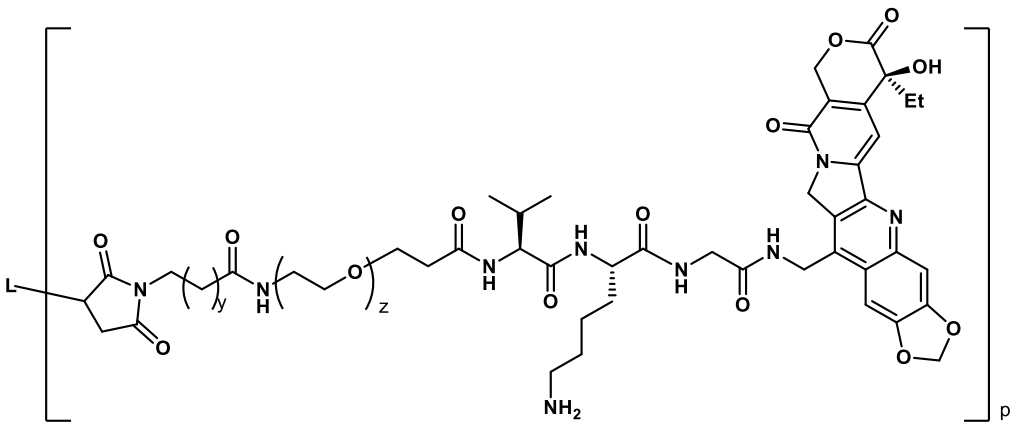
30. The Camptothecin Conjugate of claim 26, wherein the antibody or antigen-binding fragment thereof comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively.

31. The Camptothecin Conjugate of claim 30, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 8.

32. The Camptothecin Conjugate of claim 30, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8.

33. The Camptothecin Conjugate of claim 30, wherein the antibody or comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 10 and a light chain comprising the amino acid sequence of SEQ ID NO: 11.

34. The Camptothecin Conjugate of any one of claims 30 to 33, having Formula(IC):



(IC)

or a pharmaceutically acceptable salt thereof;

wherein

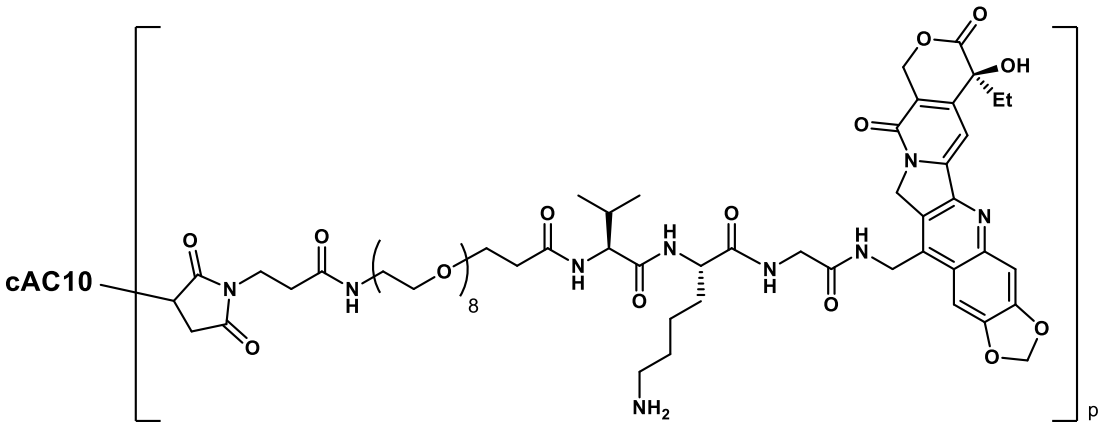
y is 1, 2, 3, or 4, or is 1 or 4; and

z is an integer from 2 to 12, or is 2, 4, 8, or 12;

and p is 1-16.

35. The Camptothecin Conjugate of claim 24, wherein p is 2, 4 or 8.

36. The Camptothecin Conjugate of claim 26, having formula:



or a pharmaceutically acceptable salt thereof;

wherein

p is 2, 4, or 8.

37. Use of a composition comprising the Camptothecin Conjugate of any one of claims 1 to 26 and 30 to 36 in the manufacture of a medicament for treating cancer or an autoimmune disease in a subject in need thereof.

38. A method of preparing a Camptothecin Conjugate of any one of claims 1 to 26 and 30 to 36, comprising reacting an antibody or antigen-binding fragment thereof with a Camptothecin-Linker Compound of any one of claims 27 to 29.

39. A pharmaceutical composition comprising the Camptothecin Conjugate of any one of claims 1 to 26 and 30 to 36 and a pharmaceutically acceptable carrier.