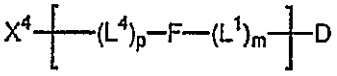
Claims

1 A compound of the formula

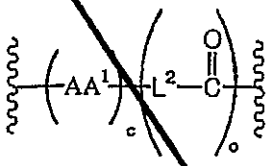


wherein

L^1 is a self-immolative linker;

m is an integer 0, 1, 2, 3, 4, 5, or 6;

F is a linker comprising the structure:



wherein

AA^1 is one or more members independently selected from the group consisting of natural amino acids and unnatural α-amino acids;

c is an integer from 1 to 20;

L^2 is a self-immolative linker;

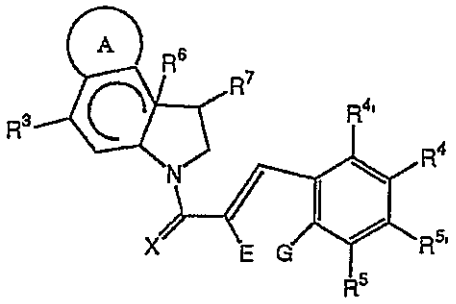
o is 0 or 1;

L^4 is a linker member;

p is 0 or 1;

X^4 is a member selected from the group consisting of protected reactive functional groups, unprotected reactive functional groups, detectable labels, and targeting agents; and

D comprises a structure:



wherein the ring system A is a member selected from substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl and substituted or unsubstituted heterocycloalkyl groups;

E and G are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, a heteroatom, a single bond, or E and G are joined to form a ring system selected from substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl and substituted or unsubstituted heterocycloalkyl;

X is a member selected from O, S and NR^{23};

R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^3 is a member selected from the group consisting of (=O), SR^{11}, NHR^{11} and OR^{11},

wherein R^{11} is a member selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted heteroalkyl, unsubstituted heteroalkyl, monophosphates, diphosphates, triphosphates, sulfonates, acyl, $C(O)R^{12}R^{13}$, $C(O)OR^{12}$, $C(O)NR^{12}R^{13}$, $P(O)(OR^{12})_2$, , $C(O)CHR^{12}R^{13}$, SR^{12} and $SiR^{12}R^{13}R^{14}$,

in which R^{12}, R^{13}, and R^{14} are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl, wherein R^{12} and R^{13} together with the nitrogen or carbon atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

R^4, $R^{4'}$, R^5 and $R^{5'}$ are members independently selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted aryl,

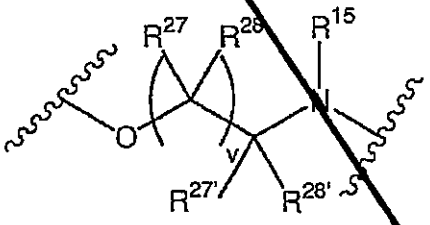
unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted heterocycloalkyl, unsubstituted heterocycloalkyl, halogen, NO_2, $NR^{15}R^{16}$, $NC(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $OC(O)OR^{15}$, $C(O)R^{15}$, SR^{15}, OR^{15}, $CR^{15}{=}NR^{16}$, and $O(CH_2)_nN(CH_3)_2$, or any adjacent pair of R^4, $R^{4'}$, R^5 and $R^{5'}$, together with the carbon atoms to which they are attached, are joined to form a substituted or unsubstituted cycloalkyl or heterocycloalkyl ring system having from 4 to 6 members,

wherein

n is an integer from 1 to 20;

R^{15} and R^{16} are independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycloalkyl, and substituted or unsubstituted peptidyl, wherein R^{15} and R^{16} together with the nitrogen atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

wherein at least one of R^4, $R^{4'}$, R^5 and $R^{5'}$ links said drug to L^1, if present, or to F, and comprises



wherein v is an integer from 1 to 6; and

each R^{27}, $R^{27'}$, R^{28}, and $R^{28'}$ is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;

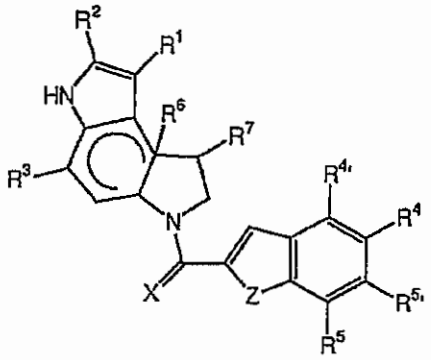
R^6 is a single bond which is either present or absent and when present R^6 and R^7 are joined to form a cyclopropyl ring; and

R^7 is CH_2-X^1 or –CH_2- joined in said cyclopropyl ring with R^6, wherein

X^1 is a leaving group;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein D has the structure:



wherein

Z is a member selected from O, S and NR^{23}

wherein

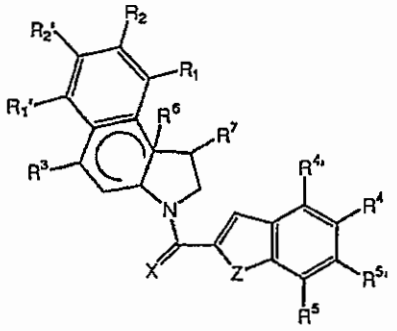
R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^1 is H, substituted or unsubstituted lower alkyl, $C(O)R^8$, or CO_2R^8, wherein R^8 is a member selected from group consisting of substituted alkyl, unsubstituted alkyl, NR^9R^{10}, NR^9NHR^{10}, and OR^9

in which R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl; and

R^2 is H, substituted alkyl or unsubstituted lower alkyl.

3. The compound of claim 1, wherein D has the structure:



wherein

Z is a member selected from O, S and NR^{23}

wherein

R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^1 is H, substituted or unsubstituted lower alkyl, $C(O)R^8$, or CO_2R^8, wherein R^8 is a member selected from NR^9R^{10} and OR^9,

in which

R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

$R^{1'}$ is H, substituted or unsubstituted lower alkyl, or $C(O)R^8$, wherein R^8 is a member selected from NR^9R^{10} and OR^9,

in which

R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

R^2 is H, or substituted or unsubstituted lower alkyl or unsubstituted heteroalkyl or cyano or alkoxy; and

$R^{2'}$ is H, or substituted or unsubstituted lower alkyl or unsubstituted heteroalkyl.

4. The compound of claim 1, wherein $(AA^1)_c$ is a peptide sequence cleavable by a protease expressed in tumor tissue.

5. The compound of claim 4, wherein the protease is a lysosomal protease.

6. The compound of claim 1, wherein the amino acid in $(AA^1)_c$ located closest to the drug moiety is selected from the group consisting of: Ala, Asn, Asp, Cit, Cys, Gln, Glu, Gly, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, and Val.

7. The compound of claim 1, . wherein $(AA^1)_c$ is a peptide sequence selected from the group consisting of Val-Cit, Val-Lys, Phe-Lys, Lys-Lys, Ala-Lys, Phe-Cit, Leu-Cit, Ile-Cit, Trp, Cit, Phe-Ala, Phe-N^9-tosyl-Arg, Phe-N^9-nitro-Arg, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Leu-Ala-Leu, Ile-Ala-Leu, Val-Ala-Val, Ala-Leu-Ala-Leu (SEQ. ID NO: 1), β-Ala-Leu-Ala-Leu (SEQ. ID NO: 2) and Gly-Phe-Leu-Gly (SEQ. ID NO: 3).

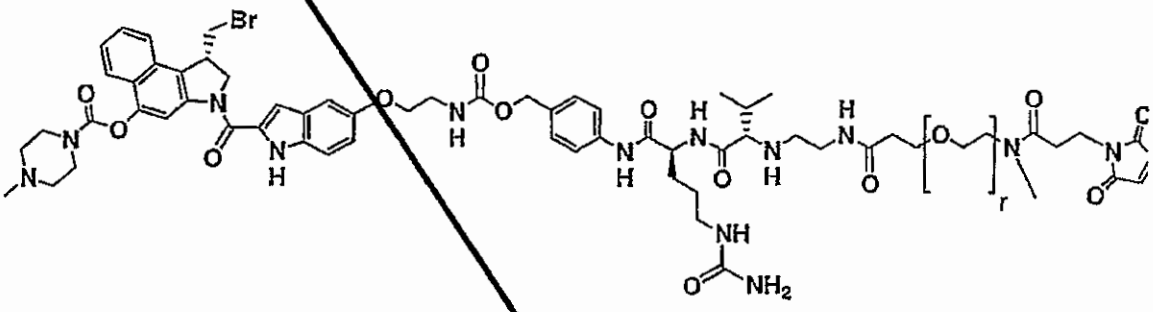
8. The compound of claim 1, wherein $(AA^1)_c$ is Val-Cit or Val-Lys.

9. The compound of claim 1, wherein R^{27}, $R^{27'}$, R^{28}, and $R^{28'}$ are independently H or lower alkyl.

10. The compound of claim 1, wherein v is 1 or 2.

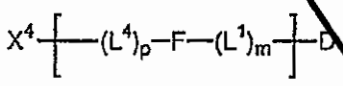
11. The compound of claim 1, wherein R^{15} is H or lower alkyl.

12. The compound of claim 1, wherein the compound is



wherein r is an integer in the range from 0 to 24.

13. A compound of the formula

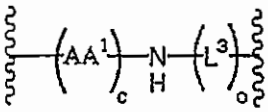


wherein

L^1 is a self-immolative linker;

m is an integer 0, 1, 2, 3, 4, 5, or 6;

F is a linker comprising the structure:



wherein

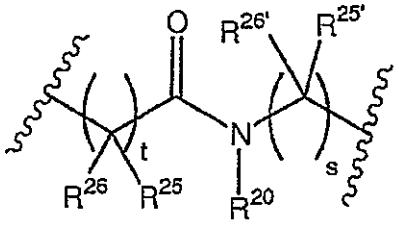
AA^1 is one or more members independently selected from the group consisting of natural amino acids and unnatural α-amino acids;

c is an integer from 1 to 20;

L^3 is a spacer group comprising a primary or secondary amine or a carboxyl functional group; wherein if L^3 is present, m is 0 and either the amine of L^3 forms an amide bond with a pendant carboxyl functional group of D or the carboxyl of L^3 forms an amide bond with a pendant amine functional group of D;

o is 0 or 1;

L^4 is a linker member, wherein L^4 comprises



directly attached to the N-terminus of $(AA^1)_c$, wherein

R^{20} is is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl,

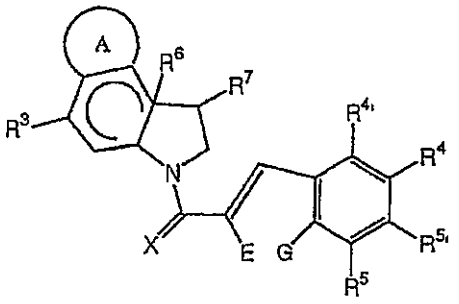
each R^{25}, $R^{25'}$, R^{26}, and $R^{26'}$ is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;

and s and t are independently integers from 1 to 6;

p is 1;

X^4 is a member selected from the group consisting of protected reactive functional groups, unprotected reactive functional groups, detectable labels, and targeting agents; and

D comprises a structure:



wherein the ring system A is a member selected from substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl and substituted or unsubstituted heterocycloalkyl groups;

E and G are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, a heteroatom, a single bond, or E and G are joined to form a ring system selected from substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl and substituted or unsubstituted heterocycloalkyl;

X is a member selected from O, S and NR^{23};

R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^3 is a member selected from the group consisting of (=O), SR^{11}, NHR^{11} and OR^{11};

wherein

R^{11} is a member selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted heteroalkyl, unsubstituted heteroalkyl, monophosphates, diphosphates, triphosphates, sulfonates, acyl, $C(O)R^{12}R^{13}$, $C(O)OR^{12}$, $C(O)NR^{12}R^{13}$, $P(O)(OR^{12})_2$, , $C(O)CHR^{12}R^{13}$, SR^{12} and $SiR^{12}R^{13}R^{14}$,

in which

R^{12}, R^{13}, and R^{14} are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl, wherein R^{12} and R^{13} together with the nitrogen or carbon atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

R^4, $R^{4'}$, R^5 and $R^{5'}$ are members independently selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted heterocycloalkyl, unsubstituted heterocycloalkyl, halogen, NO_2, $NR^{15}R^{16}$, $NC(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $OC(O)OR^{15}$, $C(O)R^{15}$, SR^{15}, OR^{15}, $CR^{15}{=}NR^{16}$, and $O(CH_2)_nN(CH_3)_2$, or any adjacent pair of R^4, $R^{4'}$, R^5 and $R^{5'}$, together with the

carbon atoms to which they are attached, are joined to form a substituted or unsubstituted cycloalkyl or heterocycloalkyl ring system having from 4 to 6 members,

wherein

n is an integer from 1 to 20;

R^{15} and R^{16} are independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycloalkyl, and substituted or unsubstituted peptidyl, wherein R^{15} and R^{16} together with the nitrogen atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

R^6 is a single bond which is either present or absent and when present R^6 and R^7 are joined to form a cyclopropyl ring; and

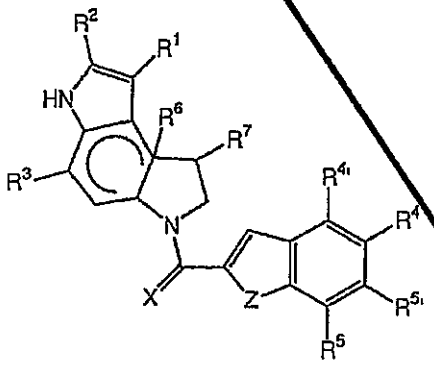
R^7 is CH_2-X^1 or –CH_2- joined in said cyclopropyl ring with R^6, wherein

X^1 is a leaving group,

wherein at least one of R^4 , $R^{4'}$, R^5, $R^{5'}$, R^{15} or R^{16} links said drug to L^1, if present, or to F;

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 13, wherein D has the structure:



wherein

Z is a member selected from O, S and NR^{23}

wherein

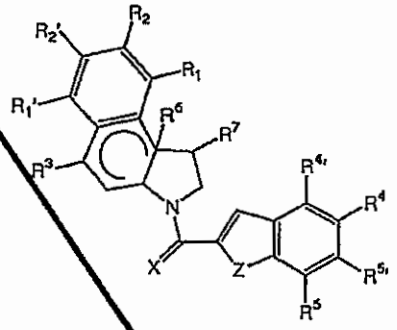
R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^1 is H, substituted or unsubstituted lower alkyl, $C(O)R^8$, or CO_2R^8, wherein R^8 is a member selected from group consisting of substituted alkyl, unsubstituted alkyl, NR^9R^{10}, NR^9NHR^{10}, and OR^9

in which R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl; and

R^3 is H, substituted alkyl or unsubstituted lower alkyl.

15. The compound of claim 13, wherein D has the structure:



wherein

Z is a member selected from O, S and NR^{23}

wherein

R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^1 is H, substituted or unsubstituted lower alkyl, $C(O)R^8$, or CO_2R^8, wherein R^8 is a member selected from NR^9R^{10} and OR^9,

in which

R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

$R^{1'}$ is H, substituted or unsubstituted lower alkyl, or $C(O)R^8$, wherein R^8 is a member selected from NR^9R^{10} and OR^9,

in which

R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

R^2 is H, or substituted or unsubstituted lower alkyl or unsubstituted heteroalkyl or cyano or alkoxy; and

$R^{2'}$ is H, or substituted or unsubstituted lower alkyl or unsubstituted heteroalkyl.

16. The compound of claim 13, wherein $(AA^1)_c$ is a peptide sequence cleavable by a protease expressed in tumor tissue.

17. The compound of claim 16, wherein the protease is a lysosomal protease.

18. The compound of claim 13, wherein the amino acid in $(AA^1)_c$ located closest to the drug moiety is selected from the group consisting of: Ala, Asn, Asp, Cit, Cys, Gln, Glu, Gly, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, and Val.

19. The compound of claim 13, wherein $(AA^1)_c$ is a peptide sequence selected from the group consisting of Val-Cit, Val-Lys, Phe-Lys, Lys-Lys, Ala-Lys, Phe-Cit, Leu-Cit, Ile-Cit, Trp, Cit, Phe-Ala, Phe-N^9-tosyl-Arg, Phe-N^9-nitro-Arg, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Leu-Ala-Leu, Ile-Ala-Leu, Val-Ala-Val, Ala-Leu-Ala-Leu (SEQ. ID NO: 1), β-Ala-Leu-Ala-Leu (SEQ. ID NO: 2) and Gly-Phe-Leu-Gly (SEQ. ID NO: 3).

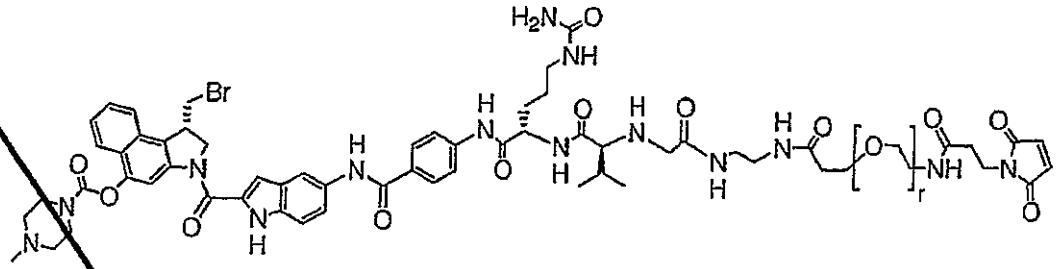
20. The compound of claim 13, wherein $(AA^1)_c$ is Val-Cit or Val-Lys.

21. The compound of claim 13, wherein R^{25}, $R^{25'}$, R^{26}, and $R^{26'}$ are independently H or lower alkyl.

22. The compound of claim 13, wherein s and t are independently 1 or 2.

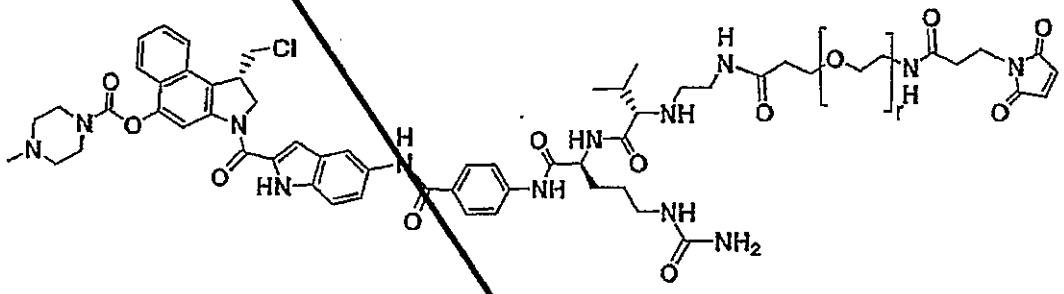
23. The compound of claim 13, wherein R^{20} is H or lower alkyl.

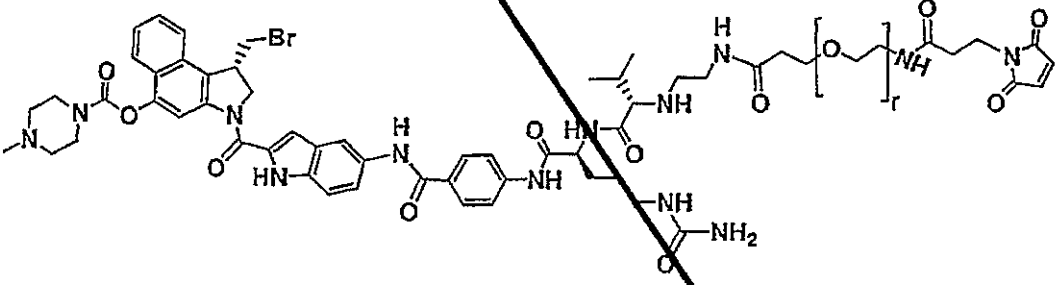
24. The compound of claim 13, wherein the compound is

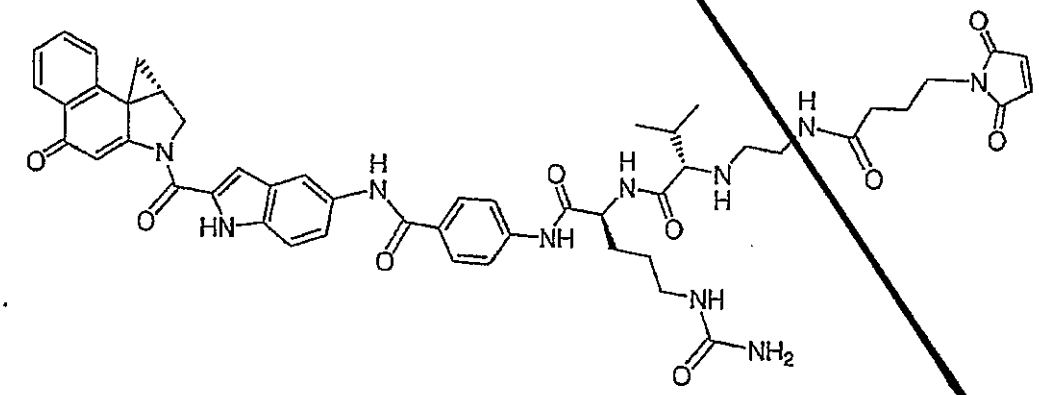


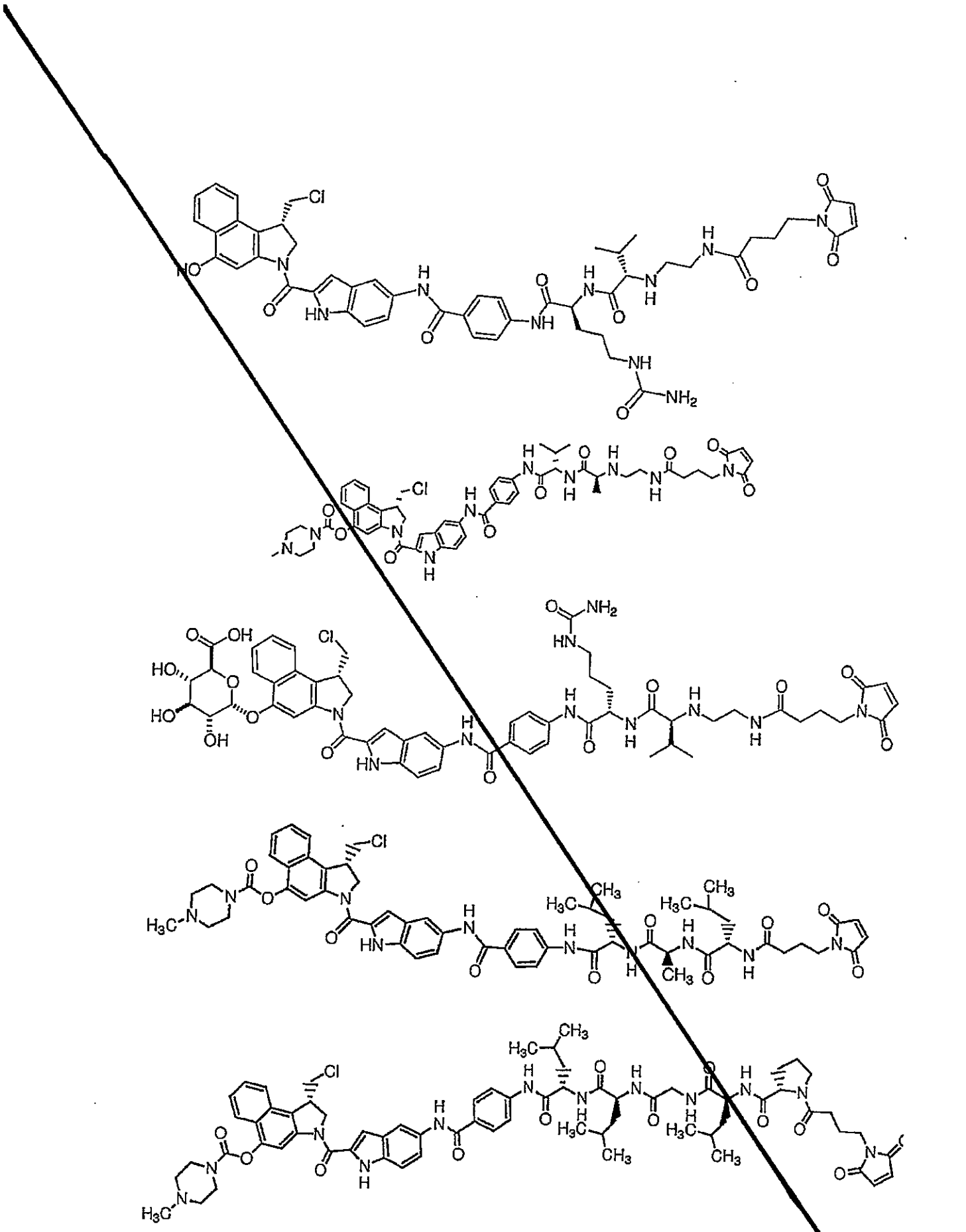
wherein r is an integer in the range from 0 to 24.

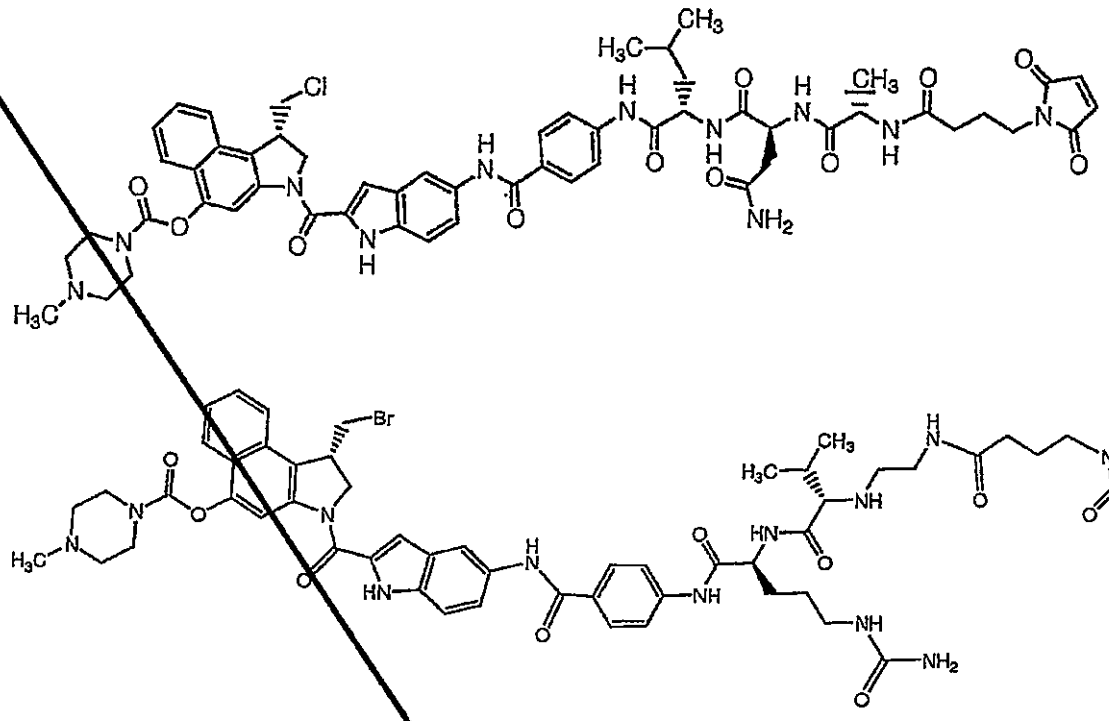
25. The compound of claim 1 or 13 where the compound is selected from:



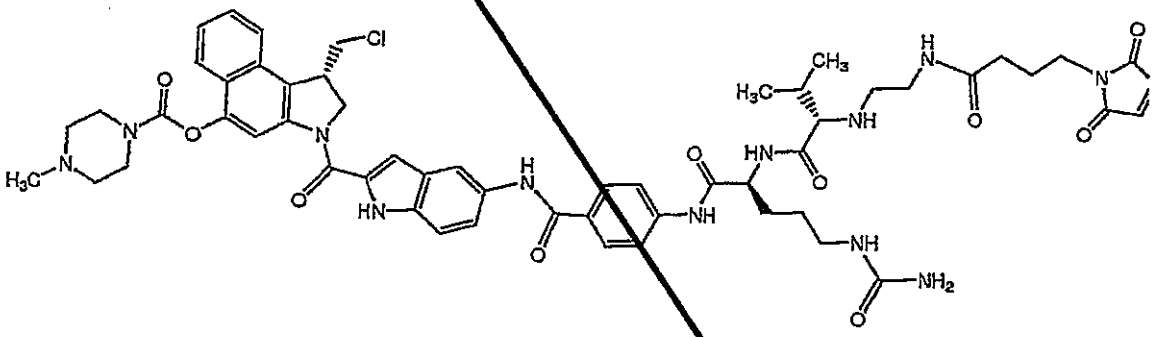


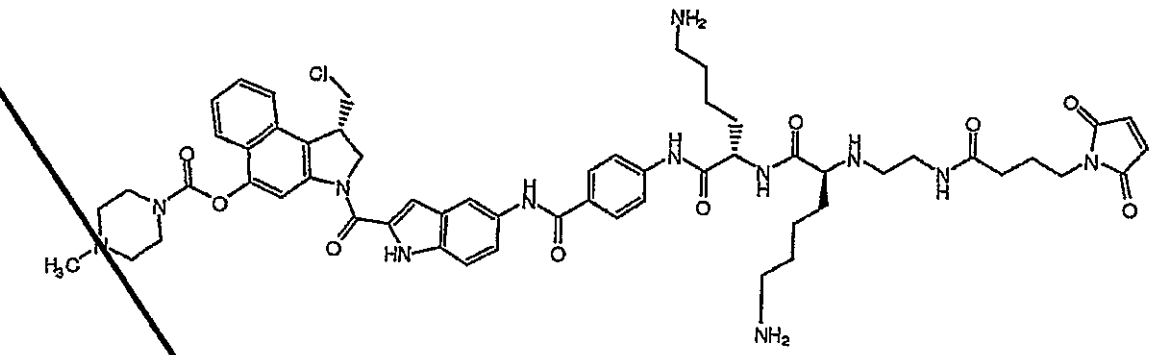


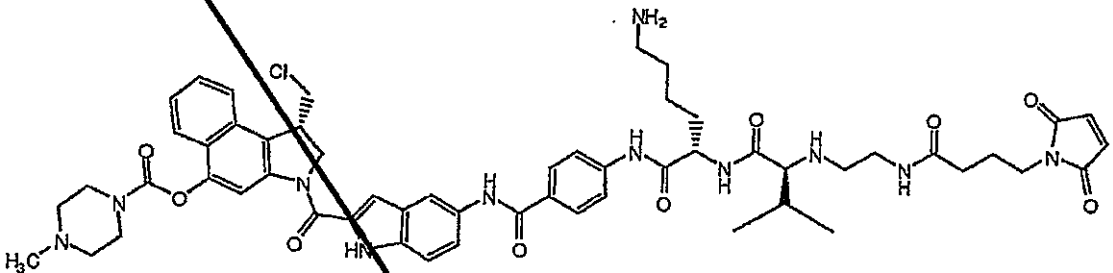


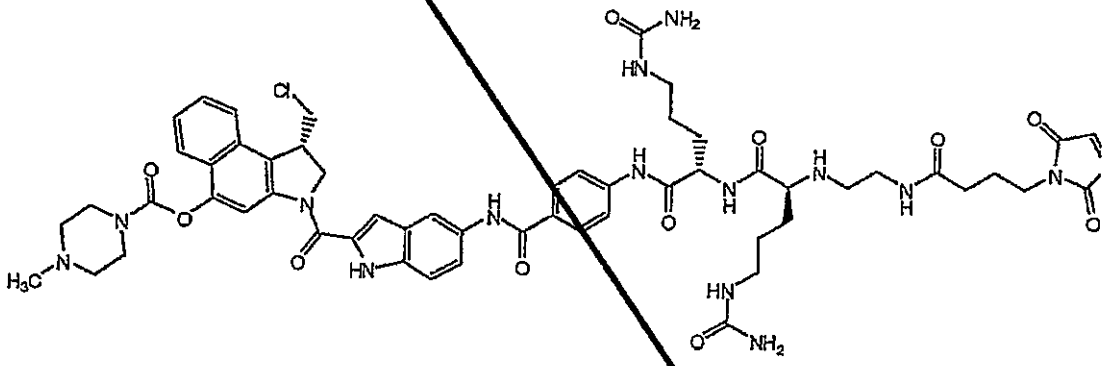


and







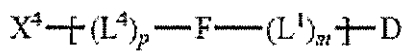


wherein r is an integer in the range from 0 to 24.

CLAIMS

What is claimed is:

1. A compound of the formula

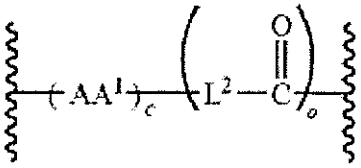


wherein

L^1 is a self-immolative linker;

m is an integer 0, 1, 2, 3, 4, 5, or 6;

F is a linker comprising the structure:



wherein

AA^1 is one or more members independently selected from the group consisting of natural amino acids and unnatural α-amino acids;

c is an integer from 1 to 20;

L^2 is a self-immolative linker;

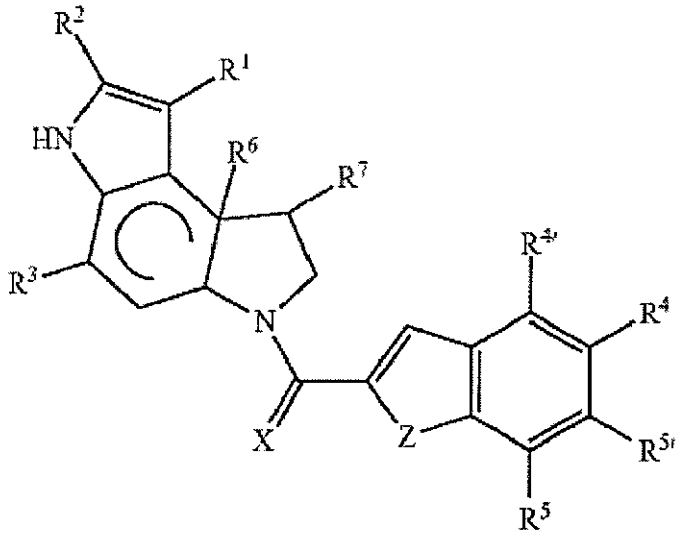
o is 0 or 1;

L^4 is a linker member;

p is 0 or 1;

X^4 is a member selected from the group consisting of protected reactive functional groups, unprotected reactive functional groups, detectable labels, and targeting agents; and

D has the structure:



wherein

Z is a member selected from O, S and NR^{23}

wherein

R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^1 is H, substituted or unsubstituted lower alkyl, $C(O)R^8$, or CO_2R^8, wherein R^8 is a member selected from group consisting of substituted alkyl, unsubstituted alkyl, NR^9R^{10}, NR^9NHR^{10}, and OR^9

in which R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl; and

R^2 is H, substituted alkyl or unsubstituted lower alkyl,

X is a member selected from O, S and NR^{23};

R^3 is a member selected from the group consisting of (=O), SR^{11}, NHR^{11} and OR^{11},

wherein R^{11} is a member selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted heteroalkyl, unsubstituted heteroalkyl, monophosphates, diphosphates, triphosphates, sulfonates, acyl, $C(O)R^{12}R^{13}$, $C(O)OR^{12}$, $C(O)NR^{12}R^{13}$, $P(O)(OR^{12})_2$, $C(O)CHR^{12}R^{13}$, SR^{12} and $SiR^{12}R^{13}R^{14}$,

in which R^{12}, R^{13}, and R^{14} are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl, wherein R^{12} and R^{13} together with the nitrogen or carbon atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

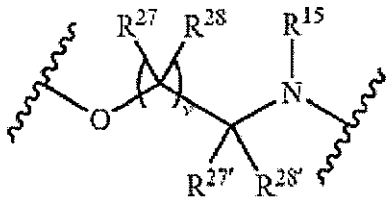
R^4, $R^{4'}$, R^5 and $R^{5'}$ are members independently selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted heterocycloalkyl, unsubstituted heterocycloalkyl, halogen, NO_2, $NR^{15}R^{16}$, $NHC(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $OC(O)OR^{15}$, $C(O)R^{15}$, SR^{15}, OR^{15}, $CR^{15}=NR^{16}$, and $O(CH_2)_nN(CH_3)_2$, or any adjacent pair of R^4, $R^{4'}$, R^5 and $R^{5'}$, together with the carbon atoms to which they are attached, are joined to form a substituted or unsubstituted cycloalkyl or heterocycloalkyl ring system having from 4 to 6 members,

wherein

n is an integer from 1 to 20;

R^{15} and R^{16} are independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycloalkyl, and substituted or unsubstituted peptidyl, wherein R^{15} and R^{16} together with the nitrogen atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

wherein at least one of R^4, $R^{4'}$, R^5 and $R^{5'}$ links said drug to L^1, if present, or to F, and comprises



wherein v is an integer from 1 to 6; and

each R^{27}, $R^{27'}$, R^{28}, and $R^{28'}$ is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;

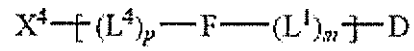
R^6 is a single bond which is either present or absent and when present R^6 and R^7 are joined to form a cyclopropyl ring; and

R^7 is CH_2—X^1 or —CH_2— joined in said cyclopropyl ring with R^6, wherein

X^1 is a leaving group;

or a pharmaceutically acceptable salt thereof.

2. A compound of the formula

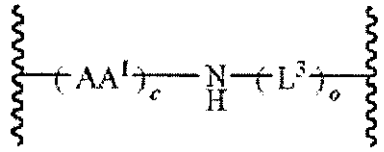


wherein

L^1 is a self-immolative linker;

m is an integer 0, 1, 2, 3, 4, 5, or 6;

F is a linker comprising the structure:



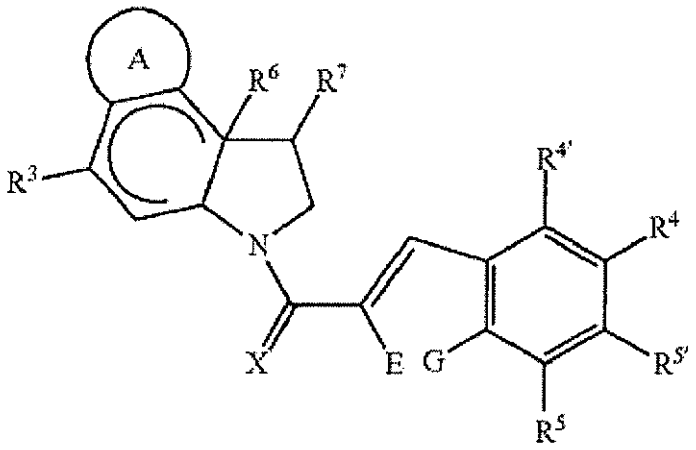
aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;

and s and t are independently integers from 1 to 6;

p is 1;

X^4 is a member selected from the group consisting of protected reactive functional groups, unprotected reactive functional groups, detectable labels, and targeting agents; and

D comprises a structure:



wherein the ring system A is a member selected from substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl and substituted or unsubstituted heterocycloalkyl groups;

E and G are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, a heteroatom, a single bond, or E and G are joined to form a ring system selected from substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl and substituted or unsubstituted heterocycloalkyl;

X is a member selected from O, S and NR^{23};

R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;

R^3 is a member selected from the group consisting of (=O), SR^{11}, NHR^{11} and OR^{11},

wherein

R^{11} is a member selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted heteroalkyl, unsubstituted heteroalkyl, monophosphates, diphosphates, triphosphates, sulfonates, acyl, $C(O)R^{12}R^{13}$, $C(O)OR^{12}$, $C(O)NR^{12}R^{13}$, $P(O)(OR^{12})_2$, $C(O)CHR^{12}R^{13}$, SR^{12} and $SiR^{12}R^{13}R^{14}$,

in which

R^{12}, R^{13} and R^{14} are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl, wherein R^{12} and R^{13} together with the nitrogen or carbon atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

R^4, $R^{4'}$, R^5 and $R^{5'}$ are members independently selected from the group consisting of H, substituted alkyl, unsubstituted alkyl, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted heterocycloalkyl, unsubstituted heterocycloalkyl, halogen, NO_2, $NR^{15}R^{16}$, $NHC(O)R^{15}$, $OC(O)NR^{15}R^{16}$, $OC(O)OR^{15}$, $C(O)R^{15}$, SR^{15}, OR^{15}, $CR^{15}=NR^{16}$, and $O(CH_2)_nN(CH_3)_2$, or any adjacent pair of R^4, $R^{4'}$, R^5 and $R^{5'}$, together with the carbon atoms to which they are attached, are joined to form a substituted or unsubstituted cycloalkyl or heterocycloalkyl ring system having from 4 to 6 members,

wherein

n is an integer from 1 to 20;

R^{15} and R^{16} are independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycloalkyl, and substituted or unsubstituted peptidyl, wherein R^{15} and R^{16} together with the nitrogen atom to which they are attached are optionally joined to form a substituted or unsubstituted heterocycloalkyl ring system having from 4 to 6 members, optionally containing two or more heteroatoms;

R^6 is a single bond which is either present or absent and when present R^6 and R^7 are joined to form a cyclopropyl ring; and

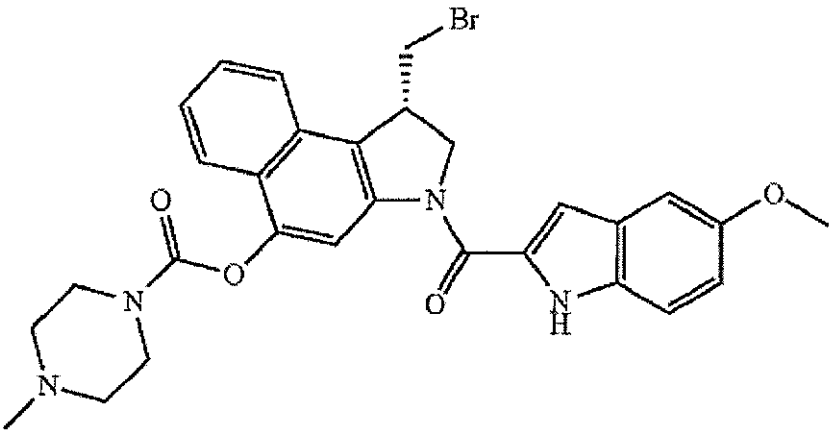
R^7 is CH_2—X^1 or —CH_2— joined in said cyclopropyl ring with R^6, wherein

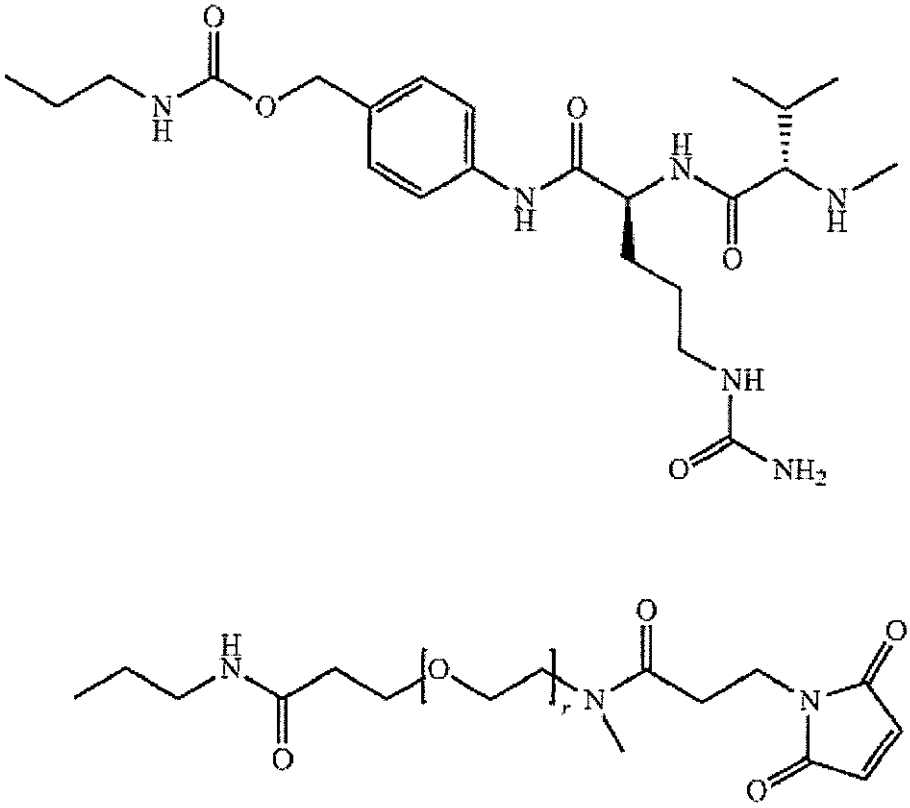
X^1 is a leaving group,

wherein at least one of R^4, $R^{4'}$, R^5, $R^{5'}$, R^{15}, R^{16} links said drug to L^1, if present, or to F;

or a pharmaceutically acceptable salt thereof.

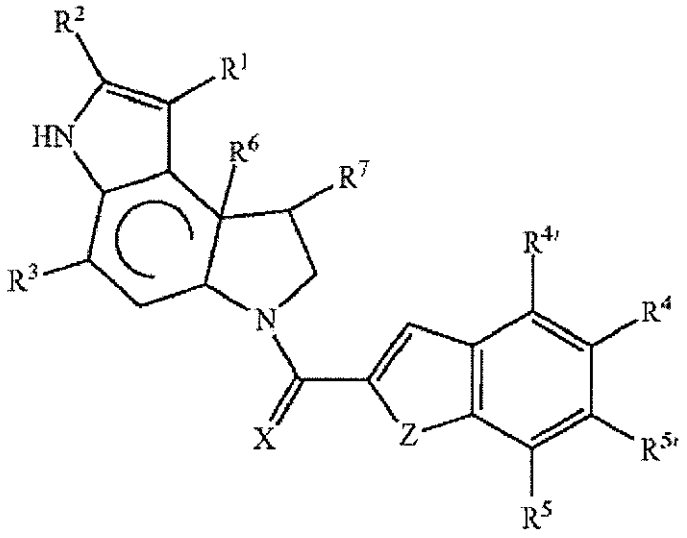
3. The compound of claim **2**, wherein the compound is





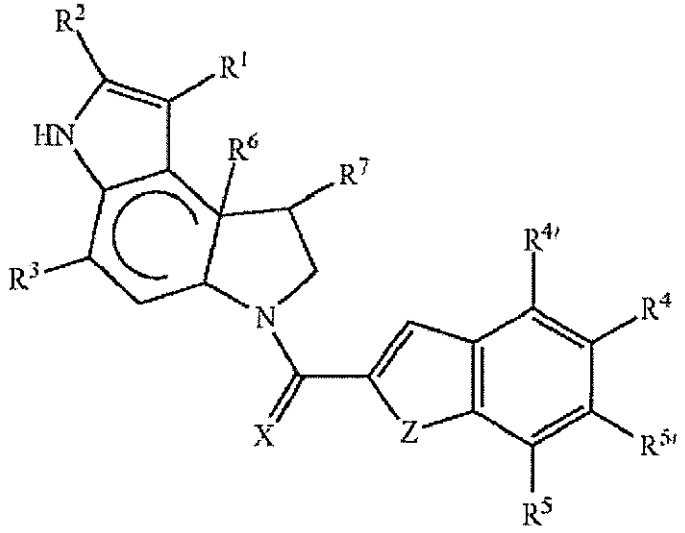
wherein r is an integer in the range from 0 to 24.

4. The compound of claim **2**, wherein D has the structure:



wherein
Z is a member selected from O, S and NR^{23}
wherein
R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;
R^1 is H, substituted or unsubstituted lower alkyl, $C(O)R^8$, or CO_2R^8, wherein R^8 is a member selected from the group consisting of substituted alkyl, unsubstituted alkyl, NR^9R^{10}, NR^9NHR^{10}, and OR^9
in which R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl; and
R^2 is H, substituted alkyl or unsubstituted lower alkyl.

5. The compound of claim **2**, wherein D has the structure:



wherein
Z is a member selected from O, S and NR^{23}
wherein
R^{23} is a member selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and acyl;
R^1 is H, substituted or unsubstituted lower alkyl, $C(O)R^8$, or CO_2R^8, wherein R^8 is a member selected from NR^9R^{10} and OR^9,
in which
R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;
R^1 is H, substituted or unsubstituted lower alkyl, or C(O) R^8, wherein R^8 is a member selected from NR^9R^{10} and OR^9,

in which

R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

R^1 is H, substituted or unsubstituted lower alkyl, or C(O) R^8, wherein R^8 is a member selected from NR^9R^{10} and OR^9,

in which

R^9 and R^{10} are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

R^2 is H, or substituted or unsubstituted lower alkyl or unsubstituted heteroalkyl or cyano or alkoxy; and

$R^{2'}$ is H, or substituted or unsubstituted lower alkyl or unsubstituted heteroalkyl.

6. The compound of claim **2**, wherein $(AA^1)_c$, is a peptide sequence selected from the group consisting of Val-Cit, Val-Lys, Phe-Lys, Lys-Lys, Ala-Lys, Phe-Cit, Leu-Cit, Ile-Cit, Trp, Cit, Phe-Ala, Phe-N^9-tosyl-Arg, Phe-N^9-nitro-Arg, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Leu-Ala-Leu, Ile-Ala-Leu, Val-Ala-Val, Ala-Leu-Ala-Leu (SEQ. ID NO: 1), β-Ala-Leu-Ala-Leu (SEQ. ID NO: 2) and Gly-Phe-Leu-Gly (SEQ. ID NO: 3).

7. The compound of claim **2**, wherein $(AA^1)_c$, is Val-Cit or Val-Lys.

8. The compound of claim **2**, wherein s and t are independently 1 or 2.

9. The compound of claim **2**, wherein R^{20} is H or lower alkyl.