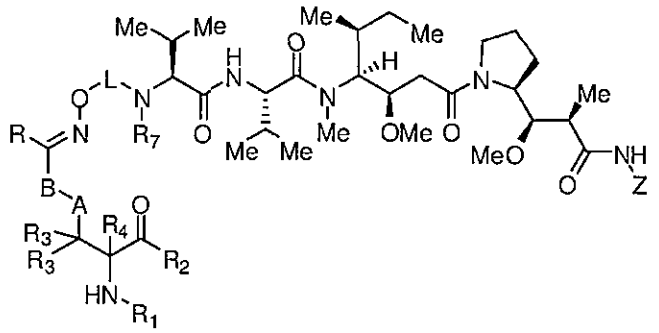
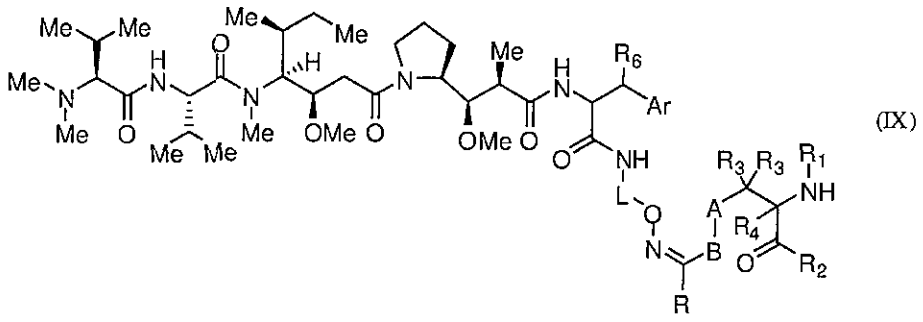
Claims

1. A compound comprising Formula (VIII) or (IX):



(VIII)

;



(IX)

;

wherein:

A is optional, and when present is lower alkylene, lower cycloalkylene, lower alkenylene, alkynylene, lower heteroalkylene, lower heterocycloalkylene, lower heterocycloalkylene, arylene, heteroarylene, alkarylene, or aralkylene;

B is optional, and when present is a linker selected from the group consisting of lower alkylene, lower alkenylene, lower heteroalkylene, -O-, -O-(alkylene)-, -S-, -S-(alkylene)-, -$S(O)_k$- where k is 1, 2, or 3, -$S(O)_k$(alkylene)-, -C(O)-, -C(O)-(alkylene)-, -C(S)-, -C(S)-(alkylene)-, -N(R')-, -NR'-(alkylene)-, -C(O)N(R')-, -CON(R')-(alkylene)-, -CSN(R')-, -CSN(R')-(alkylene)-, -N(R')CO-(alkylene)-, -N(R')C(O)O-, -$S(O)_k$N(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')$S(O)_k$N(R')-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -$C(R')_2$-N=N-, and -$C(R')_2$-N(R')-N(R')-, where each R' is independently H, or alkyl;

R is H, alkyl, or cycloalkyl;

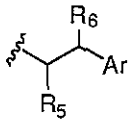
R_1 is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

provided that at least one of R_1 or R_2 is an anti-CD70 (αCD70) antibody;

R_3 and R_4 are each independently H, halogen, or lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl;

Z has the structure of:



;

R_5 is H, COR_8, C_1-C_6alkyl, or thiazole;

R_8 is OH;

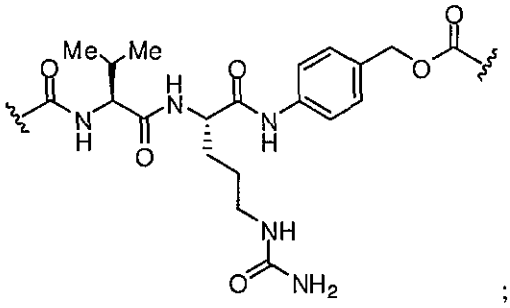
R_6 is OH or H;

Ar is phenyl or pyridine;

R_7 is C_1-C_6alkyl or hydrogen;

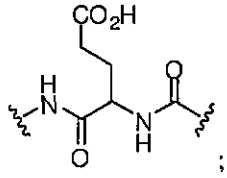
L is a linker selected from the group consisting of –alkylene–, –alkylene–C(O)–, –(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–C(O)–, –(alkylene–O)$_n$–(CH$_2$)$_{n'}$–NHC(O)–(CH$_2$)$_{n''}$–C(Me)$_2$–S–S–(CH$_2$)$_{n'''}$–NHC(O)–(alkylene–O)$_{n''''}$–alkylene–, –(alkylene–O)$_n$–alkylene–W–, –alkylene–C(O)–W–, –(alkylene–O)$_n$–alkylene–U–alkylene–C(O)–, and –(alkylene–O)$_n$–alkylene–U–alkylene–;

W has the structure of:



;

U has the structure of:



; and

each n, n', n", n"' and n"" are independently integers greater than or equal to one;

or a pharmaceutically acceptable prodrug or solvate thereof.

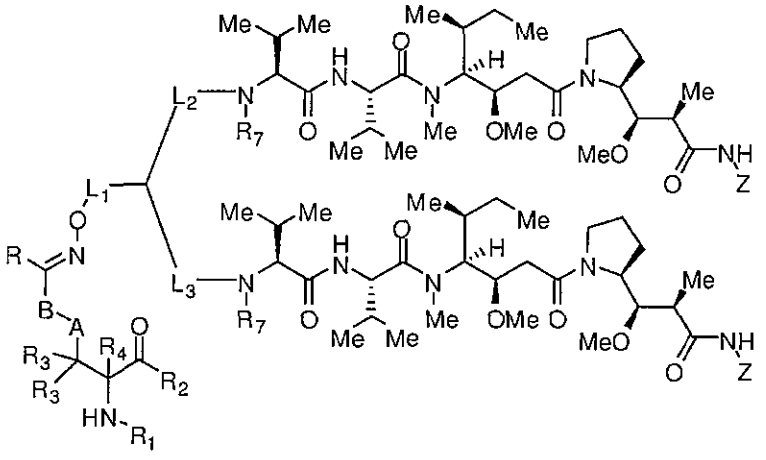
2. The compound of claim 1, wherein R_1 is an anti-CD70 (αCD70) antibody.

3. The compound of claim 1 or claim 2, wherein R_2 is an αCD70 antibody.

4. The compound of any one of claims 1 to 3, wherein the αCD70 antibody comprises one or more non-naturally encoded amino acids.

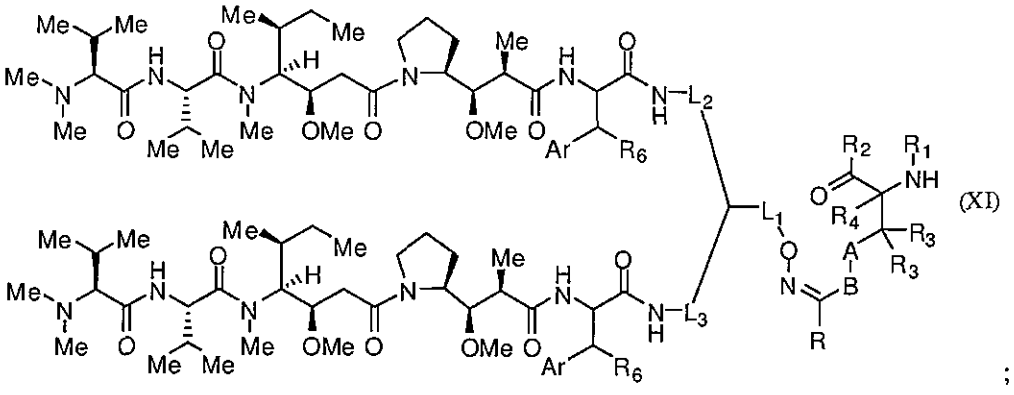
5. The compound of any one of claims 1 to 4, wherein the αCD70 antibody comprises at least one and no more than ten non-naturally encoded amino acids.

6. The compound, or salt thereof, comprising Formula (X), (XI), (XII) or (XIII):



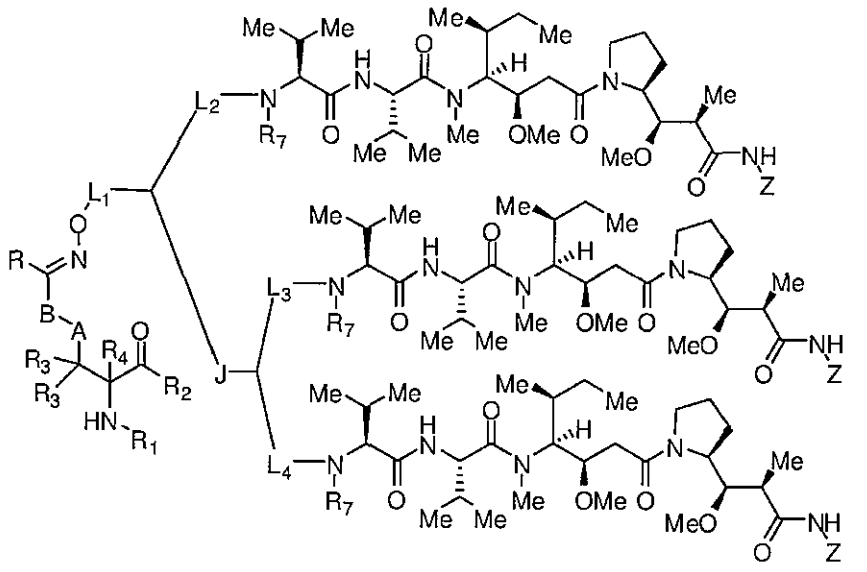
(X)

;



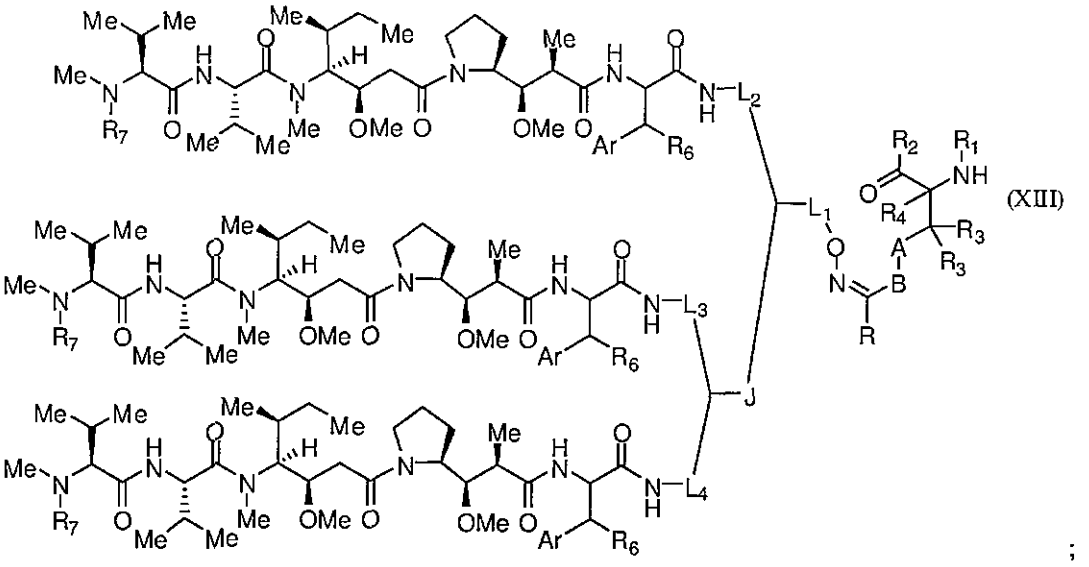
(XI)

;



(XII)

;



(XIII)

;

wherein:

A is optional, and when present is lower alkylene, lower cycloalkylene, lower alkenylene, alkynylene, lower heteroalkylene, lower heterocycloalkylene, arylene, heteroarylene, alkarylene, or aralkylene;

B is optional, and when present is a linker selected from the group consisting of lower alkylene, lower alkenylene, lower heteroalkylene, -O-, -O-(alkylene)-, -S-, -S-(alkylene)-, $-S(O)_k-$ where k is 1, 2, or 3, $-S(O)_k$(alkylene)-, -C(O)-, -C(O)-(alkylene)-, -C(S)-, -C(S)-(alkylene)-, -N(R')-, -NR'-(alkylene)-, -C(O)N(R')-, -CON(R')-(alkylene)-, -CSN(R')-, -CSN(R')-(alkylene)-, -N(R')CO-(alkylene)-, -N(R')C(O)O-, $-S(O)_kN(R')-$, -N(R')C(O)N(R')-,

-N(R')C(S)N(R')-, -N(R')S(O)$_k$N(R')-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -C(R')$_2$-N=N-, and -C(R')$_2$-N(R')-N(R')-, where each R' is independently H, or alkyl;

R is H, alkyl, or cycloalkyl;

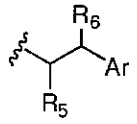
R_1 is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

provided that at least one of R_1 or R_2 is an anti-CD70 (αCD70) antibody;

R_3 and R_4 are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl;

Z has the structure of:



;

R_5 is H, CO_2H, C_1-C_6alkyl, or thiazole;

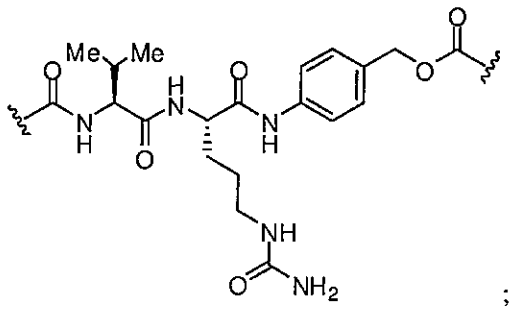
R_6 is OH or H;

Ar is phenyl or pyridine;

R_7 is C_1-C_6alkyl or hydrogen;

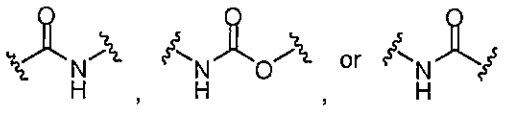
L_1, L_2, L_3, and L_4 are each linkers independently selected from the group consisting of a bond, –alkylene–, –(alkylene–O)$_n$–alkylene–J–, –alkylene'–J–(alkylene–O)$_n$–alkylene–, –J–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–J–(alkylene–O)$_n$'–alkylene–J'–, –(alkylene–O)$_n$–alkylene–J–alkylene'–, –W–, –alkylene–W–, alkylene'–J–(alkylene–NMe)$_n$–alkylene–W–, –J–(alkylene–NMe)$_n$–alkylene–W–, –J–alkylene–NMe–alkylene'–NMe–alkylene"–W–, and –alkylene–J–alkylene'–NMe–alkylene"–NMe–alkylene'"–W–;

W has the structure of:



;

each J and J' independently have the structure of:

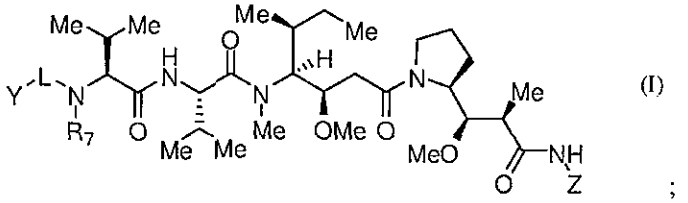

; and

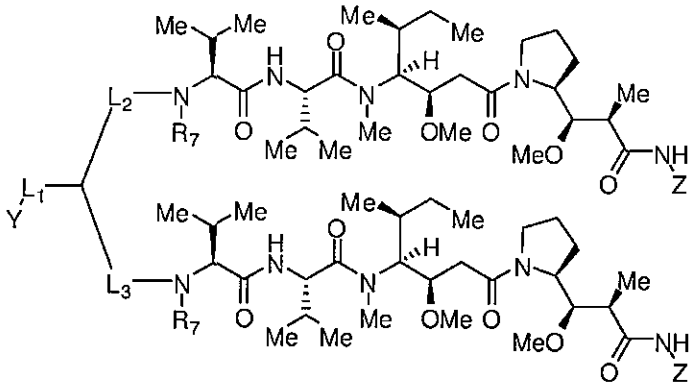
each n and n' are independently integers greater than or equal to one.

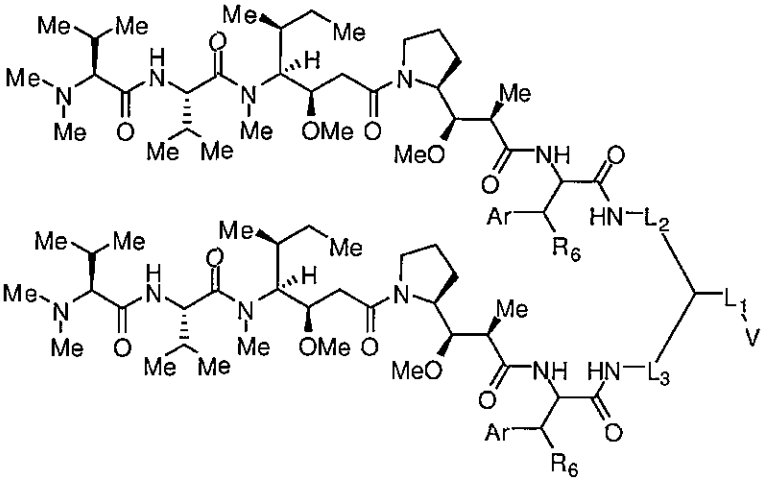
7. The compound of claim 6, wherein R_1 an αCD70 antibody.

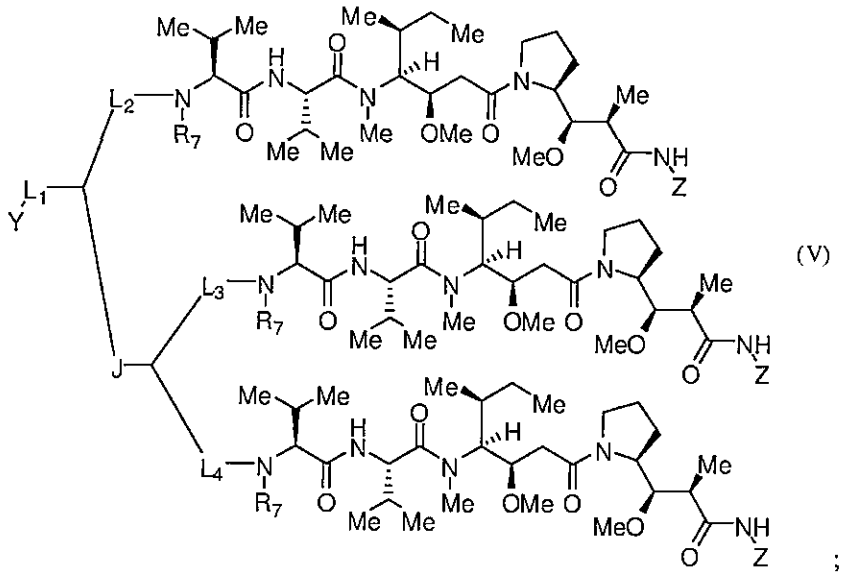
8. The compound of claim 6 or claim 7, wherein R_2 an αCD70 antibody.

9. A method for derivatizing a dolastatin analog comprising Formula (I), (III), (IV), (V), or (VI), the method comprising contacting the dolastatin analog with a reagent of Formula (XXXVII), wherein Formula (I), (III), (IV), (V), or (VI) correspond to:


(I)
;

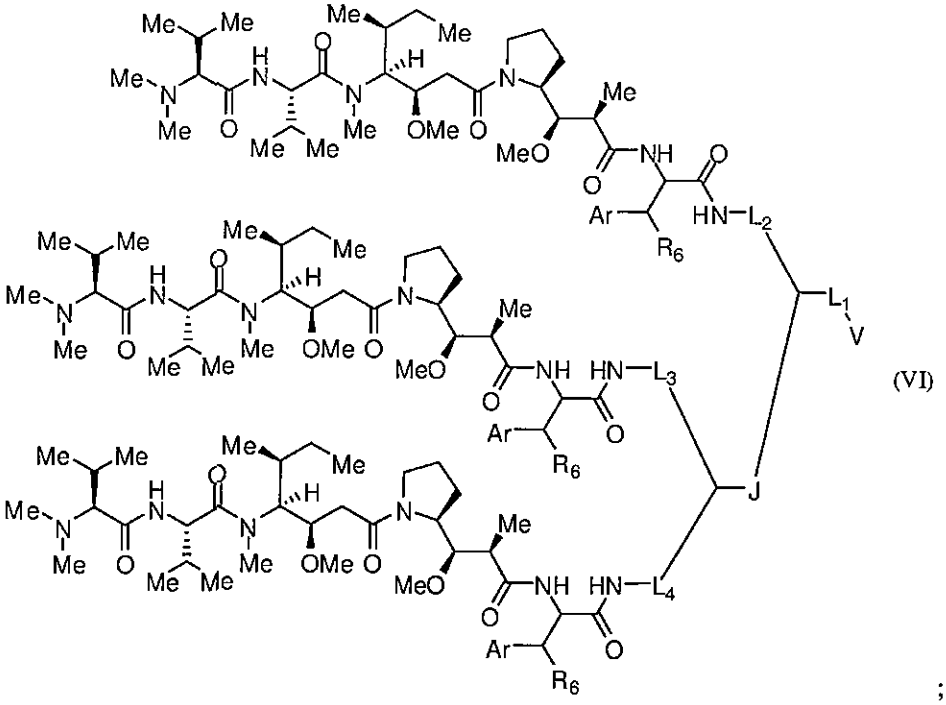

(III)
;


(IV)
;



(V)

;

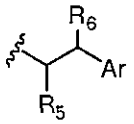


(VI)

;

wherein:

Z has the structure of:



;

R_5 is H, COR_8, C_1-C_6alkyl, or thiazole;

R_8 is OH or –NH–(alkylene–O)$_n$–NH_2;

R_6 is OH or H;

Ar is phenyl or pyridine;

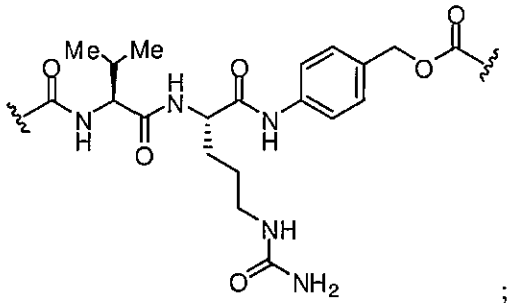
R_7 is C_1-C_6 alkyl or hydrogen;

Y is NH_2–O– or methyl;

V is selected from the group consisting of an hydroxylamine, methyl, aldehyde, protected aldehyde, ketone, protected ketone, thioester, ester, dicarbonyl, hydrazine, azide, amidine, imine, diamine, keto-amine, keto-alkyne, alkyne, cycloalkyne, and ene-dione;

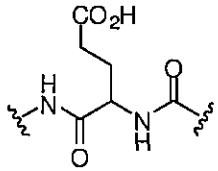
L, L_1, L_2, L_3, and L_4 are each linkers selected from the group consisting of a bond, –alkylene–, –alkylene–C(O)–, –(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–C(O)–, –(alkylene–O)$_n$–$(CH_2)_{n'}$–NHC(O)–$(CH_2)_{n''}$–$C(Me)_2$–S–S–$(CH_2)_{n'''}$–NHC(O)–(alkylene–O)$_{n''''}$–alkylene–, –(alkylene–O)$_n$–alkylene–W–, –alkylene–C(O)–W–, –(alkylene–O)$_n$–alkylene–J–, –alkylene'–J–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–J–alkylene', –J–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–J–(alkylene–O)$_n$'–alkylene–J'–, –W–, –alkylene–W–, alkylene'–J– (alkylene–NMe)$_n$–alkylene–W–, and J– (alkylene–NMe)$_n$–alkylene–W–, –(alkylene–O)$_n$–alkylene–U–alkylene–C(O)–, –(alkylene–O)$_n$–alkylene–U–alkylene–; –J–alkylene–NMe–alkylene'–NMe–alkylene"–W–, and –alkylene–J–alkylene'–NMe–alkylene"–NMe–alkylene"'–W–;

W has the structure of:

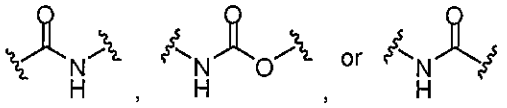


;

U has the structure of:



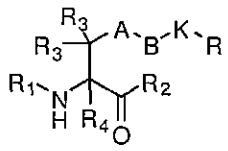
each J and J' independently have the structure of:



or L is absent, Y is methyl, R_5 is COR_8, and R_8 is –NH–(alkylene–O)$_n$–NH_2; and

each n, n', n", n"' and n"" are independently integers greater than or equal to one;

wherein Formula (XXXVII) corresponds to:

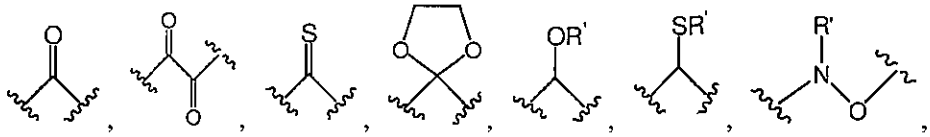
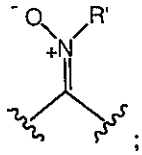

(XXXVII)

wherein:

A is optional, and when present is lower alkylene, lower alkenylene, arylene, heteroarylene, alkarylene, or aralkylene;

B is optional, and when present is a linker selected from the group consisting of lower alkylene, lower alkenylene, -O-, -O-(alkylene)-, -S-, -S-(alkylene)-, -S(O)$_k$- where k is 1, 2, or 3, -S(O)$_k$(alkylene)-, -C(O)-, -C(O)-(alkylene)-, -C(S)-, -C(S)-(alkylene)-, -N(R')-, -NR'-(alkylene)-, -C(O)N(R')-, -CON(R')-(alkylene)-, -CSN(R')-, -CSN(R')-(alkylene)-, -N(R')CO-(alkylene)-, -N(R')C(O)O-, -S(O)$_k$N(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)$_k$N(R')-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -C(R')$_2$-N=N-, and -C(R')$_2$-N(R')-N(R')-, where each R' is independently H, or alkyl;

each R' is independently H, or alkyl;

K is , or ;

R is H, alkyl, or cycloalkyl;

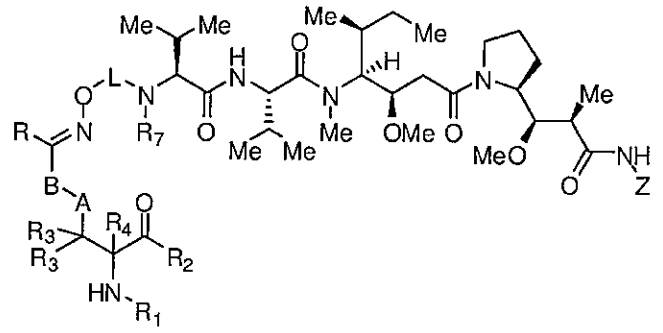
R_1 is H, an amino protecting group, resin, at least one amino acid, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, or polynucleotide;

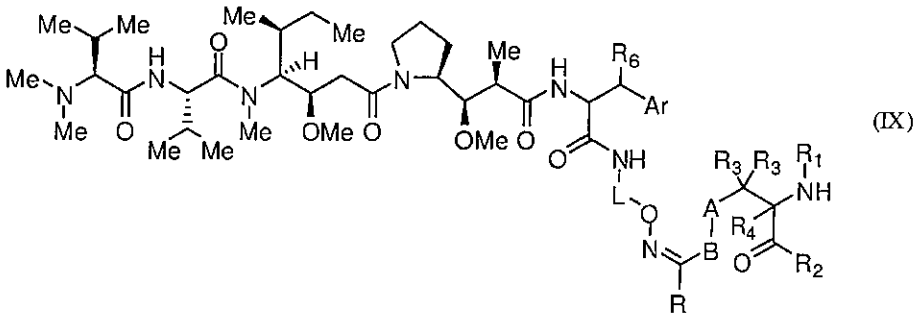
provided that at least one of R_1 or R_2 is an anti-CD70 (αCD70) antibody; and

R_3 and R_4 are each independently H, halogen, or lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl.

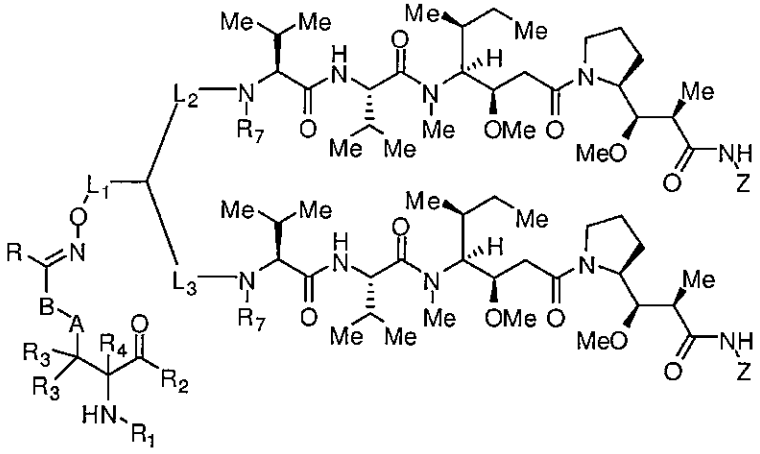
10. The method of claim 9, wherein the derivatized dolastatin analog comprises at least one oxime containing amino acid having the structure of Formula (VIII), (IX), (X), (XI), (XII), or (XIII):



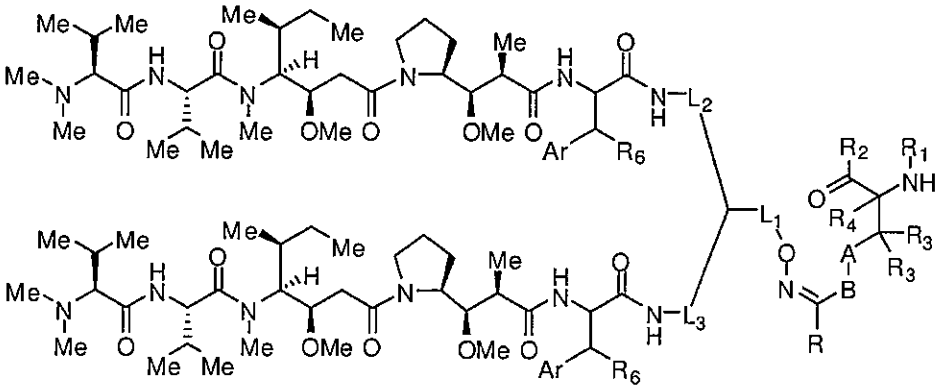
(VIII)



(IX)

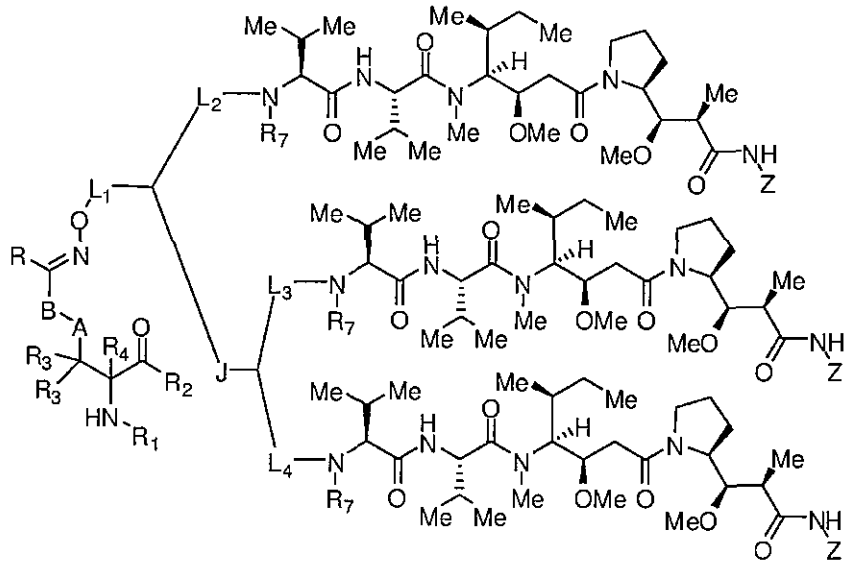


(X)



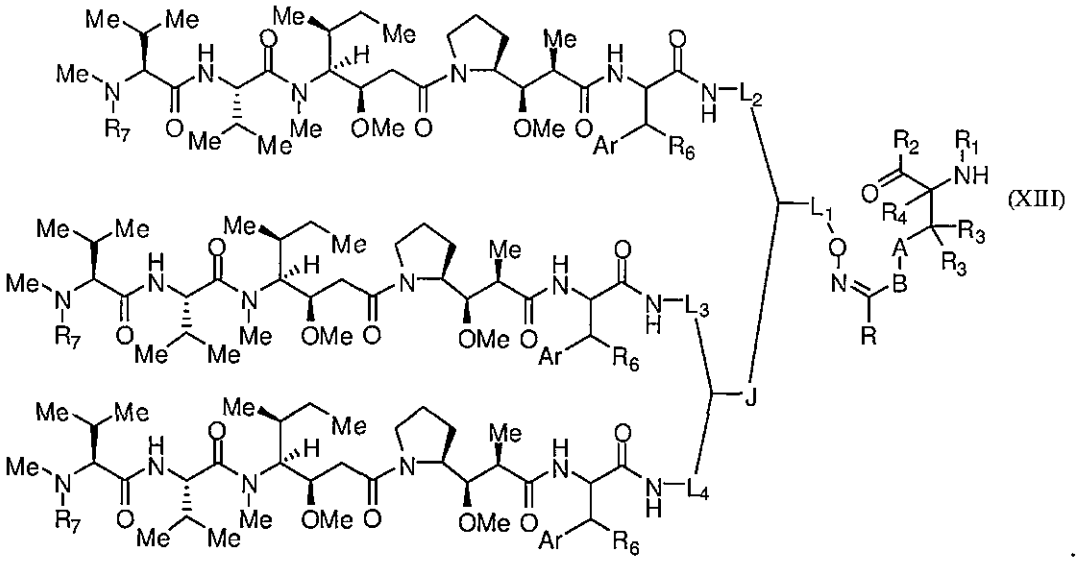
(XI)

;



(XII)

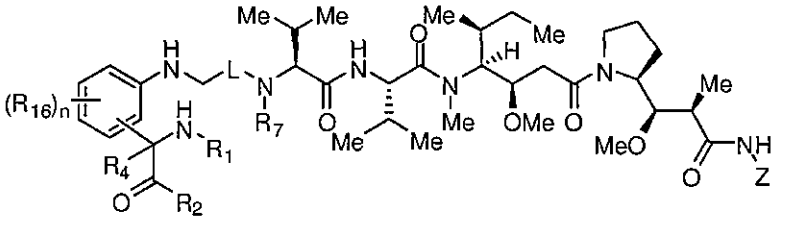
;



(XIII)

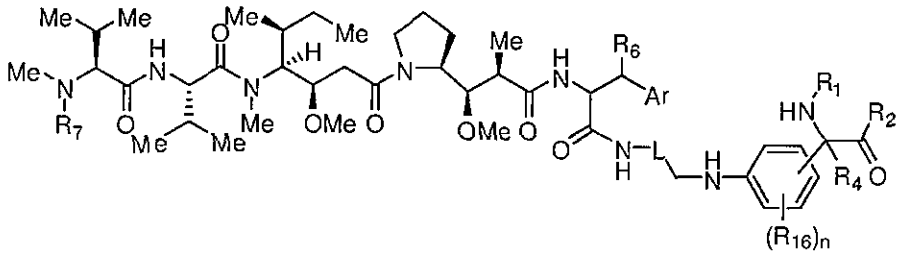
.

11. A compound comprising Formula (XXV), (XXVI), (XXVII), (XXVIII), (XXIX), or (XXX):



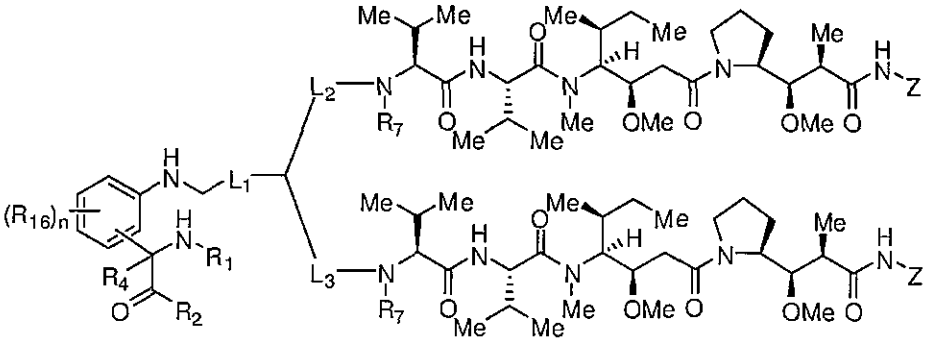
(XXV)

;



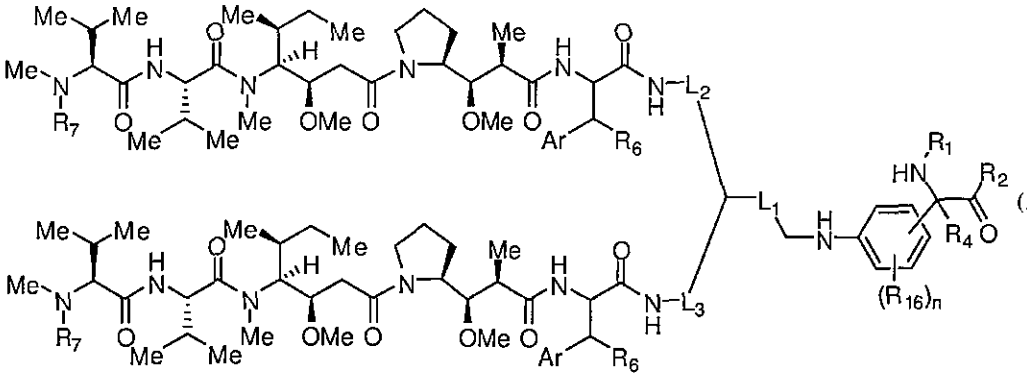
(XXVI)

;



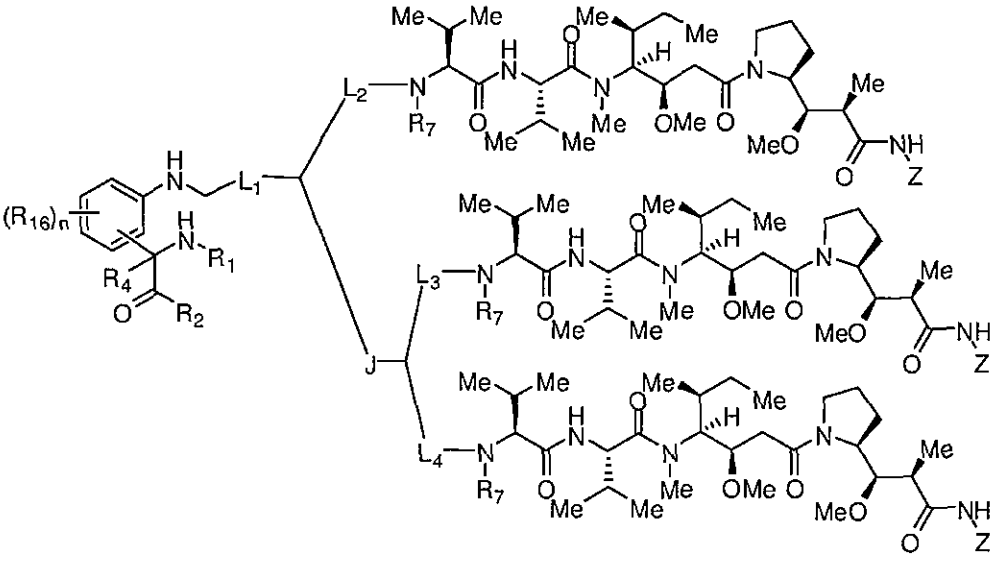
(XXVII)

;



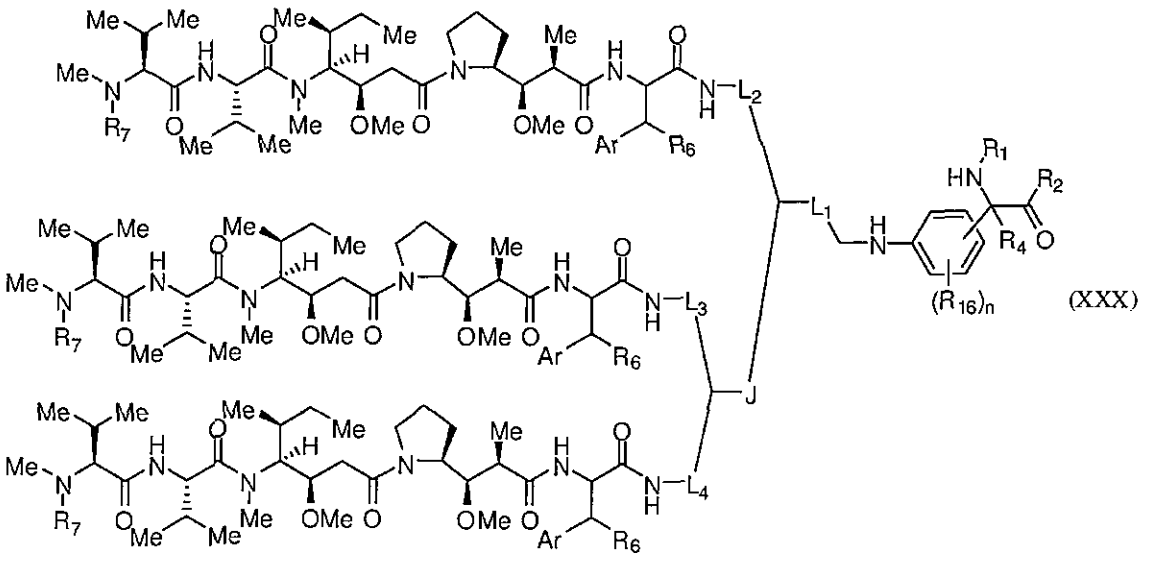
(XXVIII)

;



(XXIX)

;

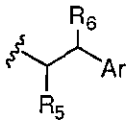


(XXX)

;

wherein:

Z has the structure of:



;

R_5 is H, CO_2H, C_1-C_6alkyl, or thiazole;

R_6 is OH or H;

Ar is phenyl or pyridine;

R_1 is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

provided that at least one of R_1 or R_2 is an anti-CD70 (αCD70) antibody;

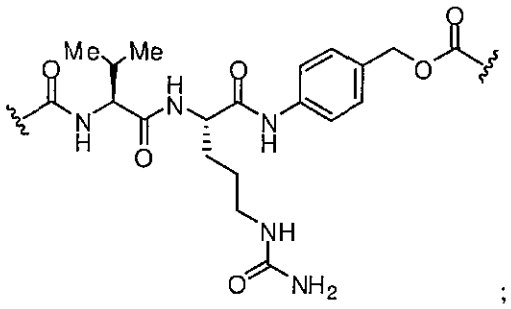
R_4 is H, halogen, lower alkyl, or substituted lower alkyl;

R_7 is C_1-C_6alkyl or hydrogen;

L, L_1, L_2, L_3, and L_4 are each linkers selected from the group consisting of a bond, –alkylene–, –alkylene–C(O)–, –alkylene–J–, –(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–C(O)–, –(alkylene–O)$_n$–J–, –(alkylene–O)$_n$–J–alkylene–, –(alkylene–O)$_n$–(CH$_2$)$_n$–NHC(O)–(CH$_2$)$_n$–C(Me)$_2$–S–S–(CH$_2$)$_n$–NHC(O)–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–W–, –alkylene–C(O)–W–, –(alkylene–O)$_n$–alkylene–J–, –alkylene'–J–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–J–alkylene', –J–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–J–(alkylene–O)$_n$'–alkylene–J'–, –W–, –alkylene–W–, alkylene'–J–(alkylene–NMe)$_n$–alkylene–W–, –J–(alkylene–NMe)$_n$–alkylene–W–, –(alkylene–O)$_n$–alkylene–U–alkylene–

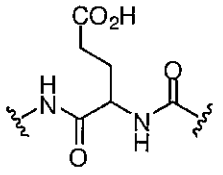
C(O)–, –(alkylene–O)$_n$–alkylene–U–alkylene–; –J–alkylene–NMe–alkylene'–NMe–alkylene"–W–, and –alkylene–J–alkylene'–NMe–alkylene"–NMe–alkylene"'–W–;

W has the structure of:

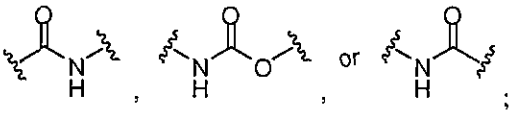


;

U has the structure of:



each J and J' independently have the structure of:

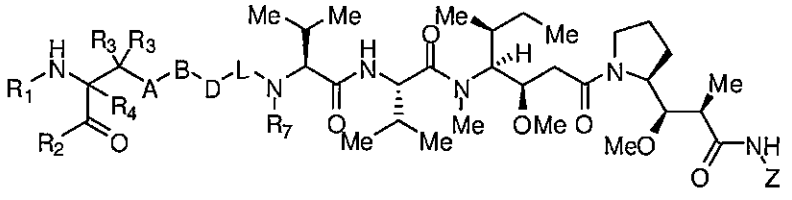


;

each n and n' are independently integers greater than or equal to one; and

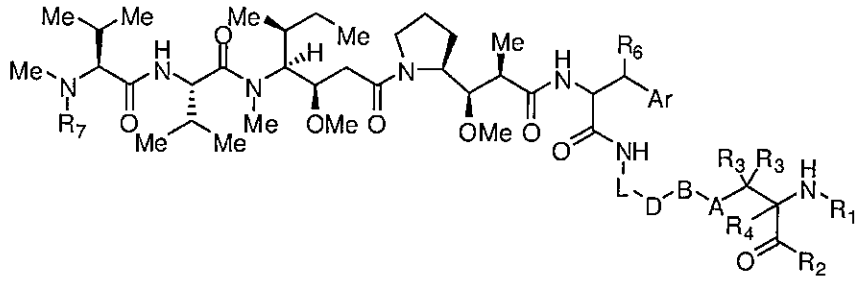
each R_{16} is independently selected from the group consisting of hydrogen, halogen, alkyl, NO_2, and CN.

12. A compound comprising Formula (XXXI), (XXXII), (XXXIII), (XXXIV), (XXXV), or (XXXVI):



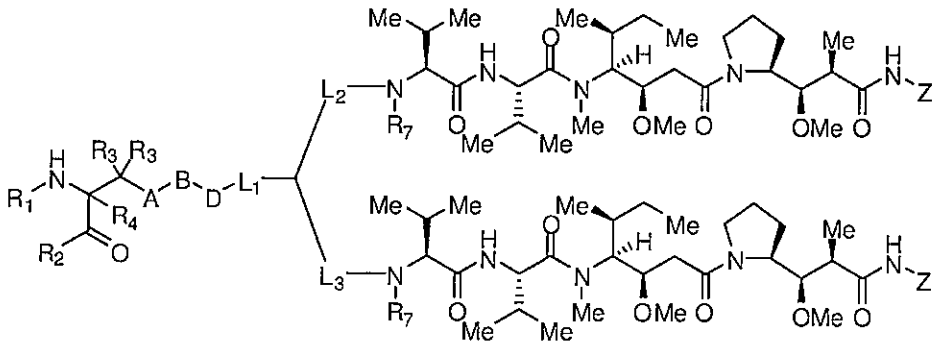
(XXXI)

;



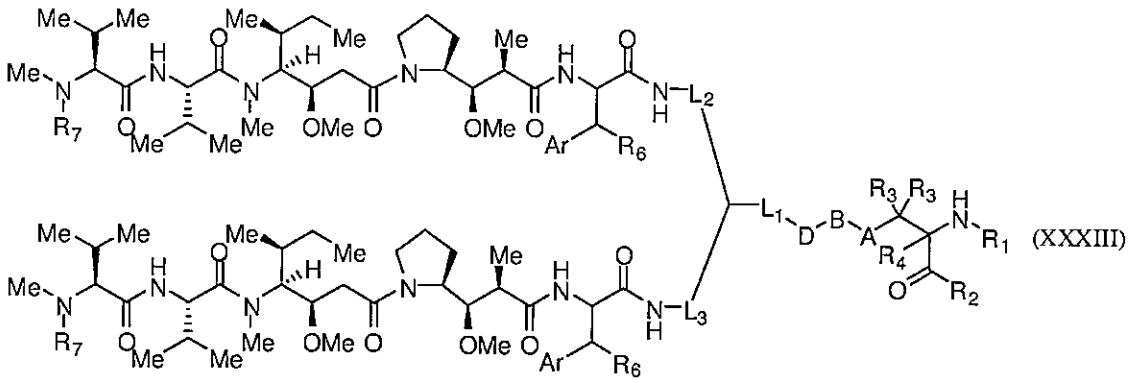
(XXXII)

;

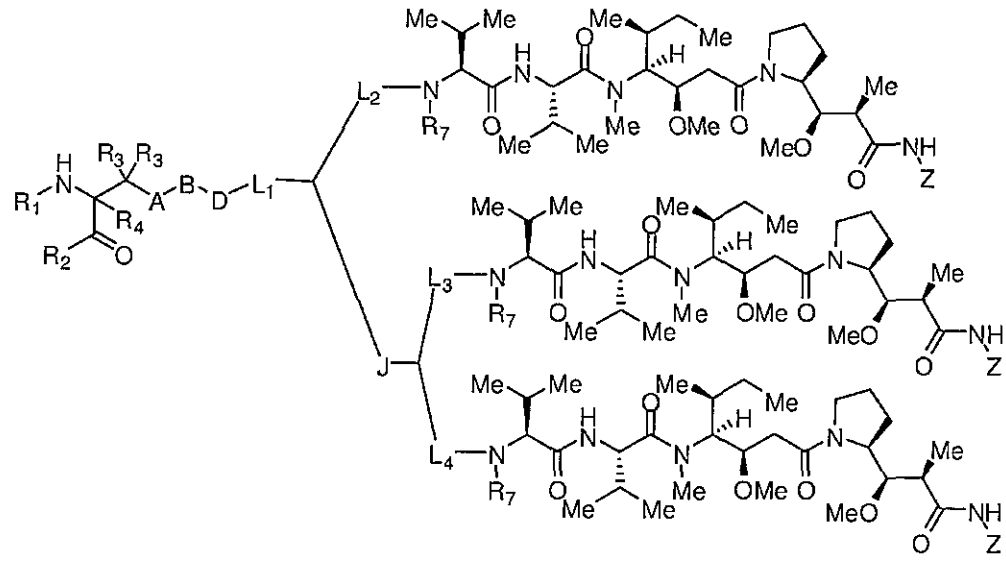


(XXXIII)

;

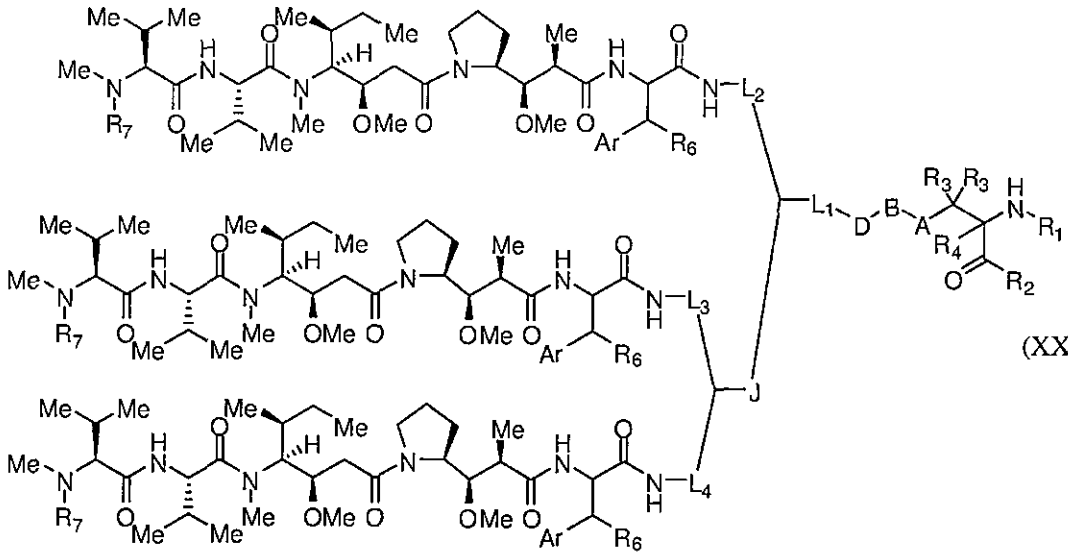


(XXXIII)



(XXXV)

;

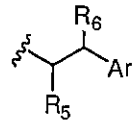


(XXXVI)

;

wherein:

Z has the structure of:



;

R_5 is H, CO_2H, C_1-C_6alkyl, or thiazole;

R_6 is OH or H;

Ar is phenyl or pyridine;

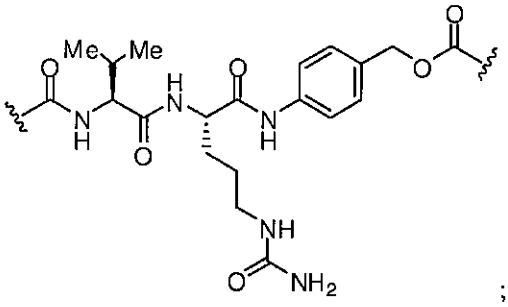
R_1 is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide; provided that at least one of R_1 or R_2 is an anti-CD70 (αCD70) antibody;

R_4 is H, halogen, lower alkyl, or substituted lower alkyl;

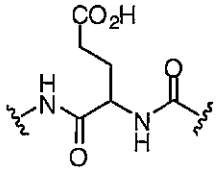
R_7 is C_1-C_6alkyl or hydrogen;

L, L_1, L_2, L_3, and L_4 are each linkers selected from the group consisting of a bond, –alkylene–, –alkylene–C(O)–, –alkylene–J–, –(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–C(O)–, –(alkylene–O)$_n$–J–, –(alkylene–O)$_n$–J–alkylene–, –(alkylene–O)$_n$–$(CH_2)_{n'}$–NHC(O)–$(CH_2)_{n'}$–$C(Me)_2$–S–S–$(CH_2)_{n''}$–NHC(O)–(alkylene–O)$_{n'''}$–alkylene–, –(alkylene–O)$_n$–alkylene–W–, –alkylene–C(O)–W–, –(alkylene–O)$_n$–alkylene–J–, –alkylene'–J–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–J–alkylene', –J–(alkylene–O)$_n$–alkylene–, –(alkylene–O)$_n$–alkylene–J–(alkylene–O)$_{n'}$–alkylene–J'–, –W–, –alkylene–W–, alkylene'–J–(alkylene–NMe)$_n$–alkylene–W–, –J–(alkylene–NMe)$_n$–alkylene–W–, –(alkylene–O)$_n$–alkylene–U–alkylene–C(O)–, –(alkylene–O)$_n$–alkylene–U–alkylene–; –J–alkylene–NMe–alkylene'–NMe–alkylene"–W–, and –alkylene–J–alkylene'–NMe–alkylene"–NMe–alkylene"'–W–;

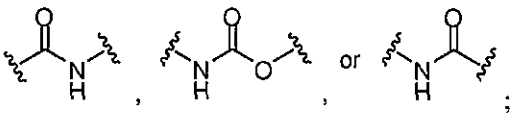


;

U has the structure of:



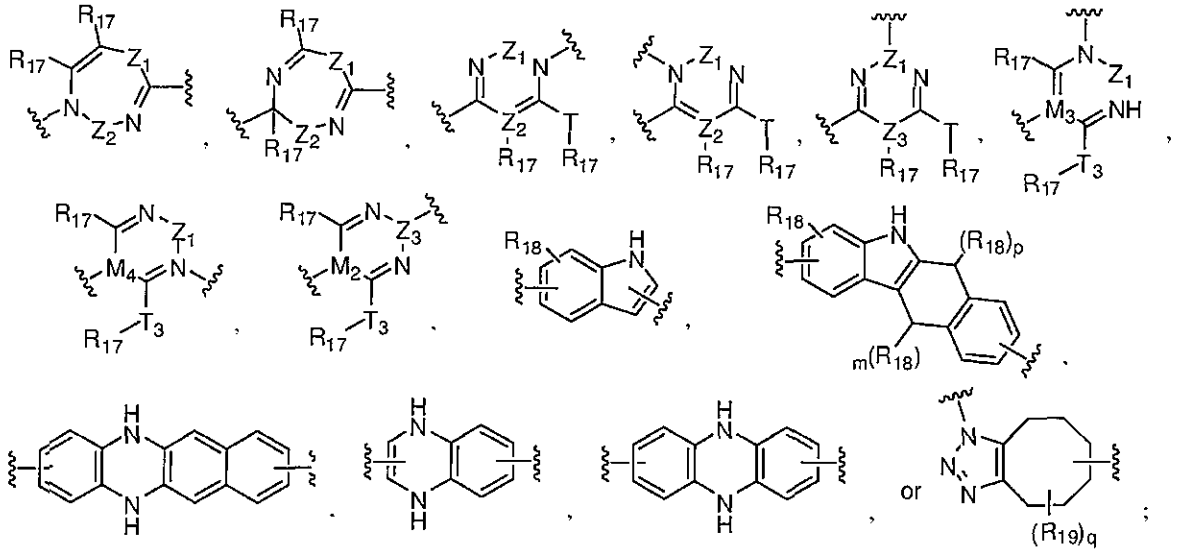
each J and J' independently have the structure of:



;

each n and n' are independently integers greater than or equal to one;

D has the structure of:



each R_{17} is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, alkylalkoxy, polyalkylene oxide, aryl, heteroaryl, alkaryl, aralkyl, -(alkylene)-ON(R")$_2$, -(alkylene)-C(O)SR", -(alkylene)-S-S-(aryl), -C(O)R", -C(O)$_2$R", or -C(O)N(R")$_2$, wherein each R" is independently hydrogen, alkyl, alkenyl, alkoxy, aryl, heteroaryl, alkaryl, or aralkyl;

each Z_1 is a bond, $CR_{17}R_{17}$, O, S, NR', $CR_{17}R_{17}$-$CR_{17}R_{17}$, $CR_{17}R_{17}$-O, O-$CR_{17}R_{17}$, $CR_{17}R_{17}$-S, S-$CR_{17}R_{17}$, $CR_{17}R_{17}$-NR', or NR'-$CR_{17}R_{17}$;

each R' is H, or alkyl;

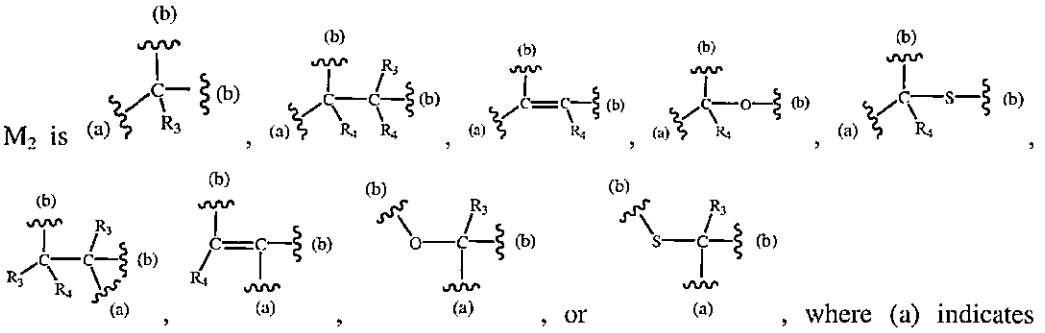
each Z_2 is selected from the group consisting of a bond, -C(O)-, -C(S)-, C_1-C_3 alkylene, C_1-C_3 alkenylene, and heteroalkyl;

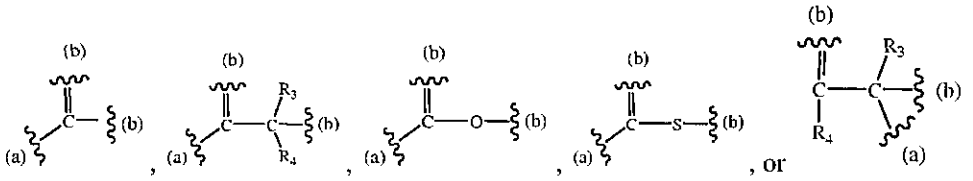
each Z_3 are independently selected from the group consisting of a bond, C_1-C_4 alkylene, C_1-C_4 alkenylene, heteroalkyl, -O-, -S-, -C(O)-, -C(S)-, and -N(R')-;

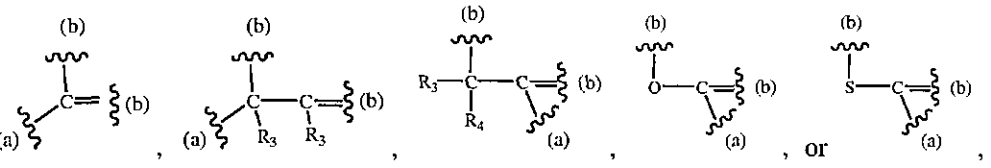
each T_3 is a bond, C(R'')(R''), O, or S; with the proviso that when T_3 is O or S, R'' cannot be halogen;

each R'' is H, halogen, alkyl, or cycloalkyl;

m and p are 0, 1, 2, or 3, provided that at least one of m or p is not 0;

M_2 is , where (a) indicates bonding to the B group and (b) indicates bonding to respective positions within the heterocycle group;

M_3 is , where (a) indicates bonding to the B group and (b) indicates bonding to respective positions within the heterocycle group;

M_4 is , where (a) indicates bonding to the B group and (b) indicates bonding to respective positions within the heterocycle group;

each R_{19} is independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, ester, ether, thioether, aminoalkyl, halogen, alkyl ester, aryl ester, amide, aryl amide, alkyl halide, alkyl amine, alkyl sulfonic acid, alkyl nitro, thioester, sulfonyl ester, halosulfonyl, nitrile, alkyl nitrile, and nitro;

q is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11; and

each R_{16} is independently selected from the group consisting of hydrogen, halogen, alkyl, NO_2, and CN.