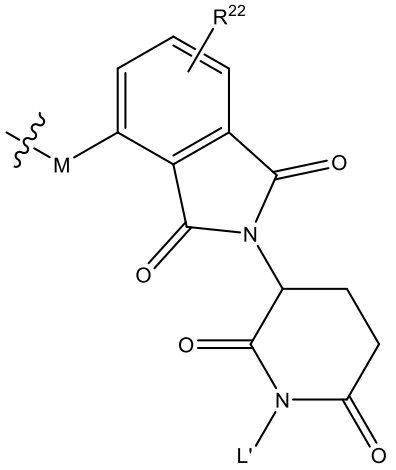
CLAIMS

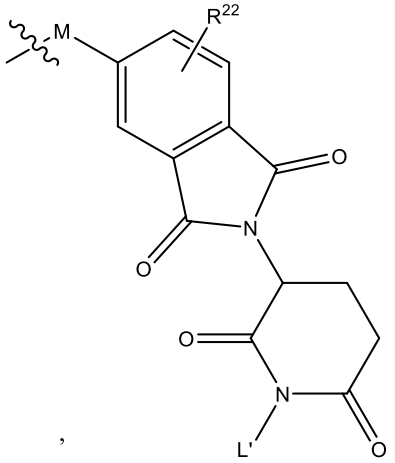
1. A compound of formula (I)

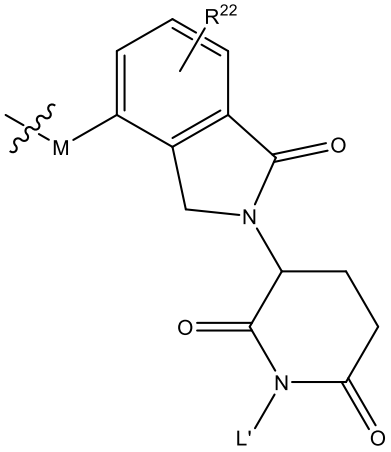
[MCL-1 ligand moiety] – linker – [ligase ligand moiety] (I)

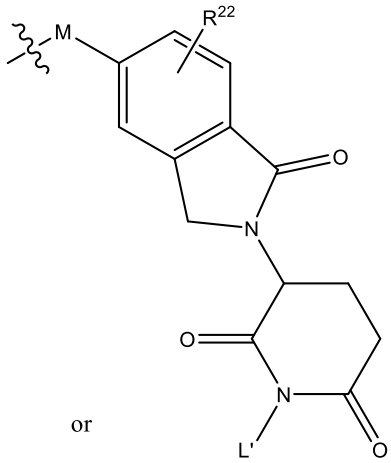
or a salt, solvate, hydrate, isomer or prodrug thereof,

in which **[ligase ligand moiety]** is:



,


,


or


in which

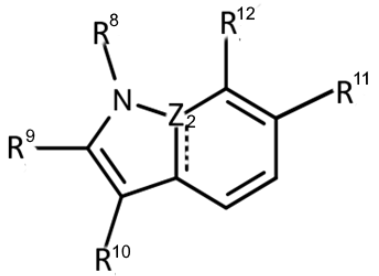
M is O, S or NH, or is absent;

 indicates attachment to **R18** of the linker;

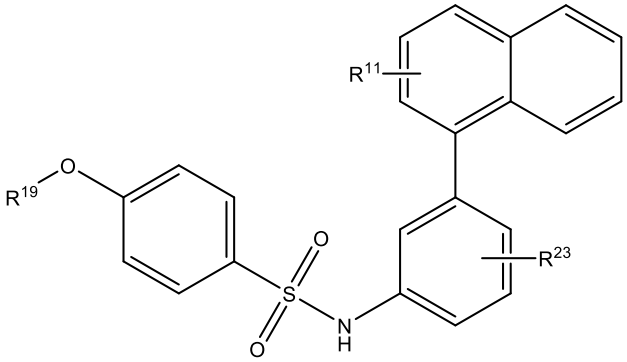
R22 is hydrogen, halogen or an amino group; and

L' is hydrogen, alkyl, benzyl, acetyl or pivaloyl;

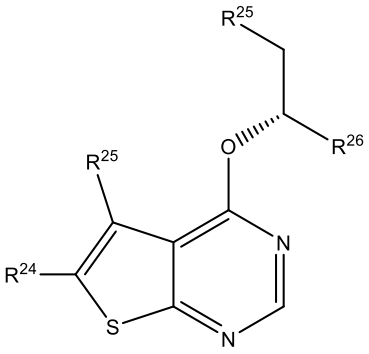
[MCL-1 ligand moiety] is a compound of Formula (A), Formula (B) or Formula (C)



(A)



(B)



(C)

in which

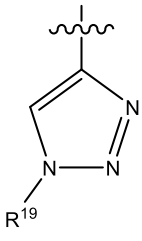
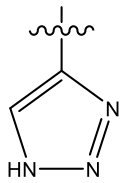
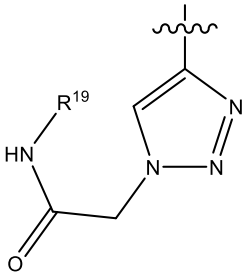
 is a single bond or a double bond;

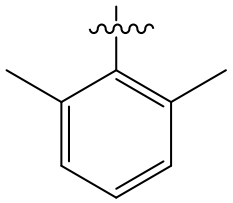
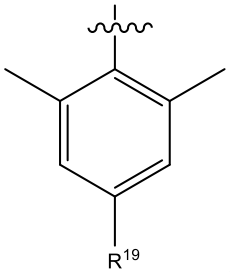
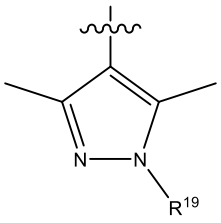
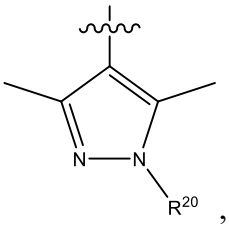
R8 is H, **R19**, or C_1-C_6 alkyl optionally substituted with morpholine;

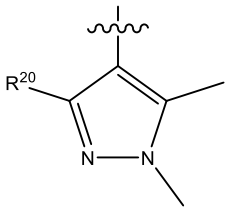
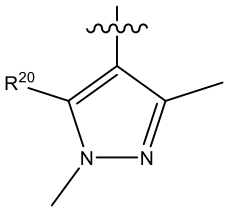
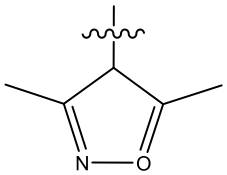
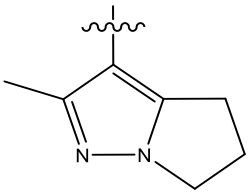
R9 is -C(O)OH, -C(O)OC_1-C_6alkyl; -C(O)NH_2; -C(O)O**R19** or -C(O)NH**R19**,

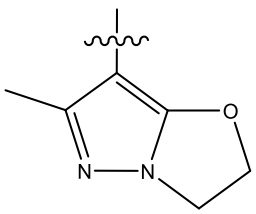
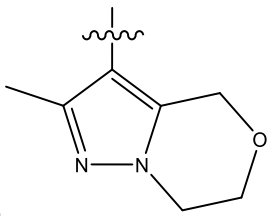
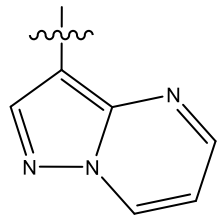
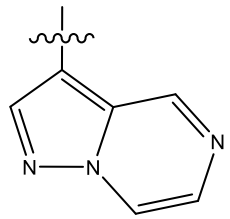
R10 is -C_{2-5}alkyl-O-R^{13} or -C_{2-5}alkyl-NMe-R^{13}, in which R^{13} is phenyl, naphthyl or tetraline, in which the phenyl, naphthyl or tetraline is optionally substituted with at least one substituent selected from halogen, C_1-C_6 alkyl and -O(C_1-C_6 alkyl); or in which the tetraline is optionally substituted with a bridging -CH_2- group; or in which the naphthyl is optionally substituted with -O- or -S-,

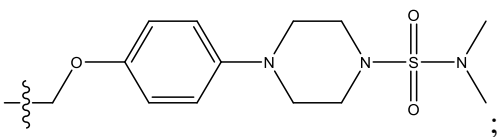
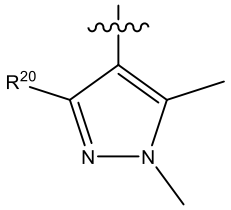
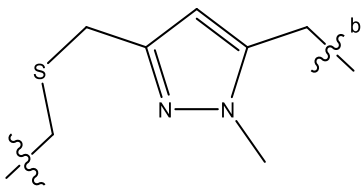
R11 is H, halogen or C_1-C_6 alkyl,

R^{12} is H,  ,  ,  ,

 ,  ,  ,  ,

 ,  ,  ,  ,

 ,  ,  , or  , in which **R**^{20} is Me, -CH_2-OMe, -CH_2-O-bromobenzaldehyde, or

 ; or when **R**^{12} is  and **R**^{10} is -O-naphthyl substituted with -O- or -S-, then **R**^{20} is  , in which

 indicates attachment to -O- or -S- of **R**^{10};

and in which

R^{19} is a bond connected to **R**^{14} of the linker;

$\mathbf{R^{23}}$ is -C(O)OH or -C(O)OC_1-C_6alkyl;

$\mathbf{Z_2}$ is N or C, in which when $\mathbf{Z_2}$ is N, then  is a single bond; and when $\mathbf{Z_2}$ is C, then  is a double bond,

$\mathbf{R^{24}}$ is furan optionally substituted with at least one halogen,

each $\mathbf{R^{25}}$ is independently phenyl substituted with -O$\mathbf{R^{28}}$ and optionally further substituted with at least one substituent selected from halogen and C_1-C_6 alkyl;

$\mathbf{R^{26}}$ is -C(O)O$\mathbf{R^{19}}$ or -C(O)NH$\mathbf{R^{19}}$; and

each $\mathbf{R^{28}}$ is independently -$C_{1\text{-}3}$alkyl-(N-alkyl piperazine) or -$C_{1\text{-}3}$alkyl-(N-haloalkylpyrazole)

and in which each of Formula (A), Formula (B) and Formula (C) contains a single $\mathbf{R^{19}}$**;**

and in which **[linker]** has the following formula

$\mathbf{R^{14}}$-$\mathbf{R^{15}}$-$\mathbf{R^{16}}$-$\mathbf{R^{17}}$-$\mathbf{R^{18}}$

in which

$\mathbf{R^{14}}$ is -$C_{1\text{-}6}$ alkyl, -$C_{2\text{-}6}$ alkenyl, -$C_{2\text{-}6}$ alkynyl, $C_{1\text{-}6}$ alkyl-N($C_{1\text{-}6}$ alkyl)-, -C(O)-, -SO_2- or is absent

$\mathbf{R^{15}}$ is cycloalkyl, heterocycloalkyl, aryl, heteroaryl, $C_{1\text{-}6}$ alkyl-NH-, -$C_{1\text{-}6}$ alkyl-N($C_{1\text{-}6}$ alkyl)-, -cycloalkyl-NH-, -heterocycloalkyl-NH- or is absent

$\mathbf{R^{16}}$ is -$C_{1\text{-}6}$ alkyl, -C(O)-, -C(O)-NH-, -C(O)O-, -CH_2-C(O)-, -CH_2-C(O)-NH-, -CH_2-C(O)O- or is absent

$\mathbf{R^{17}}$ is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

x is 1-10

y is 2-10

$\mathbf{R^{18}}$ is -$C_{1\text{-}6}$ alkyl, heterocycloalkyl, or is absent

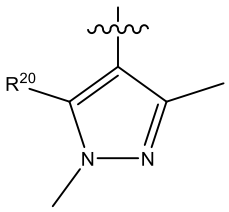
in which at least one of R^{14}-R^{18} is present

with the proviso that:

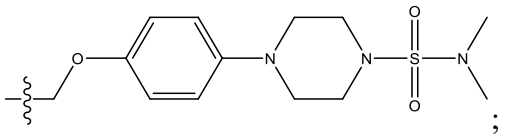
when

R^{10} is -C_3H_6-O-naphthyl,

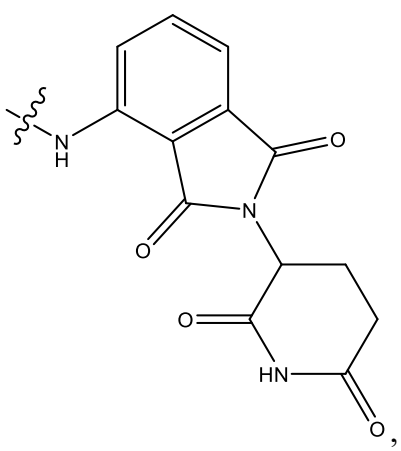
R^{12} is



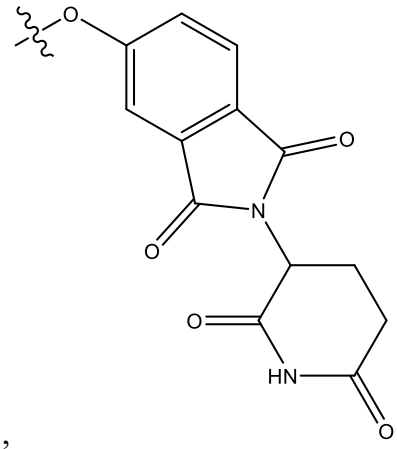
, and

R^{20} is  ;

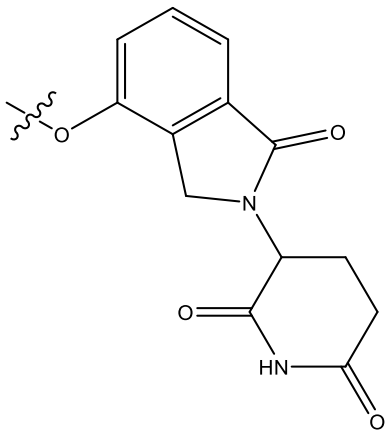
then **R^{9}** is -C(O)OH, -C(O)OC$_1$-C$_6$alkyl or -C(O)NH$_2$, and **[ligase ligand moiety]** is



,



or

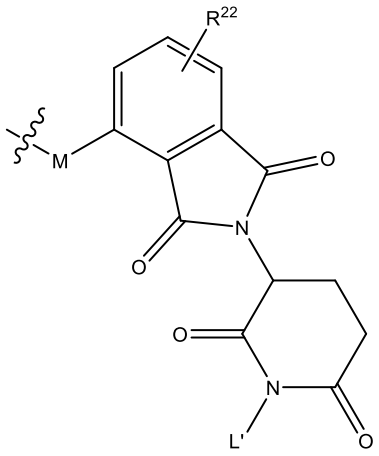
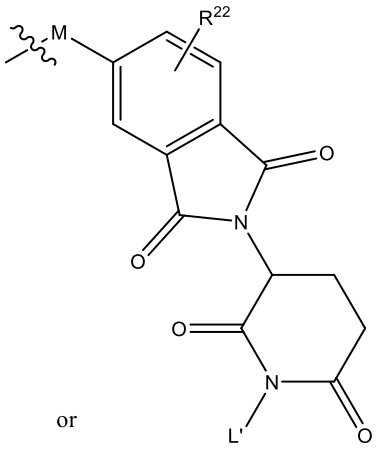


2. A compound according to Claim 1, in which **R^{22}** is hydrogen or an amino group, optionally in which **R^{22}** is hydrogen.

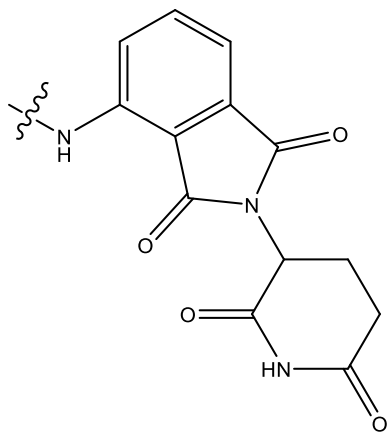
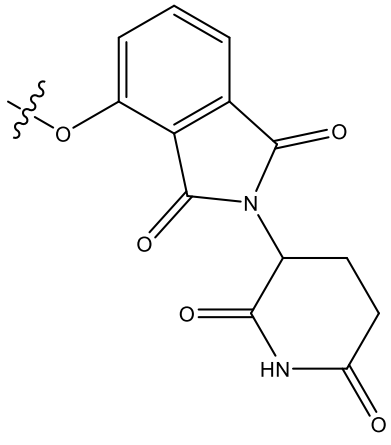
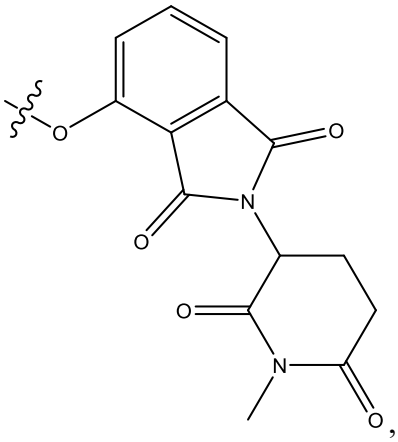
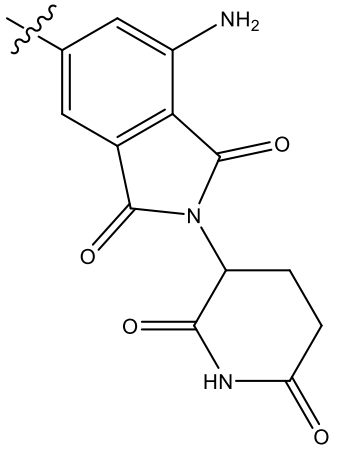
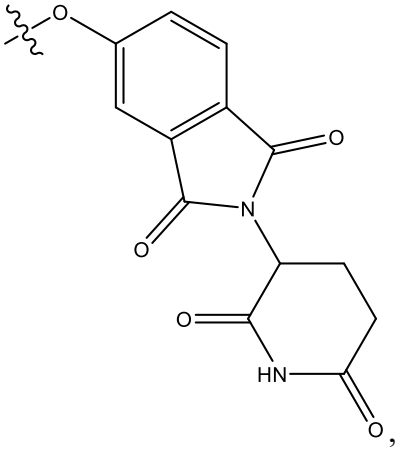
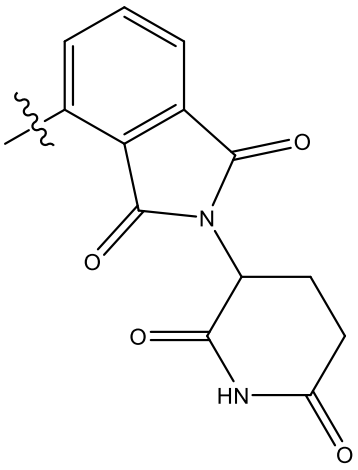
3. A compound according to Claim 1 or 2, in which **L'** is hydrogen or methyl, optionally in which **L'** is hydrogen.

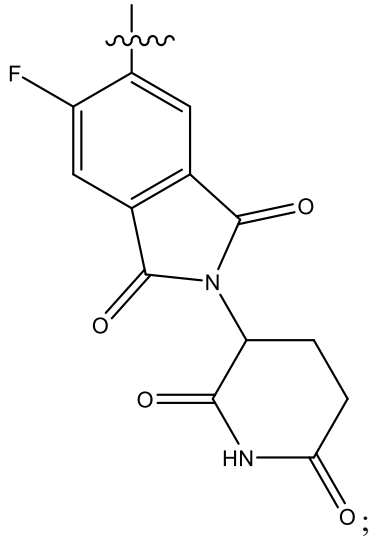
4. A compound according to Claim 1, 2 or 3, in which **M** is O or NH, or is absent.

5. A compound according to any preceding claim, in which **[ligase ligand moiety]** is:

(a)  or 

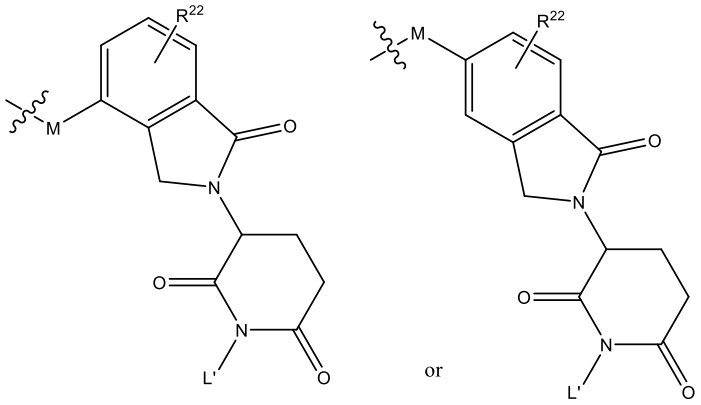
optionally in which **[ligase ligand moiety]** is


,

,

,

,

,

or

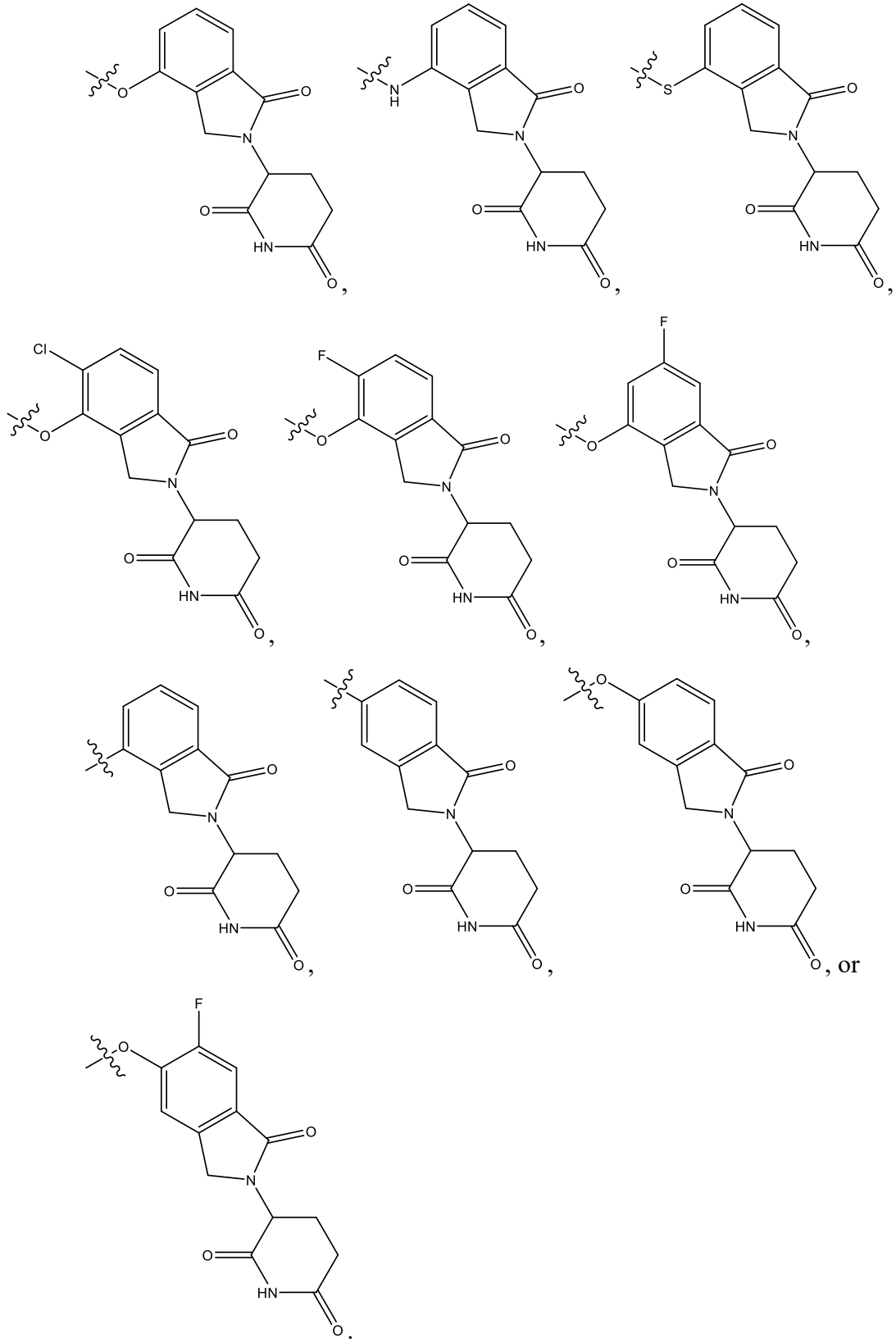


or

(b)



optionally in which **[ligase ligand moiety]** is



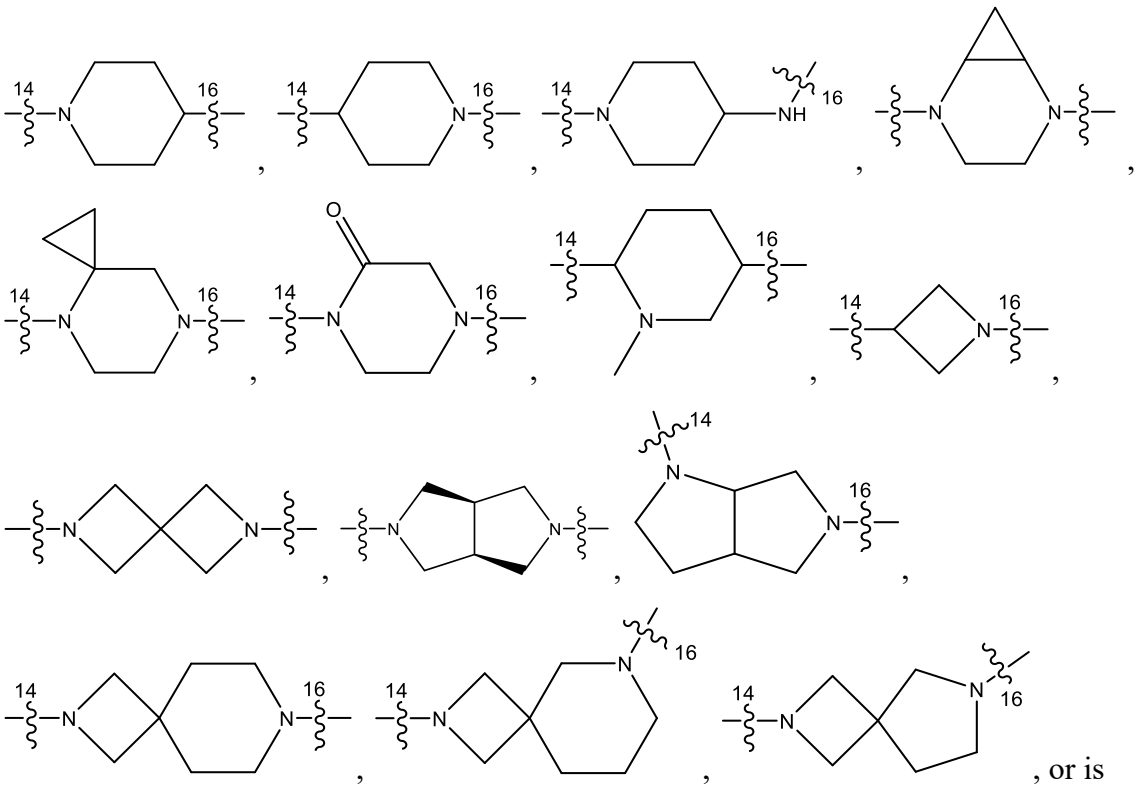
6. A compound according to any preceding claim, in which $\mathbf{R^{14}}$ is -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C(O)-, -SO_2- or is absent.

7. A compound according to any preceding claim, in which **R[15]** is cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_{1-6} alkyl-NH-, -cycloalkyl-NH- or is absent.

8. A compound according to any of Claims 1 to 5, in which

R[14] is -C_{1-6} alkyl, -C_{1-6} alkyl-N(Me)-, -SO_2- or is absent

R[15] is piperazine, bridged piperazine, piperazine N-oxide, piperazine cation, -C_{1-6} alkyl-NH-, -C_{1-6} alkyl-N(Me)-,



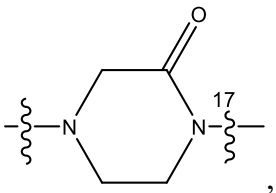
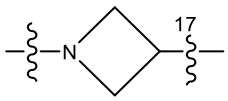
, or is absent,

in which  indicates attachment to **R[14]** and  indicates attachment to **R[16]**,

R[17] is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

x is 1-6

y is 2-6

R[18] is -C_{1-6} alkyl, piperazine,  ,  , or is absent,

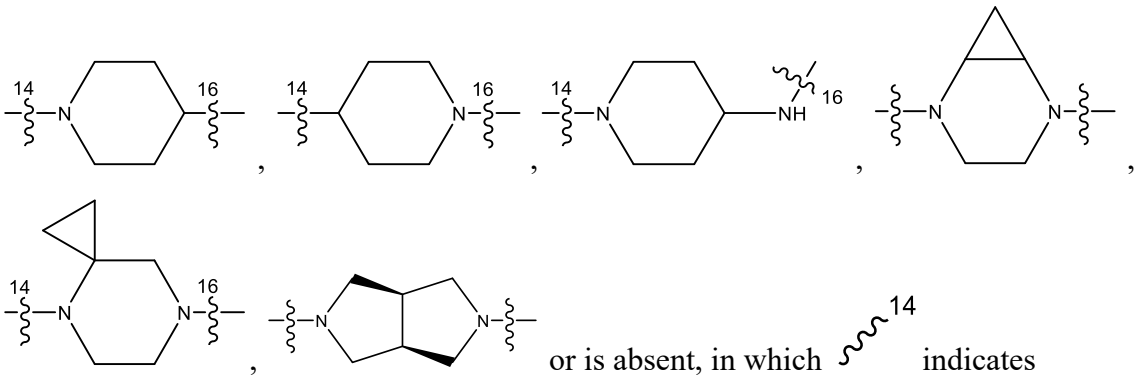
in which  indicates attachment to **R**[17],

in which at least one of **R**[14]-**R**[18] is present.

9. A compound according to any preceding claim, in which

R[14] is -C_{1-6} alkyl, -SO_2- or is absent

R[15] is piperazine, bridged piperazine, piperazine N-oxide, piperazine cation, -C_{1-6} alkyl-NH-,



attachment to **R**[14] and  indicates attachment to **R**[16],

R[16] is -C_{1-6} alkyl, -C(O)-, -C(O)-NH-, -CH_2-C(O)-NH- or is absent

R[17] is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

x is 1-6

y is 2-6

R[18] is -C_{1-6} alkyl, piperazine, or is absent

in which at least one of R^{14}-R^{18} is present.

10. A compound according to any preceding claim, in which **R**[18] is -C_{1-6} alkyl or is absent.

11. A compound according to any preceding claim, in which when **R**[14] is -SO_2-, at least two of **R**[15]-**R**[18] are present, and at least one of **R**[15]-**R**[18] is not C_{1-6} alkyl.

12. A compound according to any preceding claim, in which

R[14] is -SO_2-

R[15] is -C_{1-6} alkyl-NH-

R[16] is -C(O)-

R[17] is $-CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$ or is absent

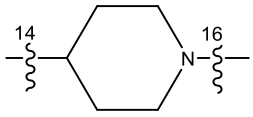
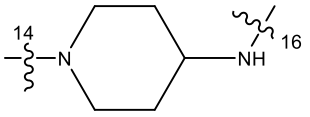
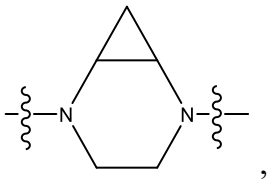
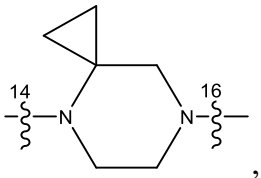
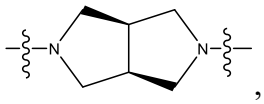
R[18] is $-C_{2\text{-}4}$ alkyl, optionally in which

R[15] is $-C_2$alkyl-NH-

x is 1 or 2

y is 1.

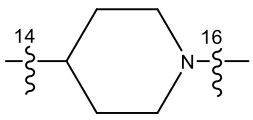
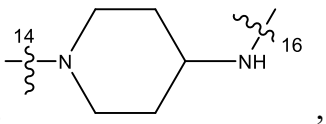
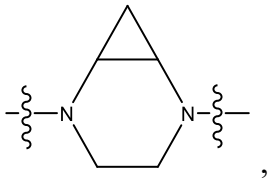
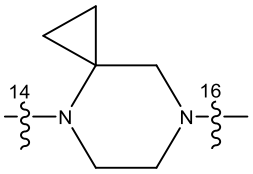
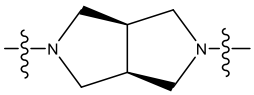
13. A compound according to any of Claims 1 to 10, in which

(a) when **R[15]** is piperazine, bridged piperazine, piperazine N-oxide, piperazine cation, $-C_{1\text{-}6}$ alkyl-NH-,  ,  ,  ,  , or  ,

then **R[14]** is $-C_{1\text{-}6}$ alkyl; or

(b) **R[14]** is $-C_{1\text{-}6}$ alkyl,

R[15] is piperazine, bridged piperazine, piperazine N-oxide,

 ,  ,  ,  or  ,

R[16] is -C(O)-, $-CH_2$-C(O)-NH-, or is absent

R[17] is $-CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

R[18] is $-C_{1\text{-}6}$ alkyl.

in which when **R[16]** and **R[17]** are absent, **R[18]** is -C_{3-6} alkyl;

optionally in which

R[14] is -C_2 alkyl,

x is 1, 2 or 6

y is 2; or

(c) **R[14]** is absent

R[15] is absent

R[16] is -C(O)-NH-, or is absent

R[17] is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

R[18] is -C_{1-6} alkyl.

14. A compound according to any preceding claim, in which at least one of **R[14]-R[18]** is not -C_{1-6} alkyl.

15. A compound according to Claim 13(c) or 14, in which

x is 1, 2 or 3

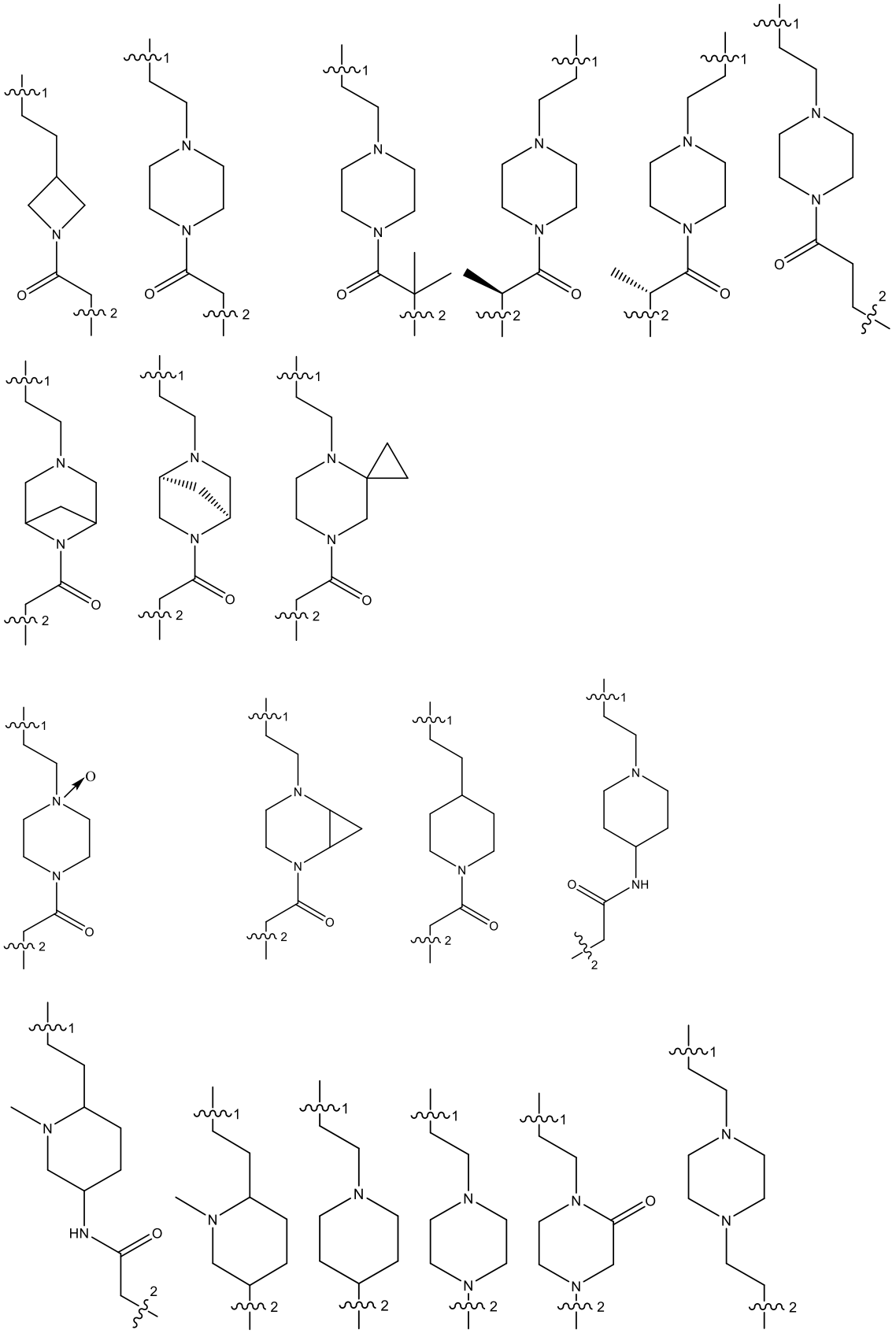
y is 2

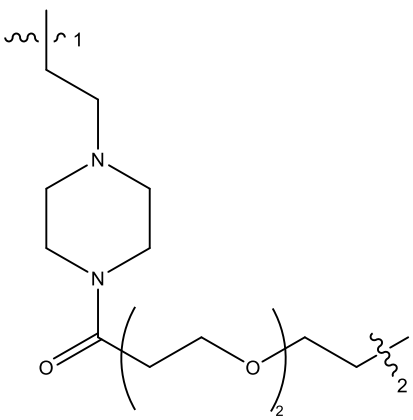
R[18] is -C_{2-6} alkyl.

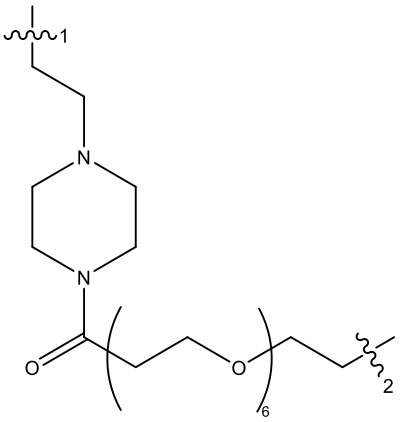
16. A compound according to any preceding claim, in which when **R[15]** is -C_{1-6} alkyl-NH-, at least one of **R[16]-R[18]** is present.

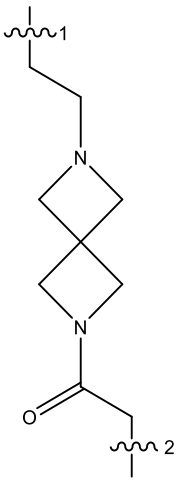
17. A compound according to any of Claims 1 to 15, in which when **R[17]** is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$ or $(C_3H_6\text{-}O)_x$, at least one of **R[14]-R[16]** and **R[18]** is present, in which at least one of **R[14]** and **R[18]** is not -C_{1-6} alkyl.

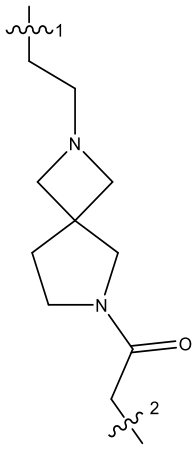
18. A compound according to any preceding claim, in which **[linker]** is selected from

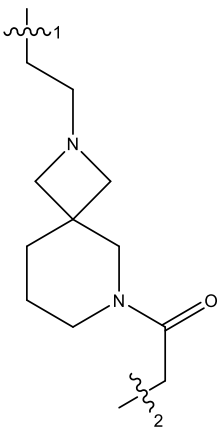


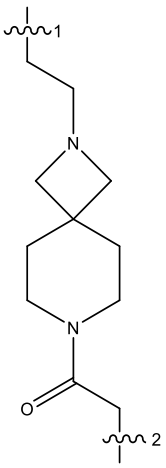


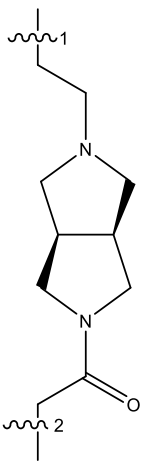


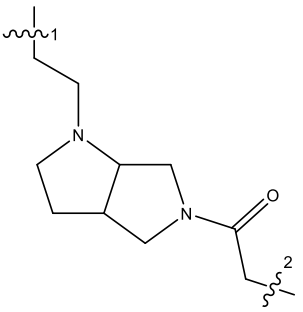


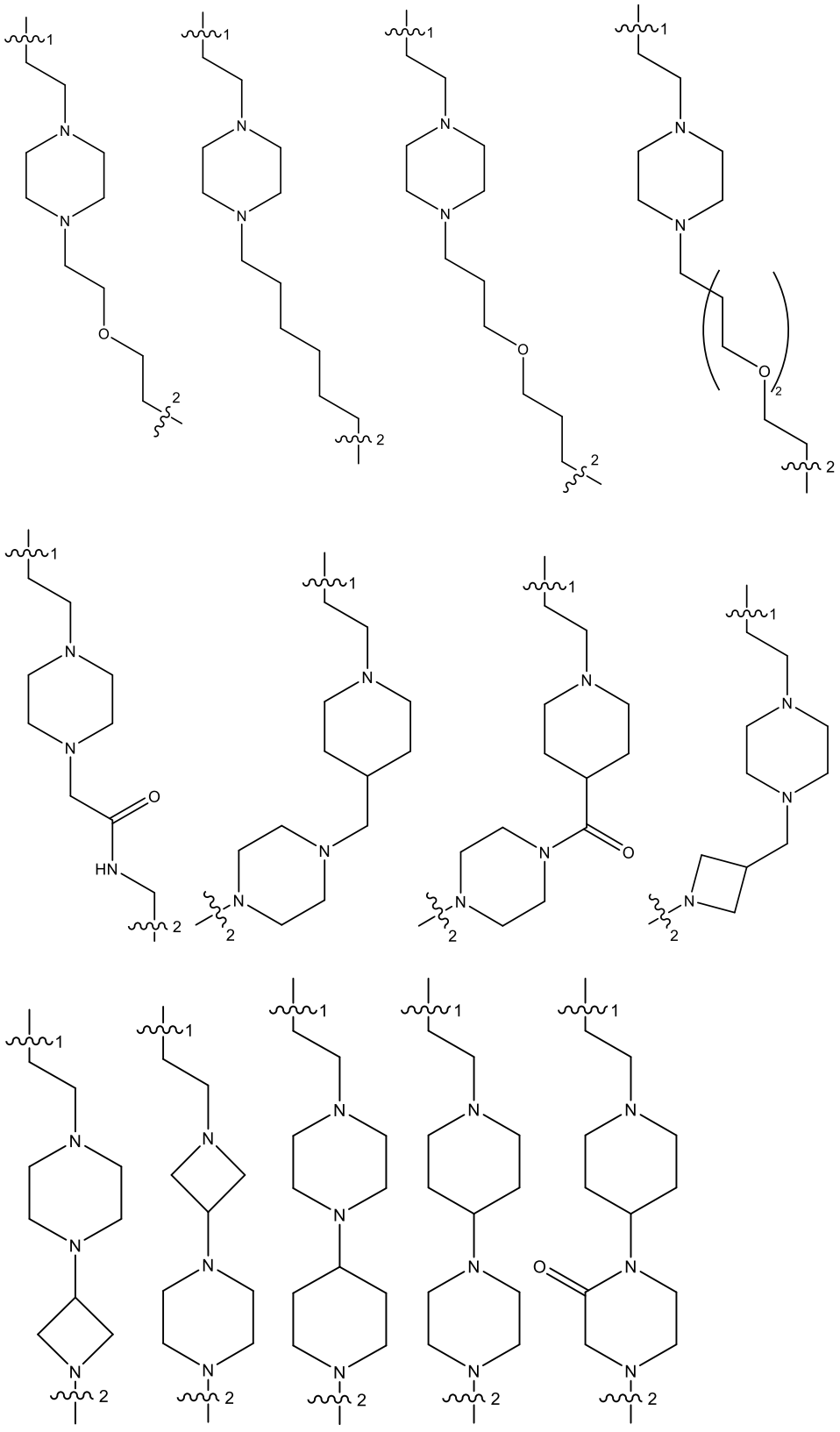


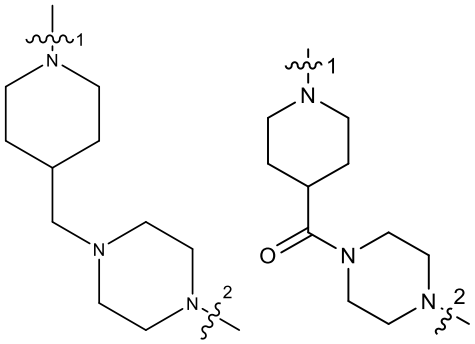


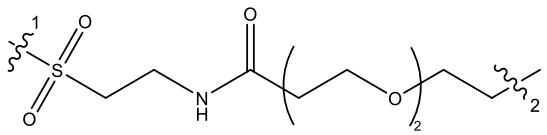


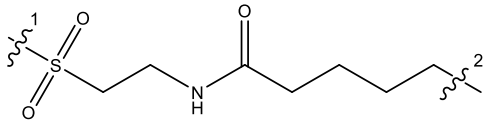


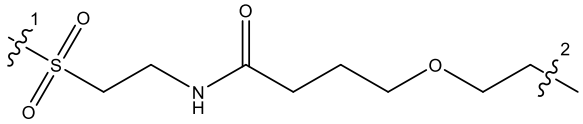


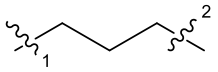


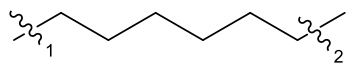


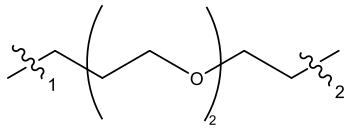


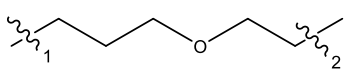


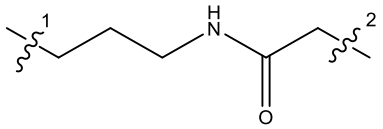


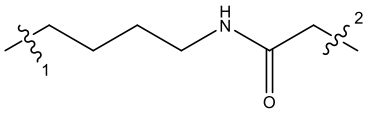


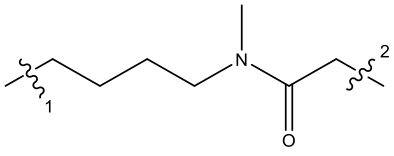


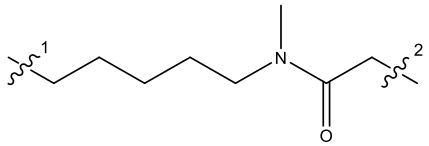


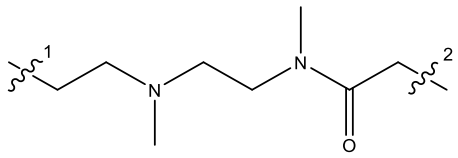


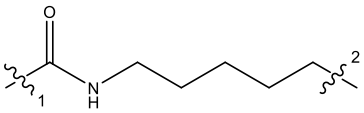


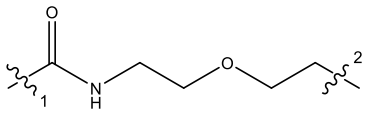


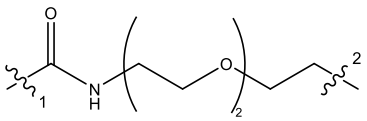




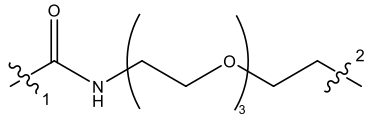








and



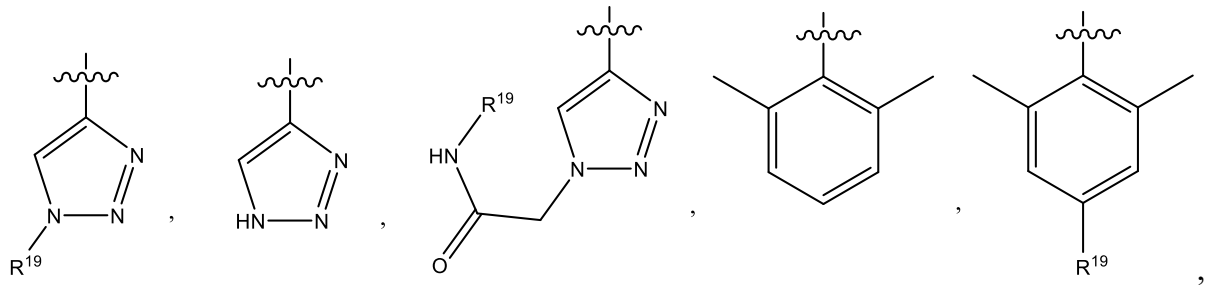
in which

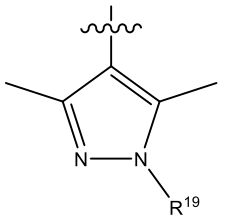
 indicates attachment to **[MCL-1 ligand moiety]** and

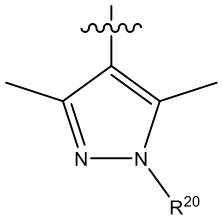
 indicates attachment to **[ligase ligand moiety]**.

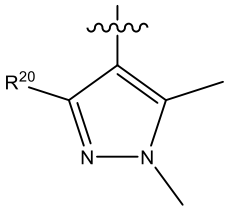
19. A compound according to any preceding claim, in which **R^{10}** is -$C_{2\text{-}5}$alkyl-O-R^{13}, in which R^{13} is phenyl, naphthyl or tetraline, in which the phenyl, naphthyl or tetraline is optionally substituted with at least one substituent selected from halogen, C_1-C_6 alkyl and -O(C_1-C_6 alkyl); or in which the naphthyl is optionally substituted with -O- or -S-.

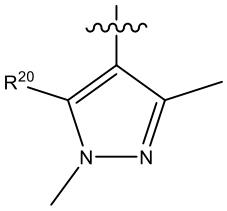
20. A compound according to any preceding claim, in which **R^{12}** is H,

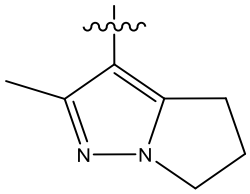


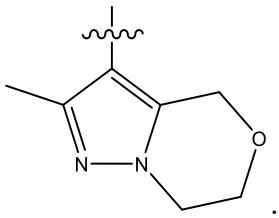


,


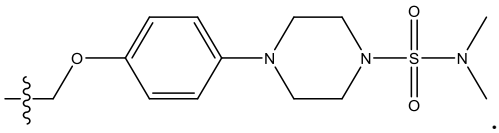
,


,


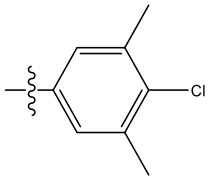
,


or


.

21. A compound according to any preceding claim, in which $\mathbf{R^{20}}$ is Me, $-CH_2-O-$ bromobenzaldehyde, or 

.

22. A compound according to any preceding claim in which when $\mathbf{R^8}$ is H, $\mathbf{R^{13}}$ is 

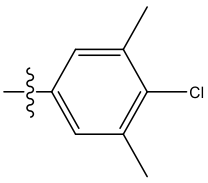
.

23. A compound according to any preceding claim, in which

$\mathbf{R^8}$ is H, $\mathbf{R^{19}}$, methyl, or $-CH_2CH_2$-morpholine;

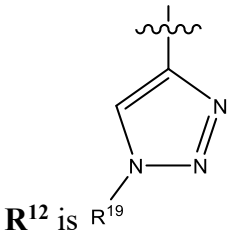
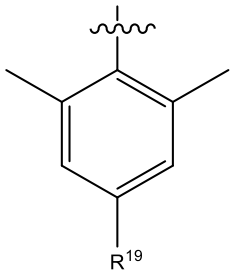
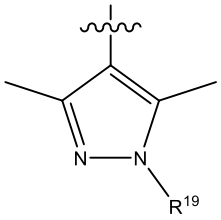
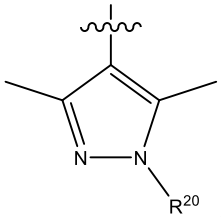
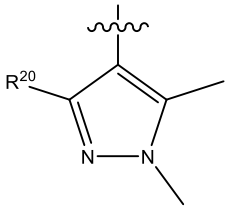
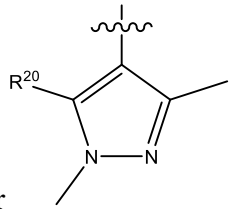
$\mathbf{R^9}$ is -C(O)OH or -C(O)NH$\mathbf{R^{19}}$,

$\mathbf{R^{10}}$ is $-C_3H_6O-R^{13}$,

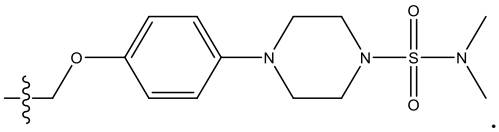
in which $\mathbf{R^{13}}$ is 

, tetraline, or naphthyl optionally substituted with fluorine;

$\mathbf{R^{11}}$ is H, Cl, F or methyl,

R[12] is  ,  ,  ,  ,  ,  , or

in which **R[20]** is Me, -CH_2-O-bromobenzaldehyde, or

 .

24. A compound according to any preceding claim in which:

(a) **Z_2** is N and  is a single bond; or

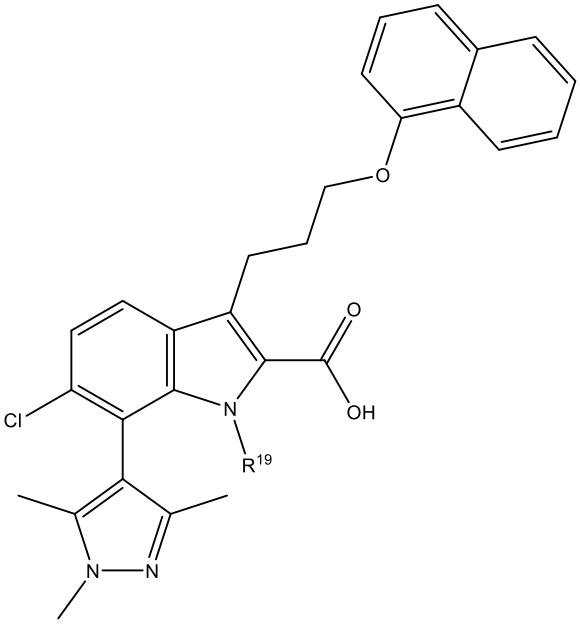
(b) **Z_2** is C and  is a double bond.

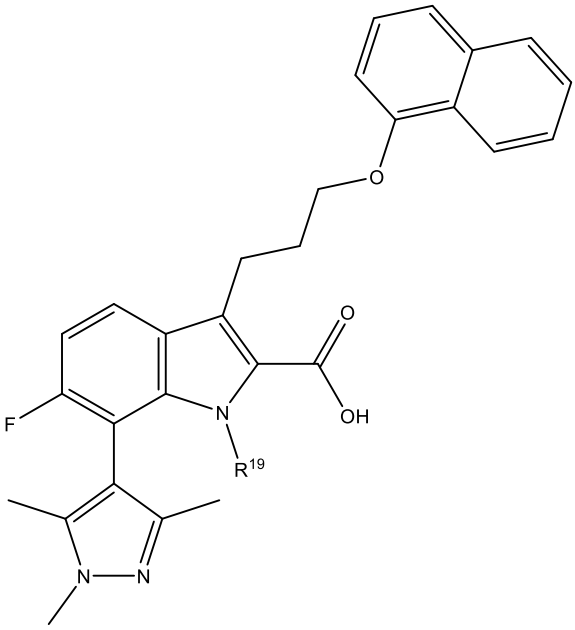
25. A compound according to any preceding claim, in which:

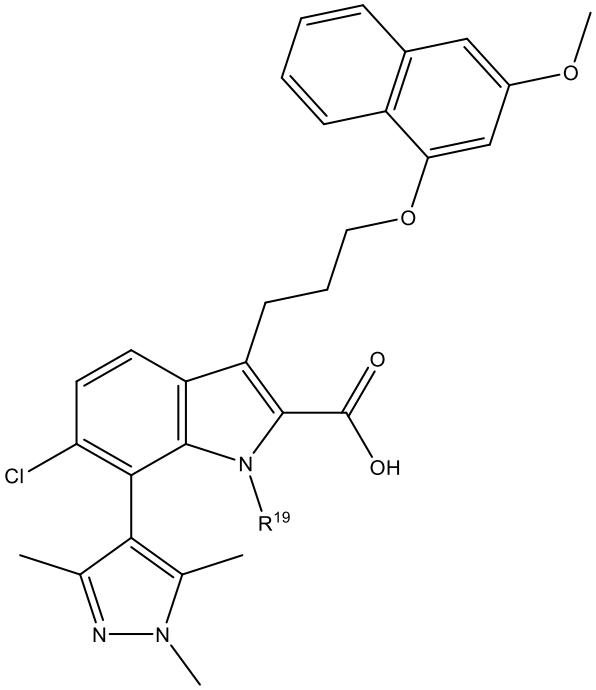
(a) **R[11]** is hydrogen; or

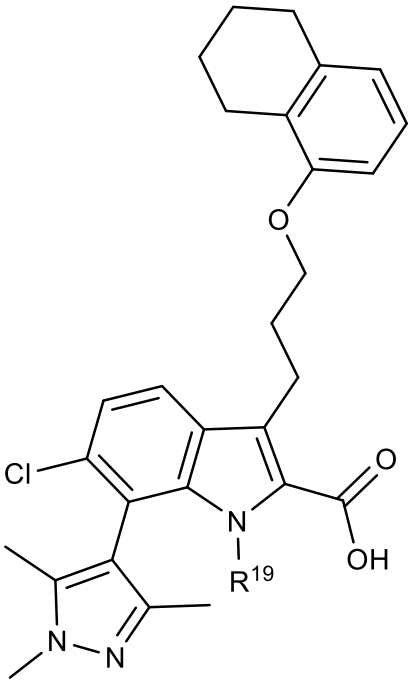
(b) **R[11]** is halogen or C_1-C_6 alkyl; optionally halogen.

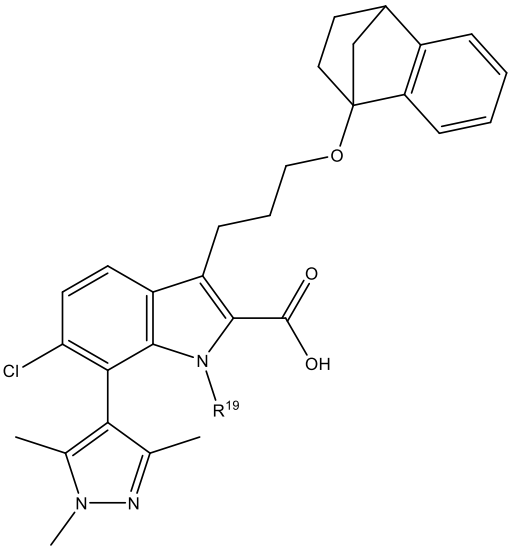
26. A compound according to any preceding claim, in which **[MCL-1 ligand moiety]** is selected from:

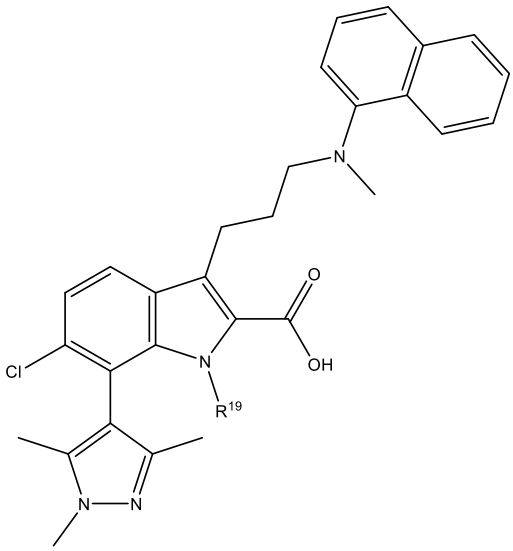

O
O
OH
Cl
N
R19
N
N

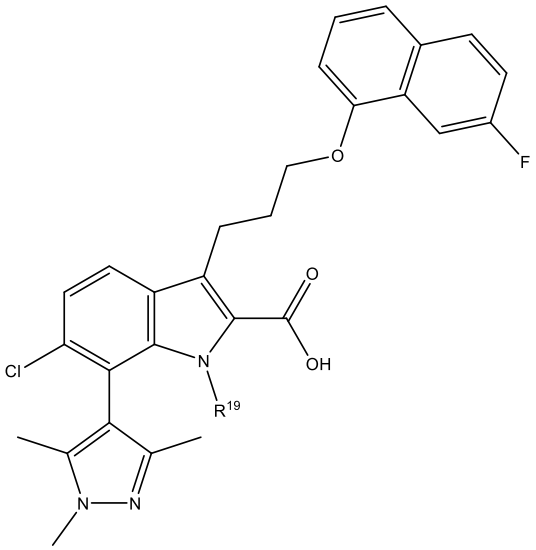

O
O
OH
F
N
R19
N
N

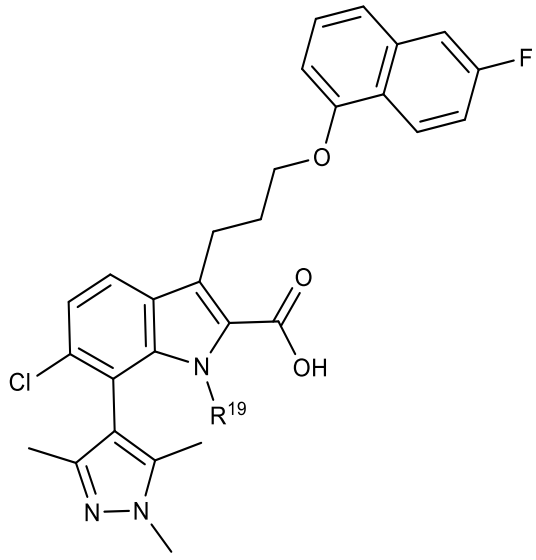

O
O
O
Cl
N
OH
R19
N
N

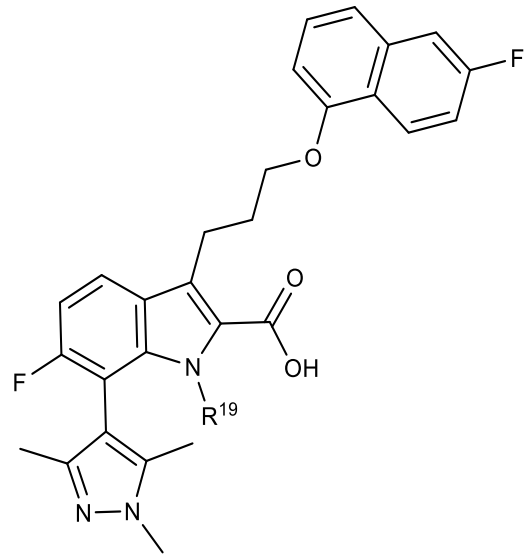

O
O
Cl
N
OH
R19
N
N

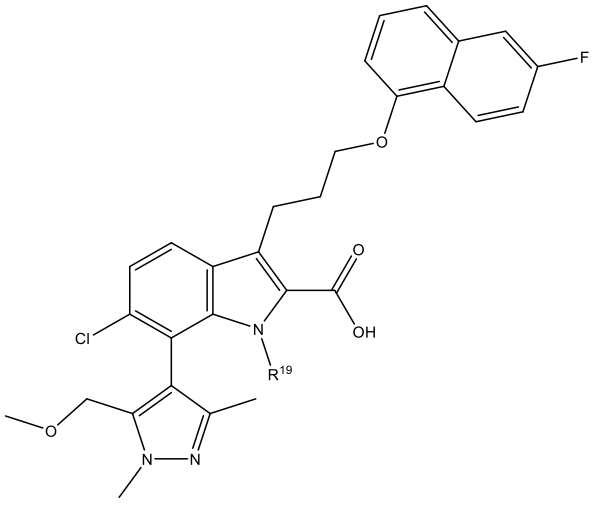

O
O
Cl
N
OH
R19
N
N

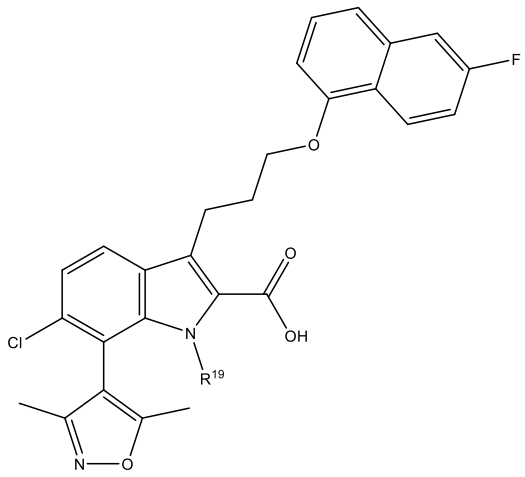

N
O
Cl
N
OH
R19
N
N

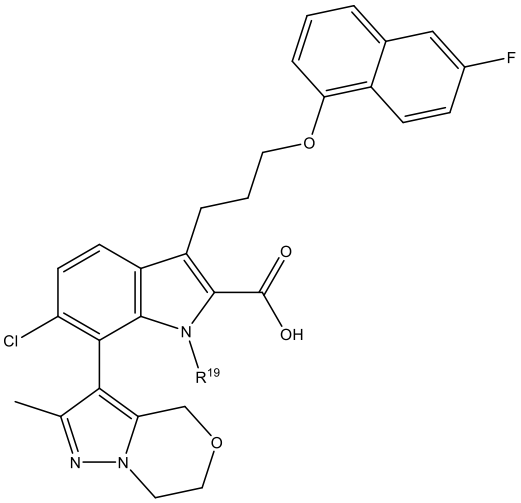

F
O
O
OH
Cl
N
R19
N
N

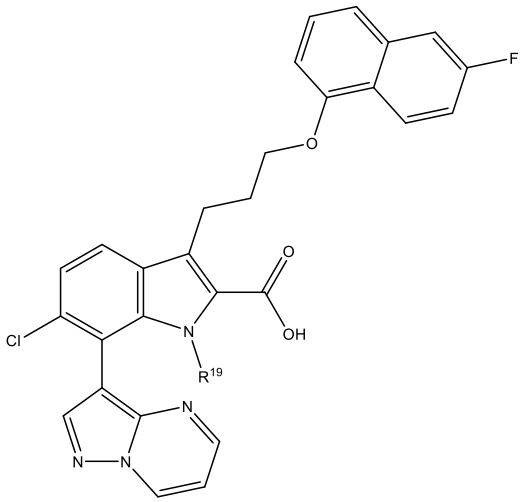

F
O
O
OH
Cl
N
R19
N
N

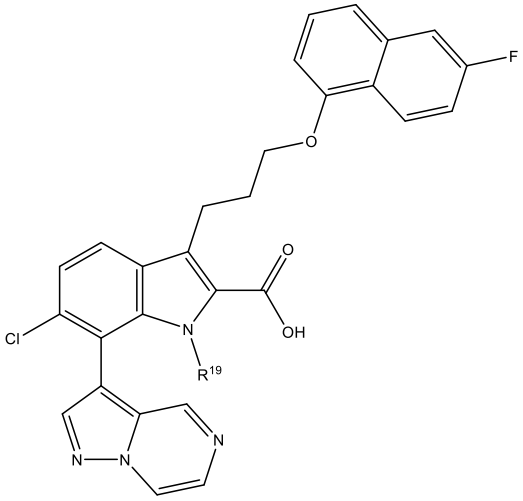

F
O
O
OH
F
N
R19
N
N

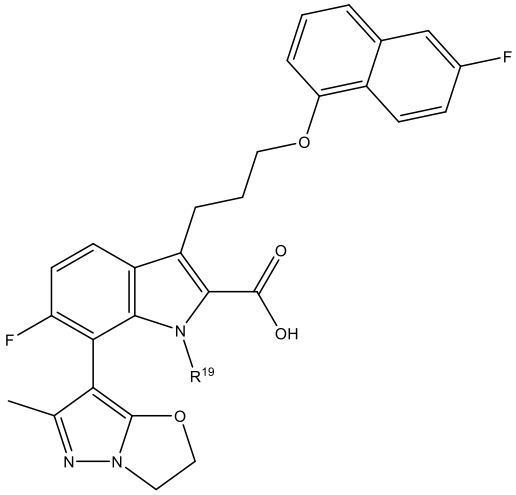

F
O
O
OH
Cl
N
R19
O
N
N

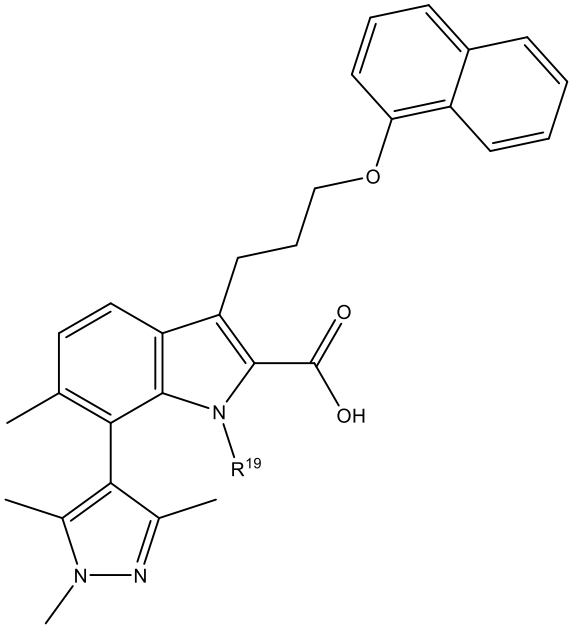

F
O
O
OH
Cl
N
R19
N
O

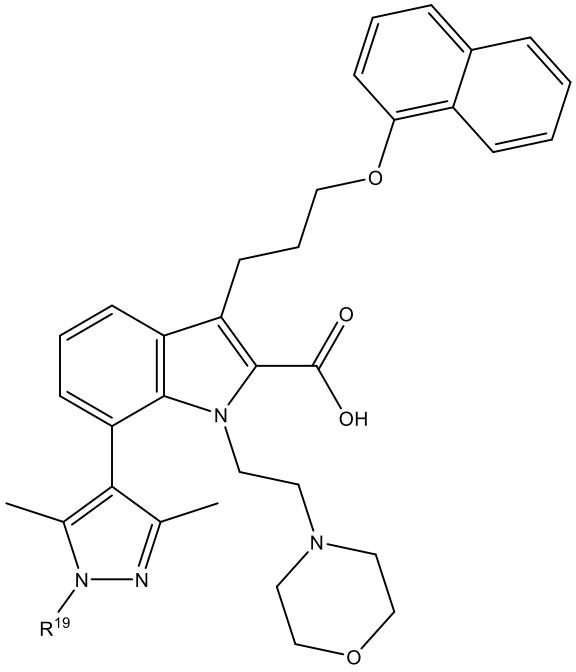

F
O
O
OH
Cl
N
R19
O
N
N

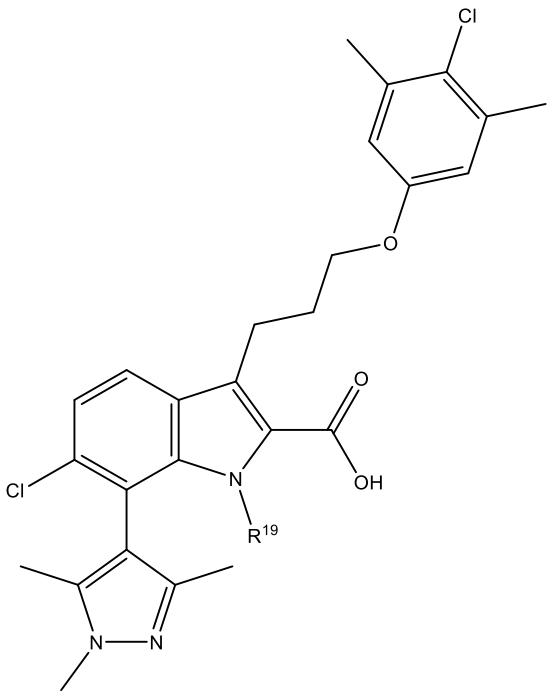

F
O
O
OH
Cl
N
R19
N
N
N

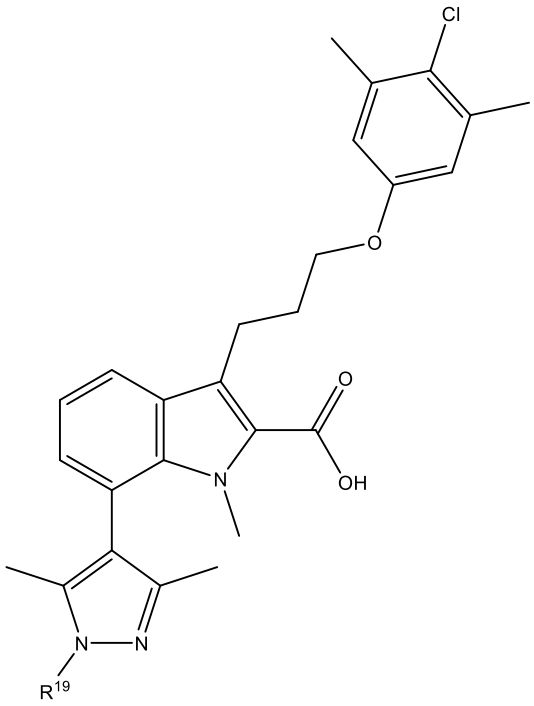

F
O
O
OH
Cl
N
R19
N
N
N

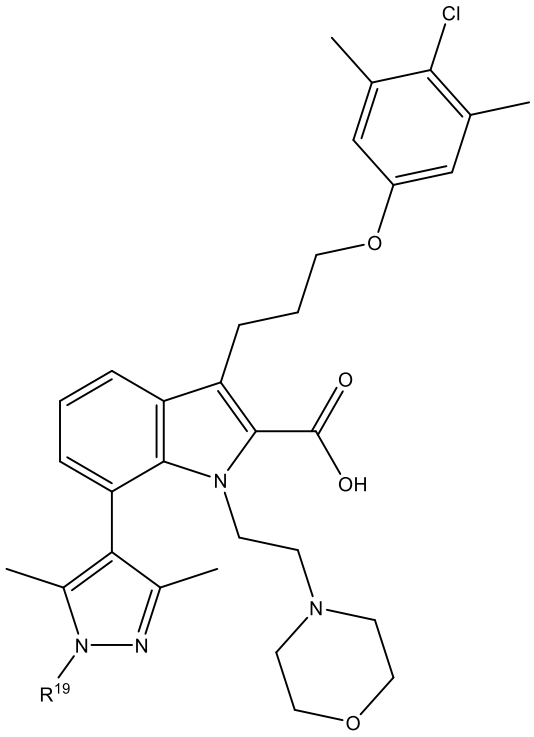

F
O
O
OH
F
N
R19
O
N
N

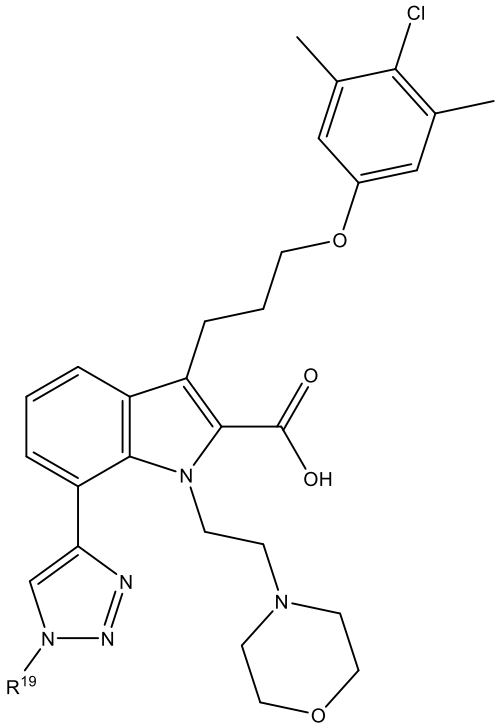

O
O
OH
N
R19
N
N

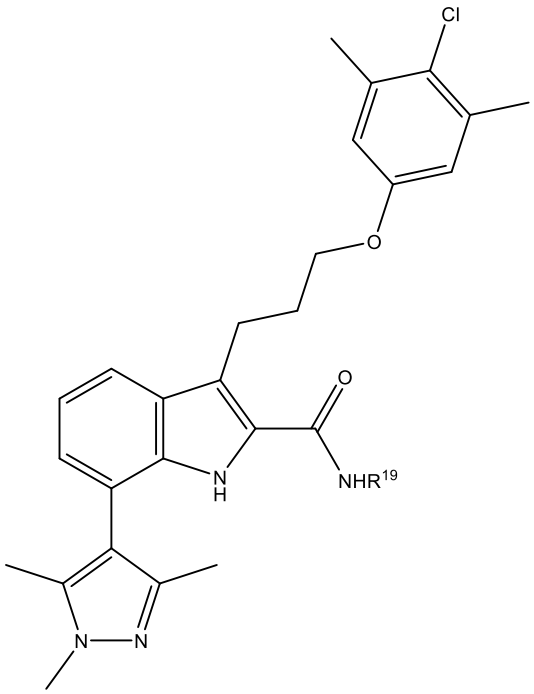

O
O
OH
N
N
N
N
R19
O

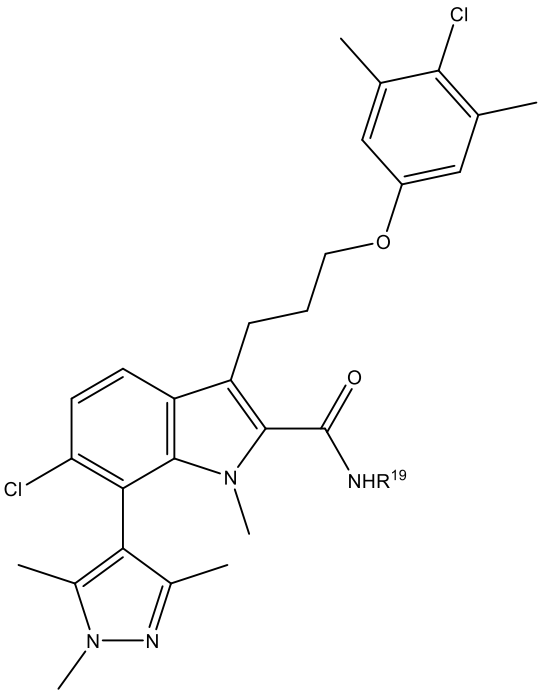

Cl
O
O
OH
Cl
N
R19
N
N

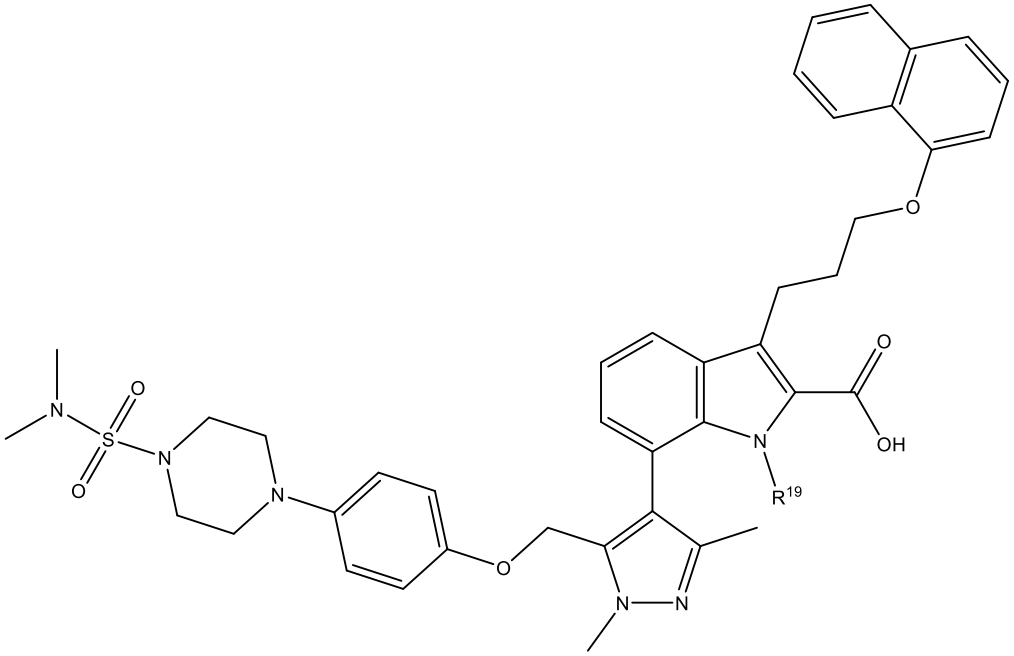

Cl
O
O
OH
N
N
N
R19

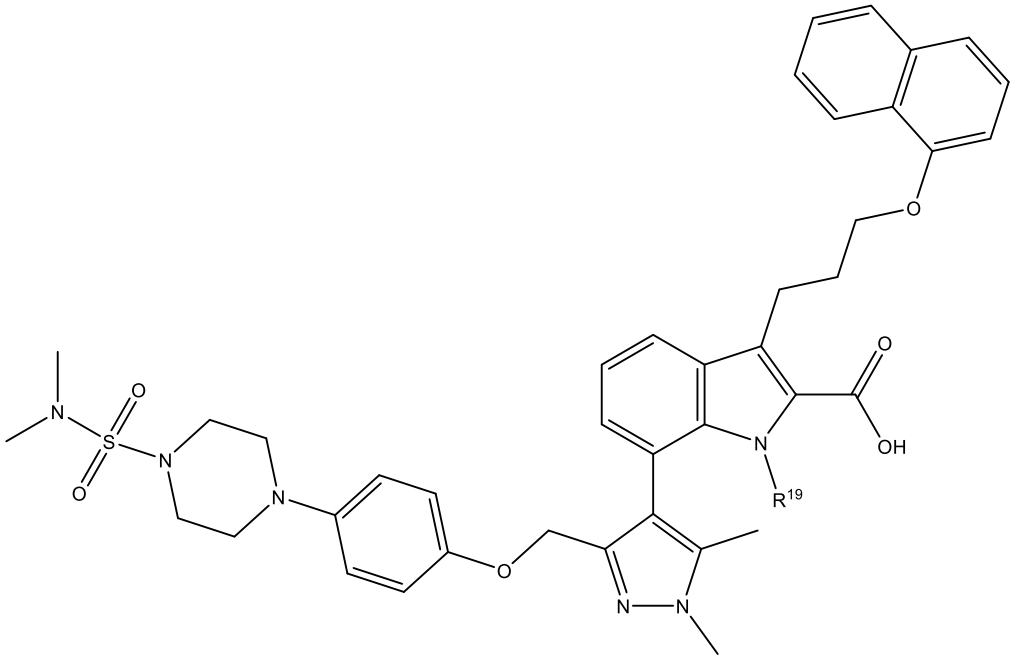

Cl
O
O
OH
N
N
N
R19
N
O

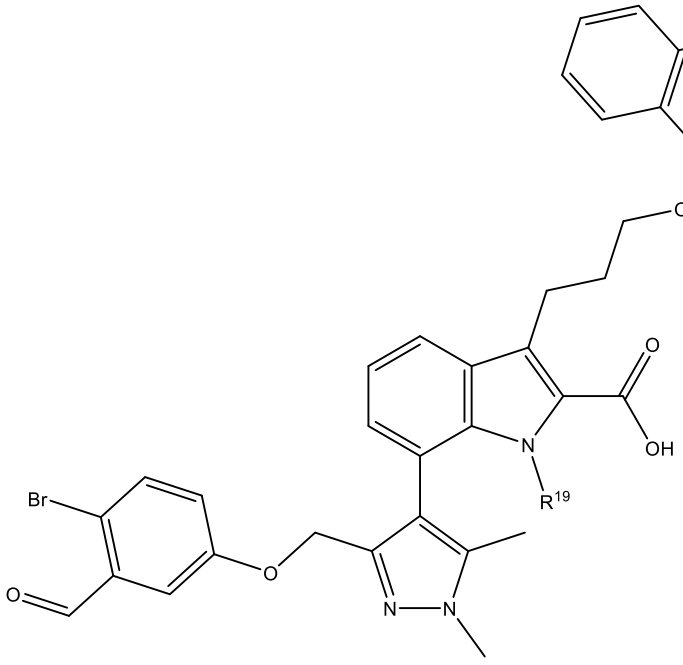

Cl
O
O
OH
N
N
N
R19
N
O

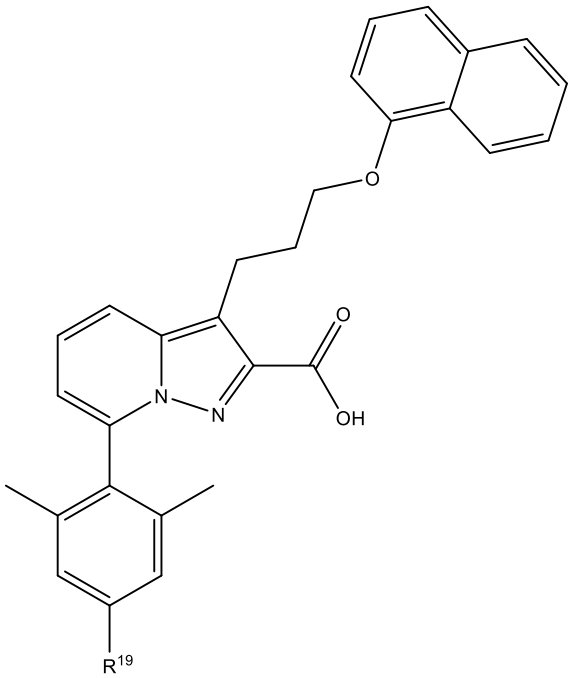

Cl
O
O
N
H
NHR19
N
N

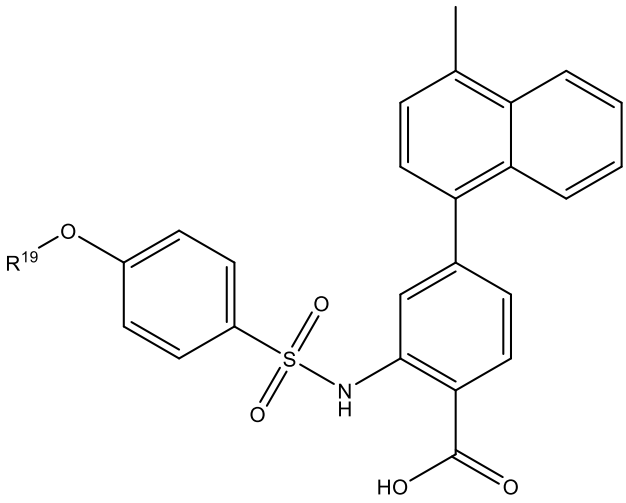

Cl
O
O
Cl
N
NHR19
N
N

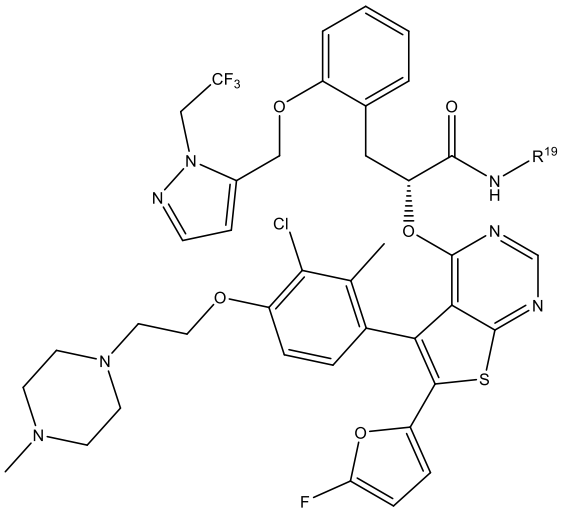

O
O
N
S
O
O
N
N
O
N
N
OH
R19


O
O
OH
N
R19
N
S
O
O
N
N
O
N
N

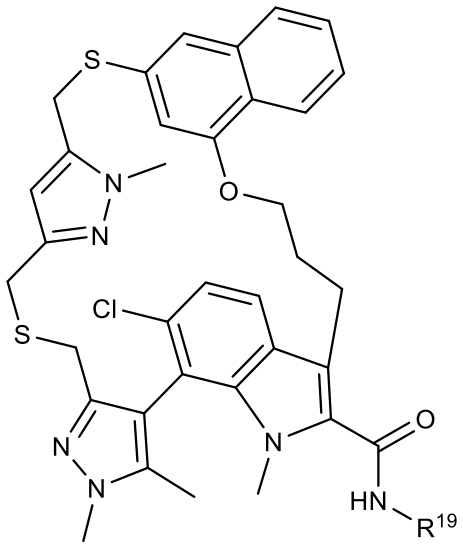

O
O
OH
N
R19
Br
O
O
N
N



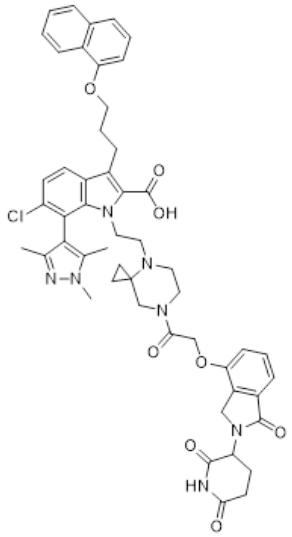
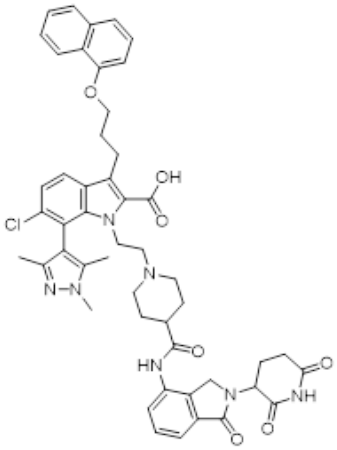
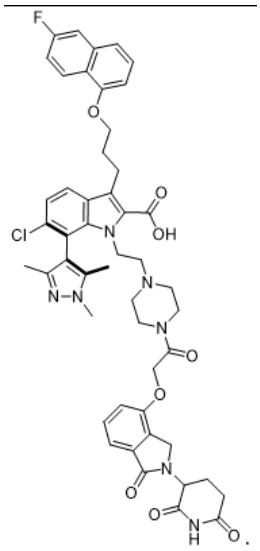
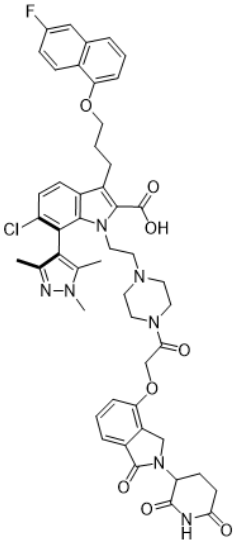
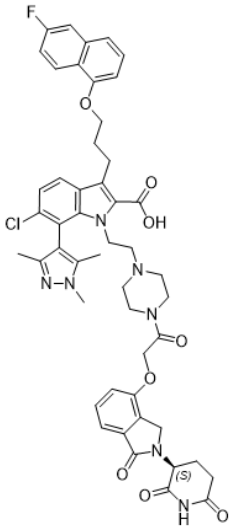
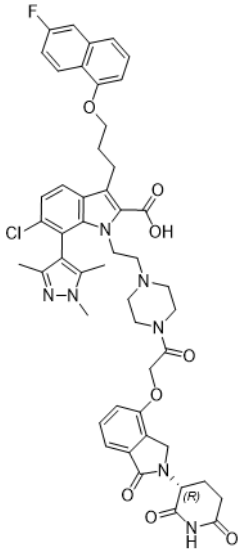


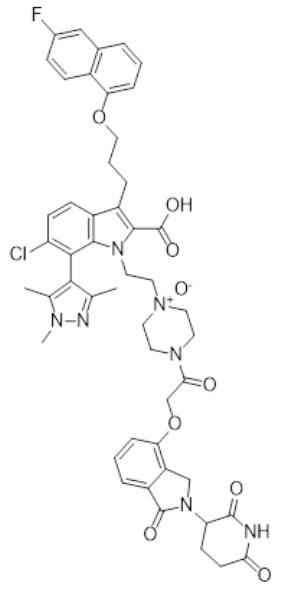
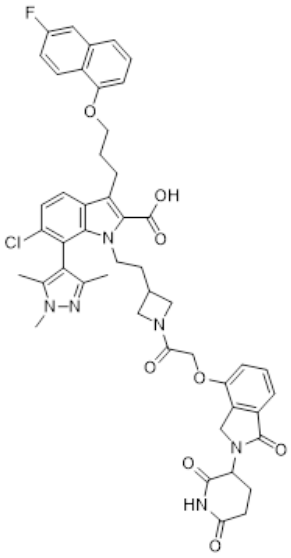
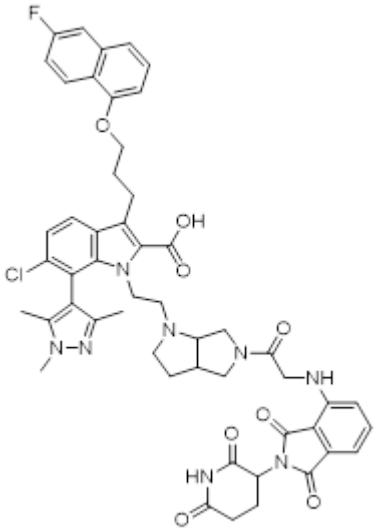
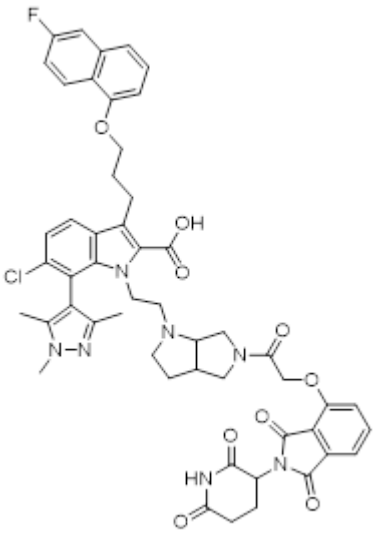
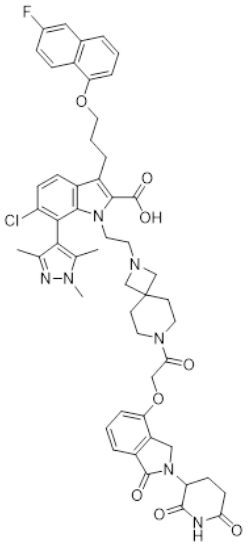
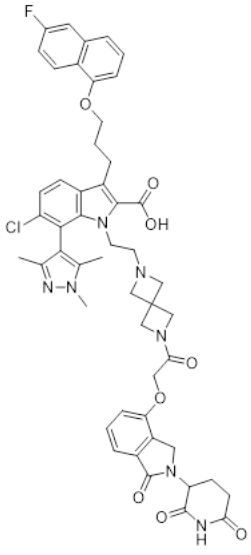


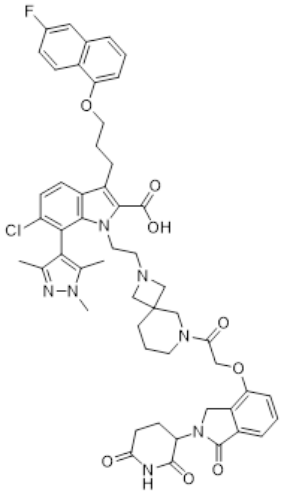
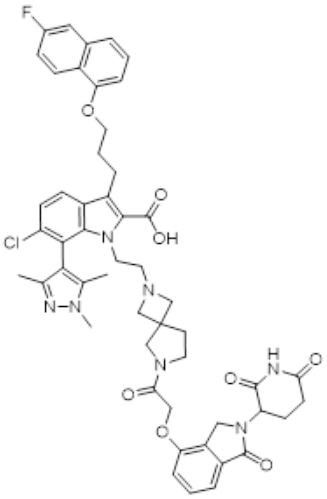
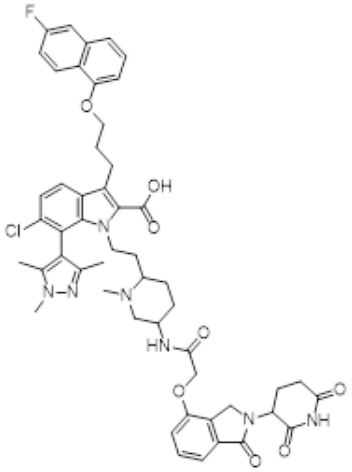
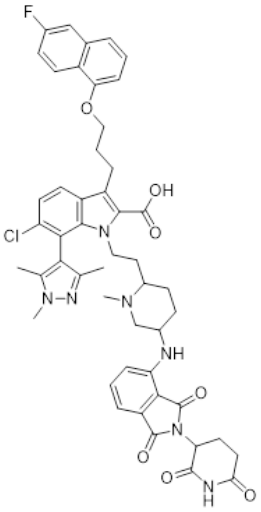
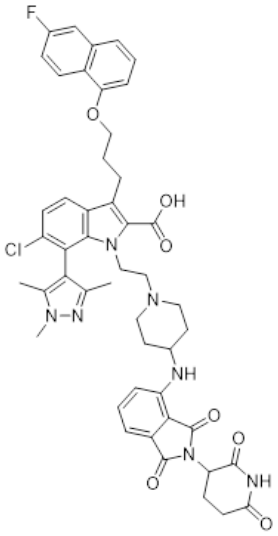
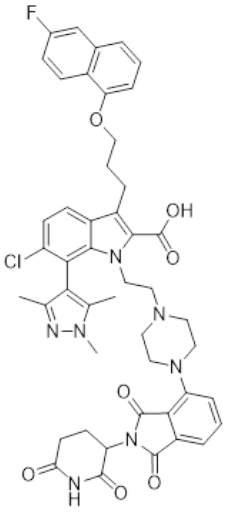
and

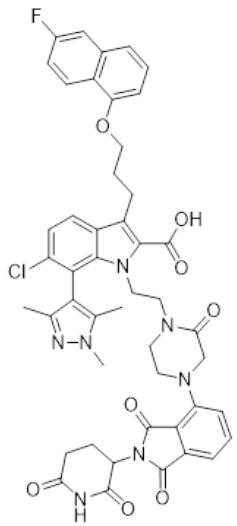
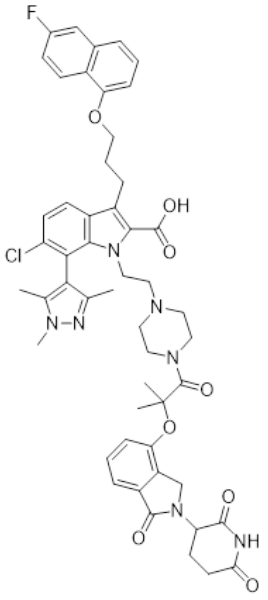
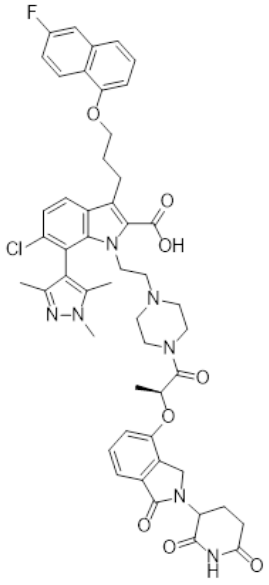
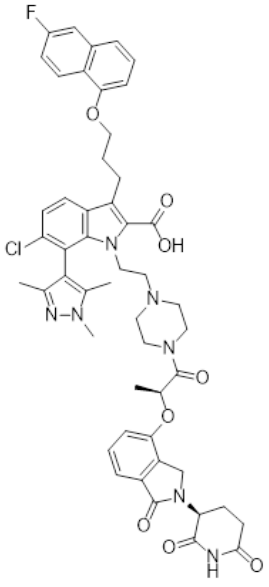
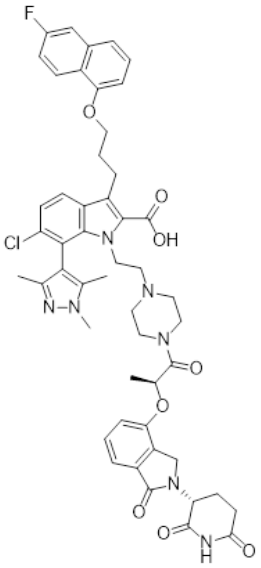
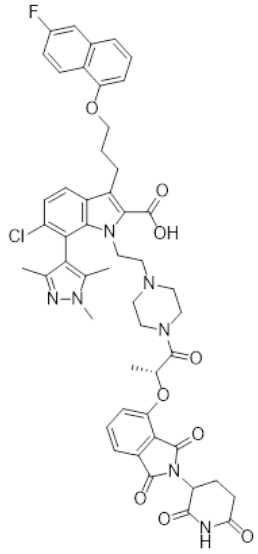


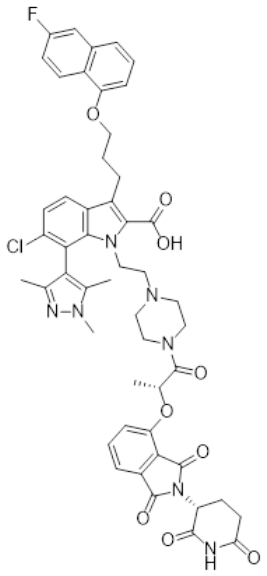
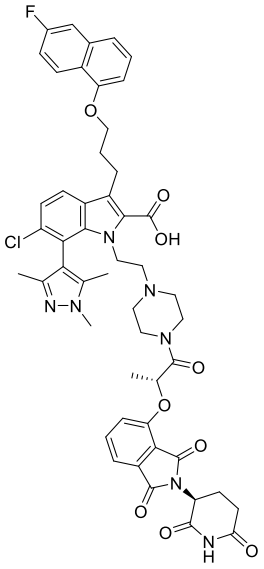
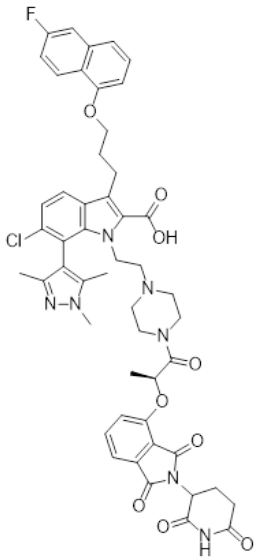
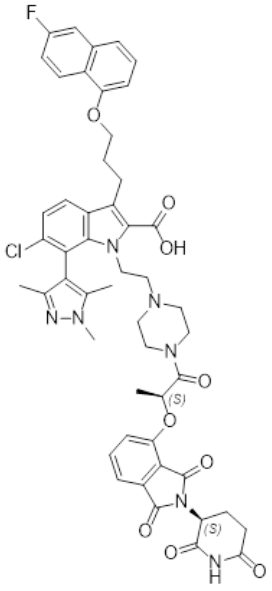
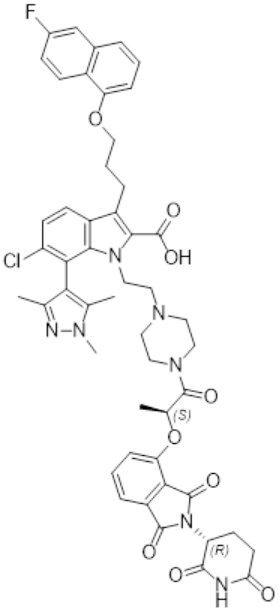
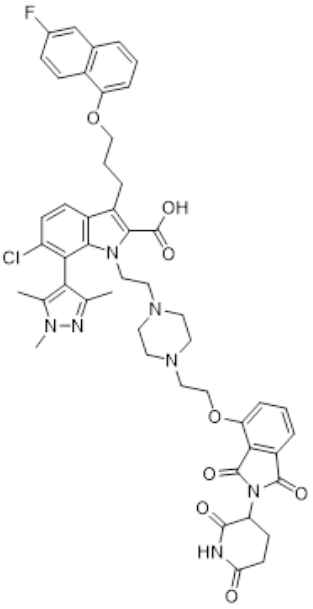
27. A compound according to Claim 1, which is selected from:

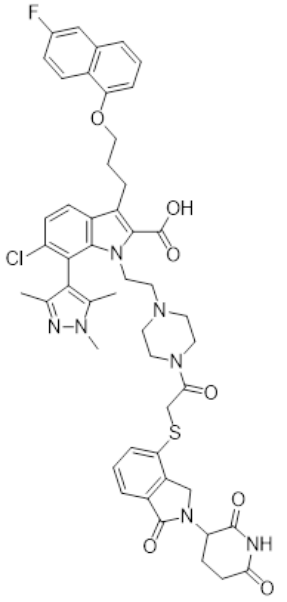
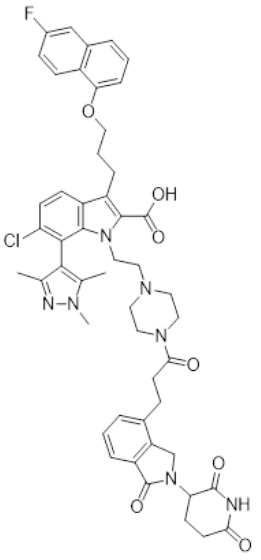
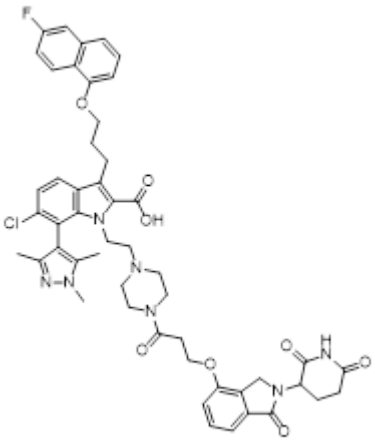
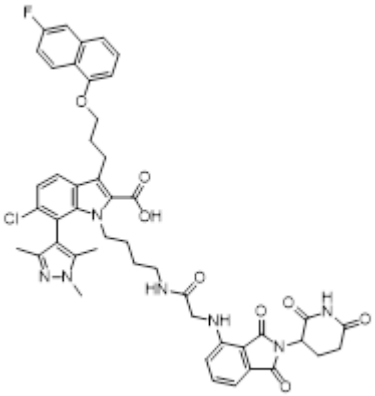
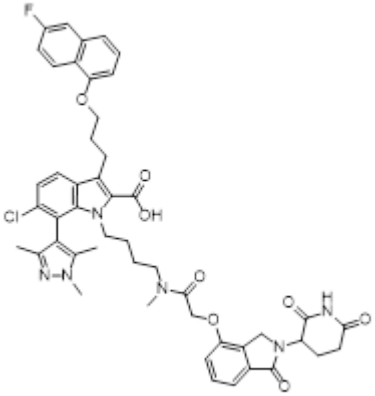
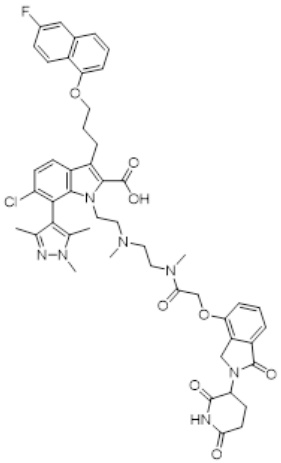
 292	 293	 294
 295	 296	 297

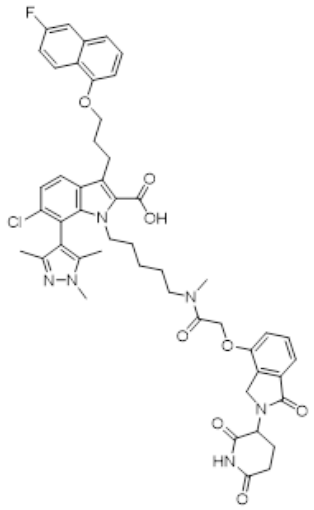
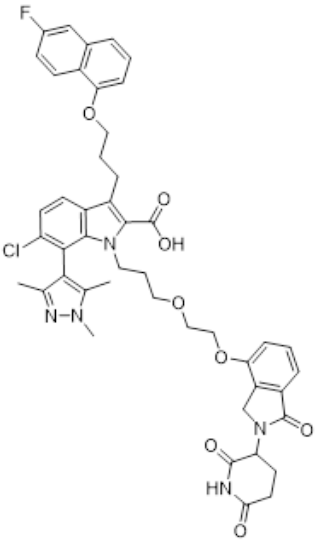
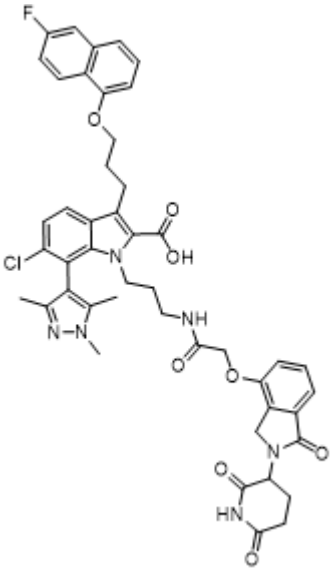
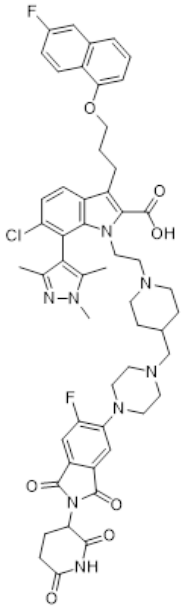
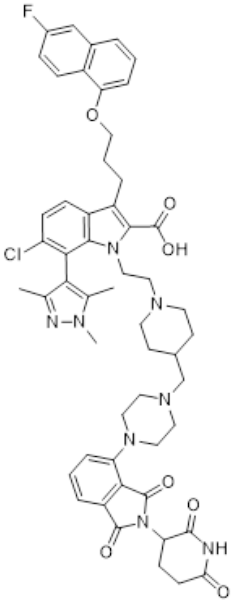
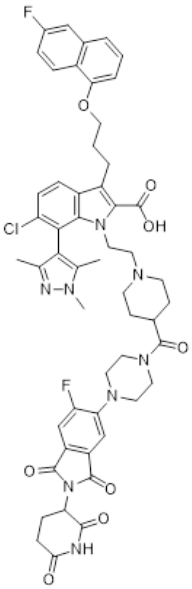
 298	 299	 300
 301	 302	 303

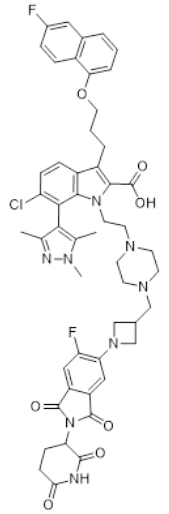
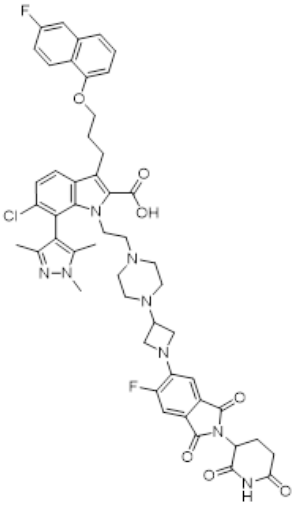
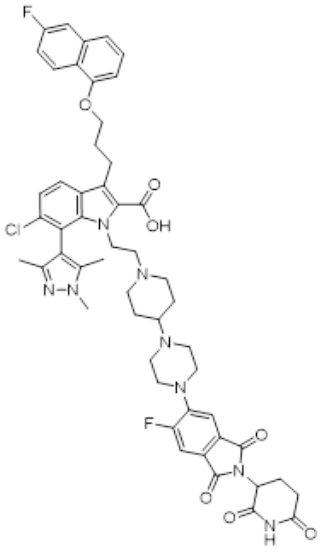
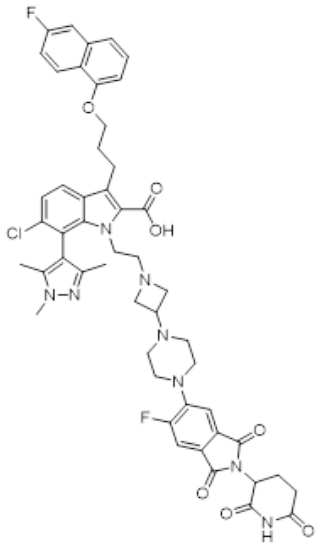
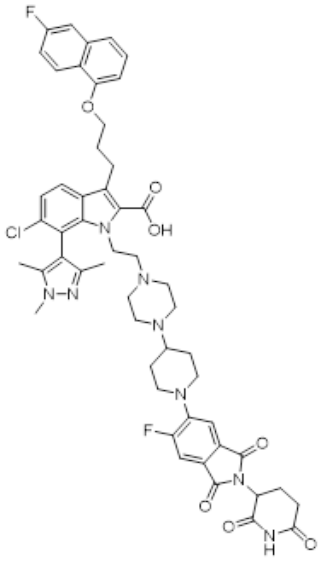
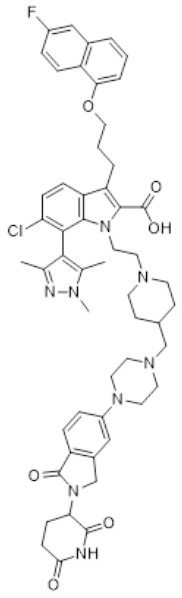
 304	 305	 306
 307	 308	 309

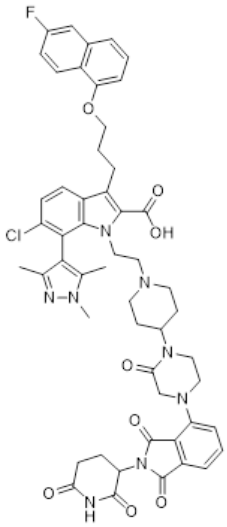
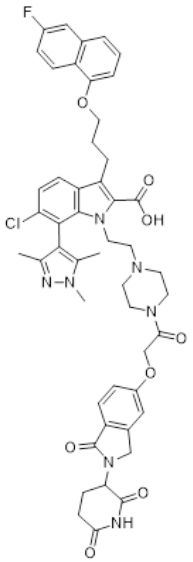
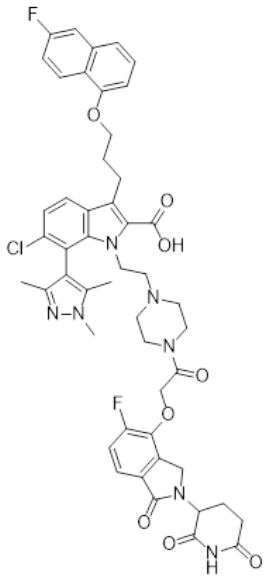
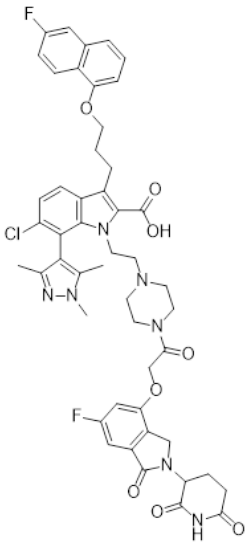
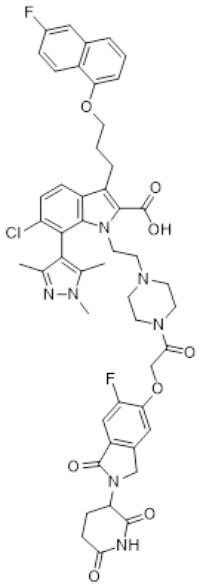
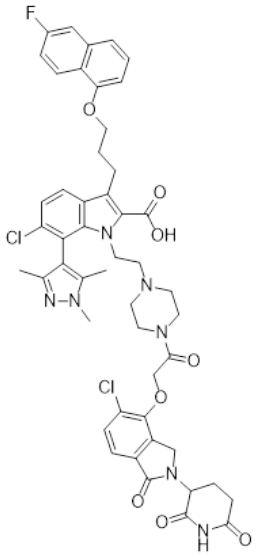
 310	 311	 312
 313	 314	 315

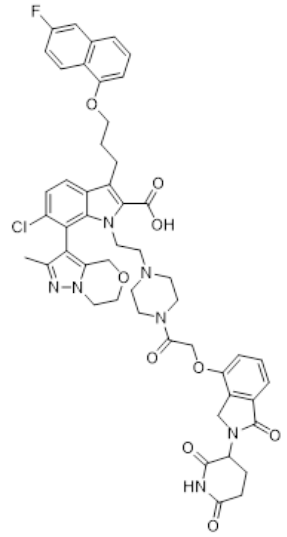
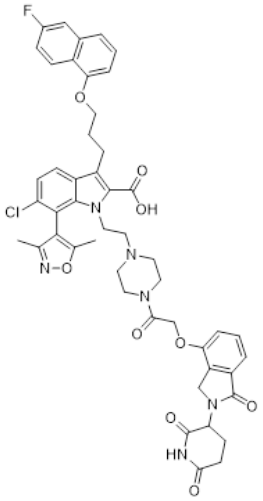
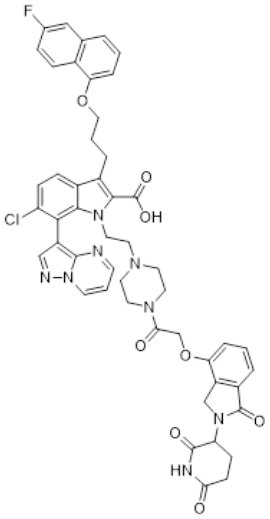
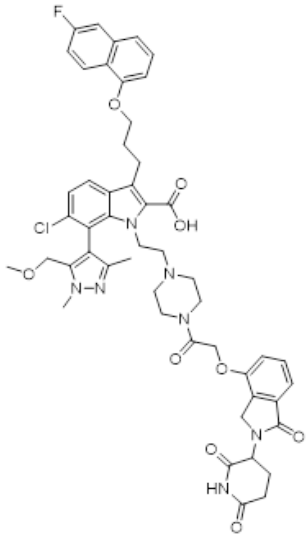
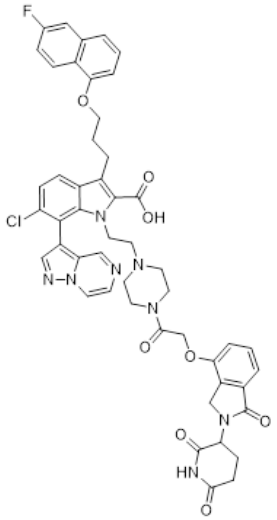
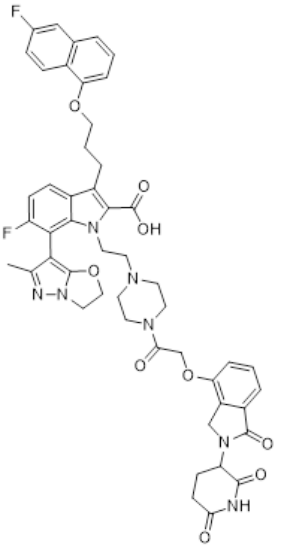
 316	 317	 318
 319	 320	 321

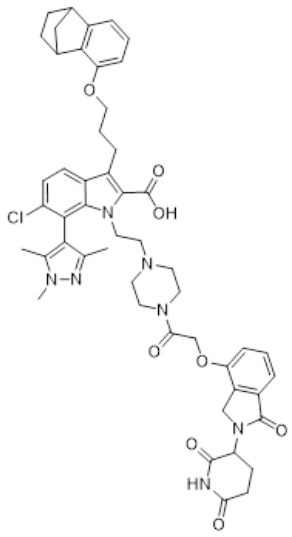
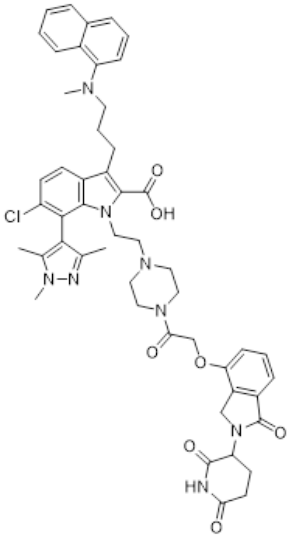
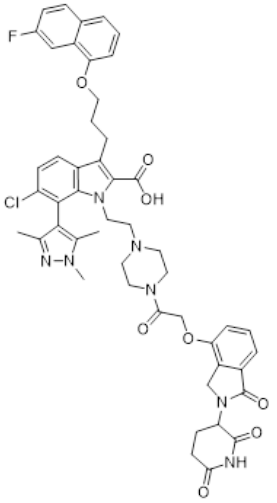
 322	 323	 324
 325	 326	 327

 328	 329	 330
 331	 332	 333

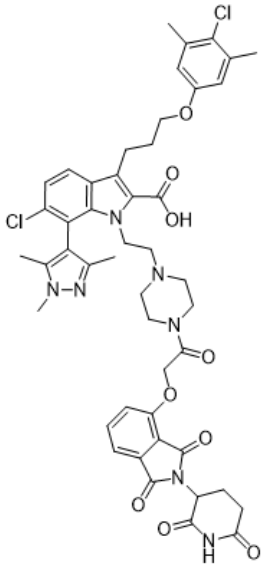
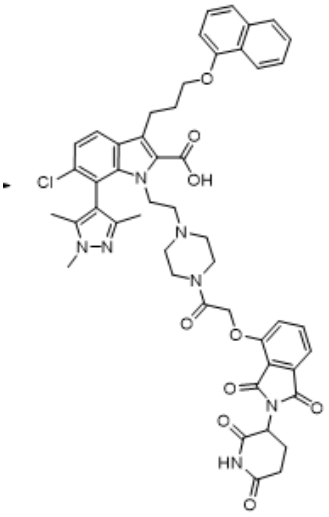
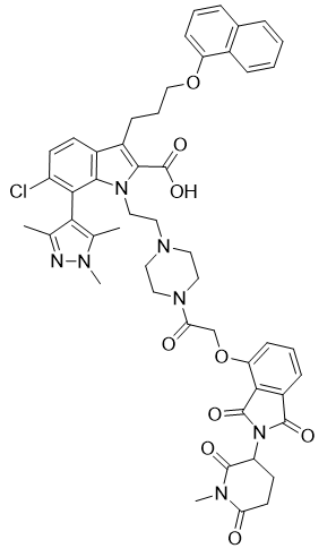
 334	 335	 336
 337	 338	 339

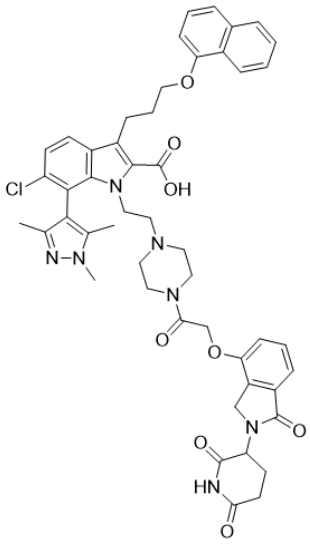
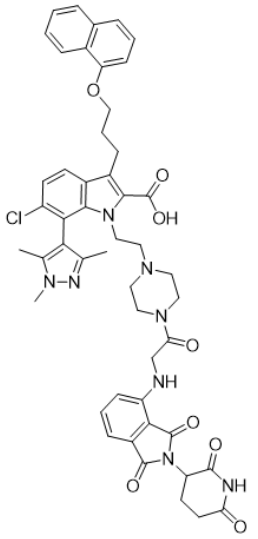
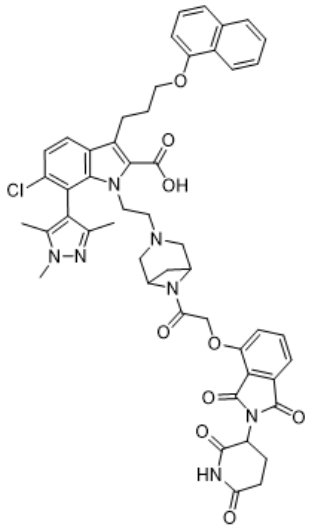
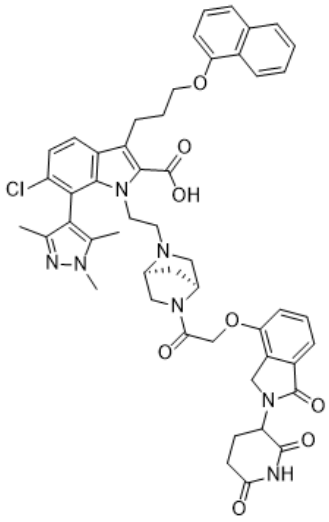
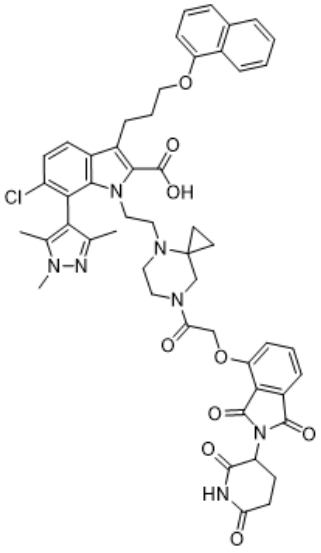
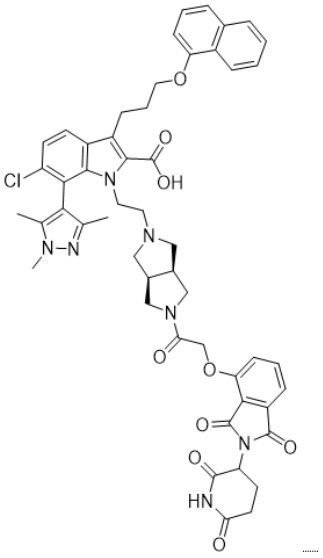
 340	 341	 342
 343	 344	 345

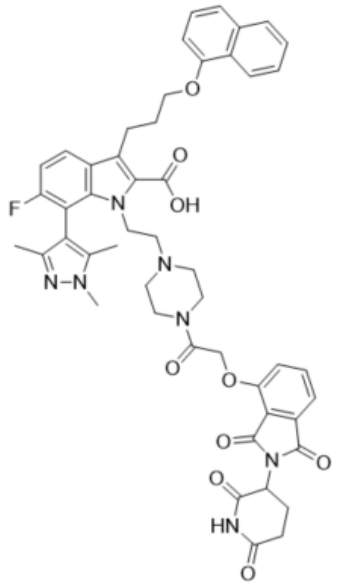
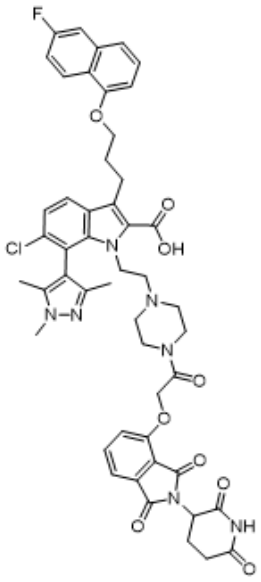
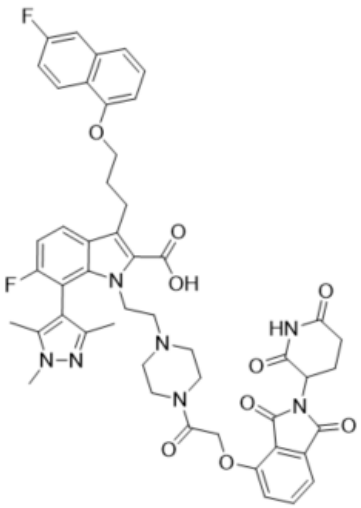
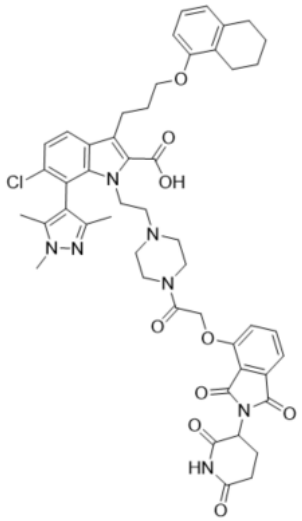
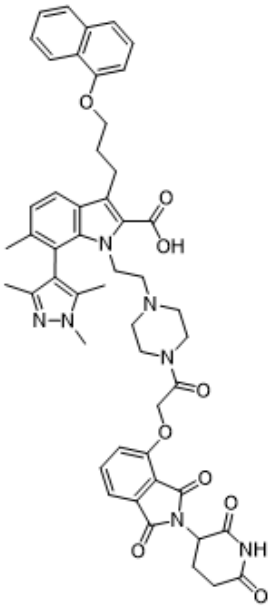
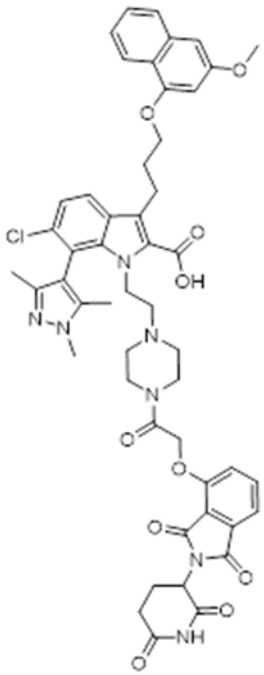
 346	 347	 348
 349	 350	 351

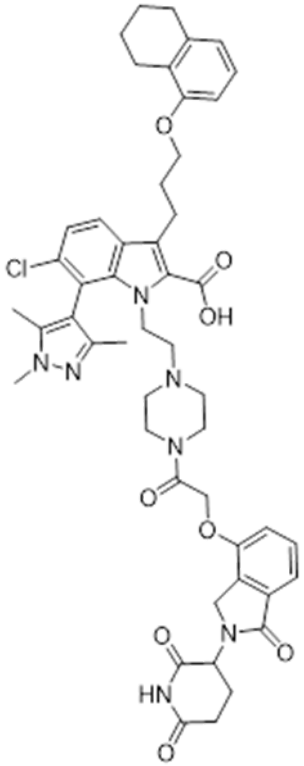
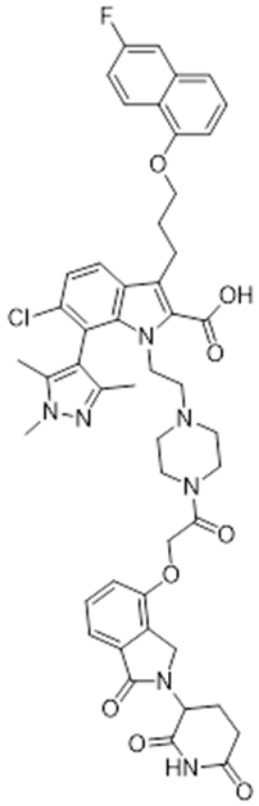
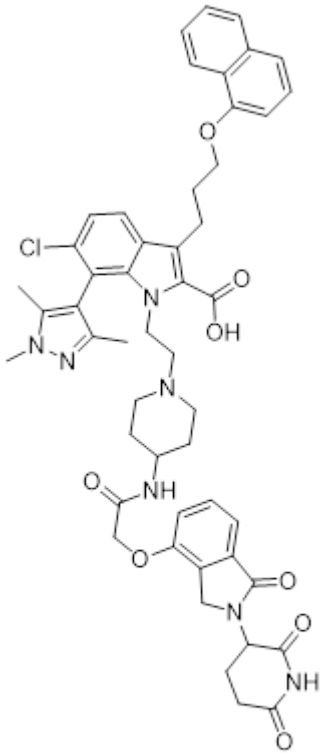
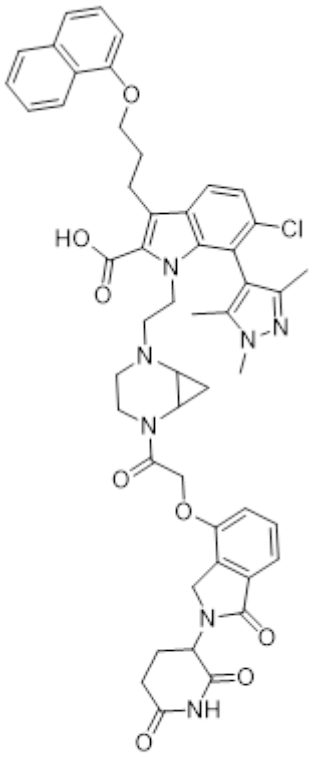
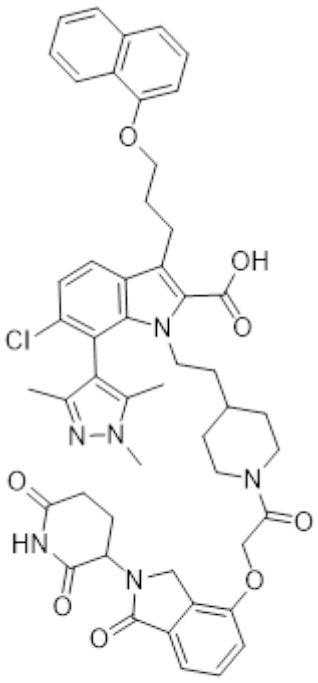
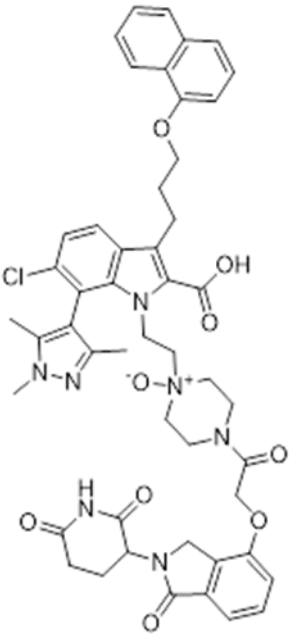
		
352	353	354

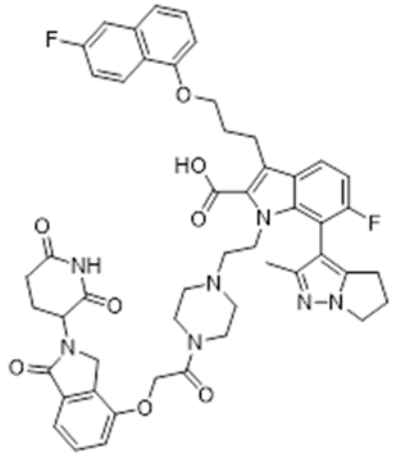
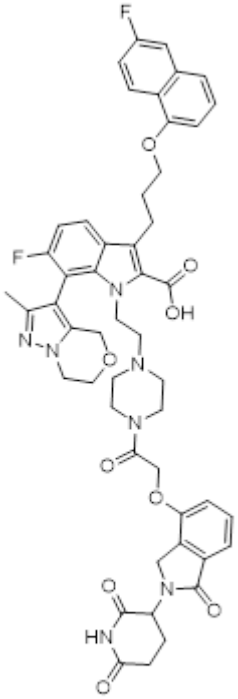
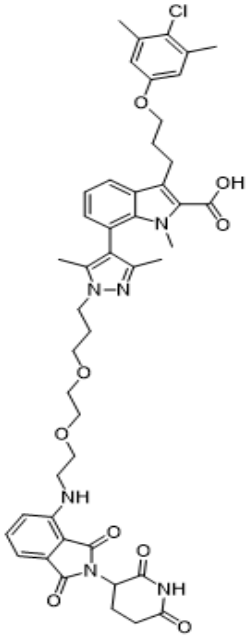
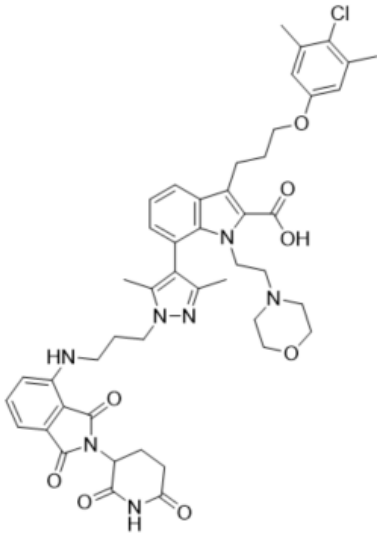
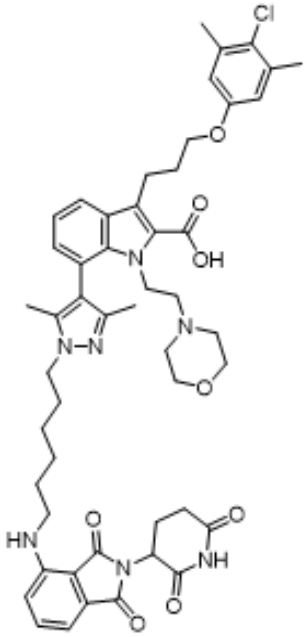
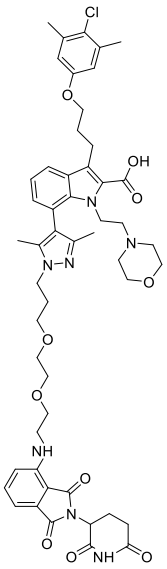
or which is selected from:

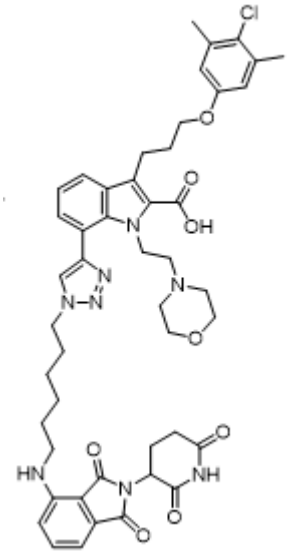
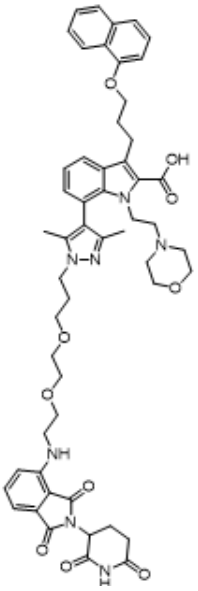
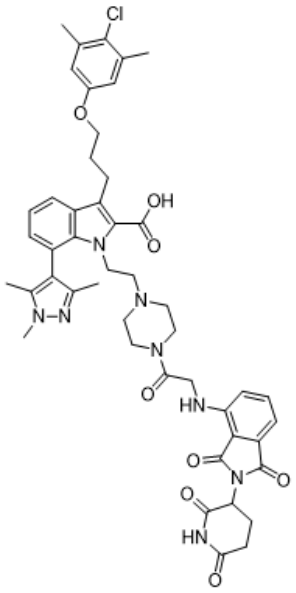
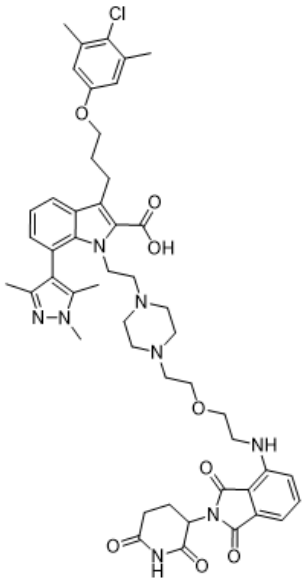
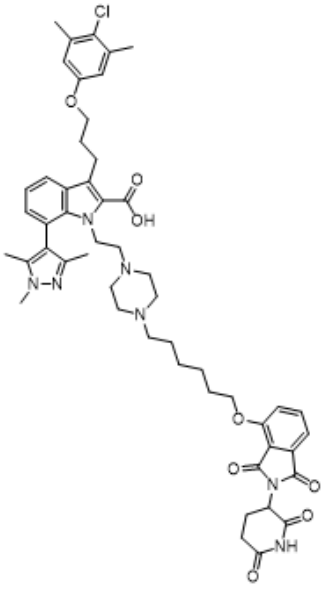
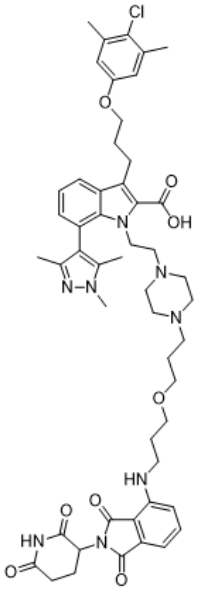
		
201	204	205

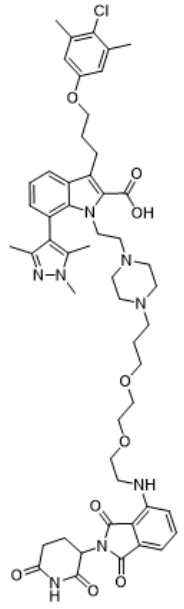
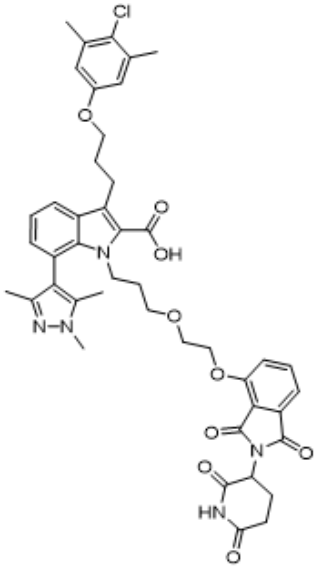
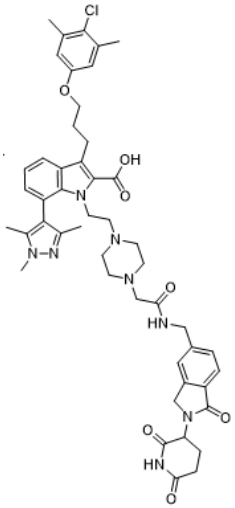
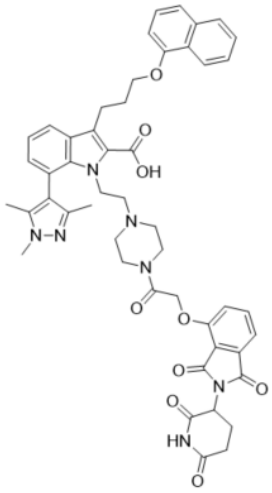
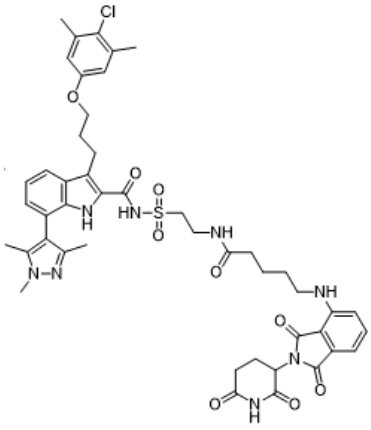
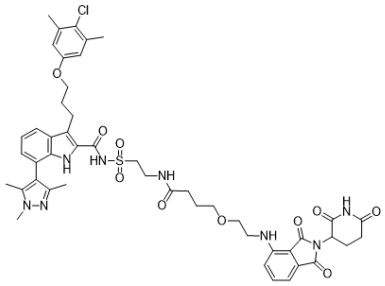
		
206	207	208
		
209	210	211

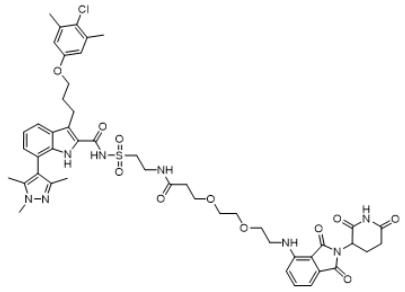
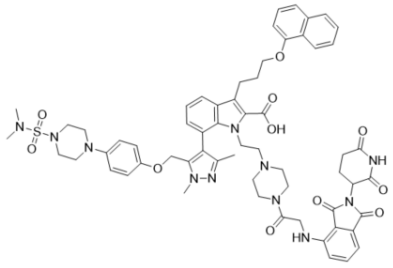
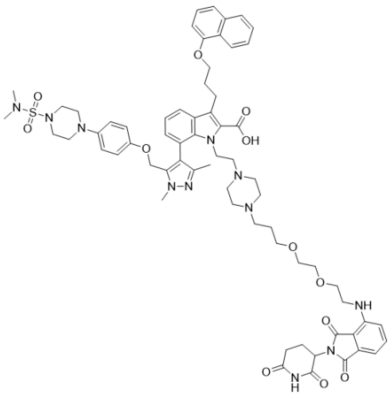
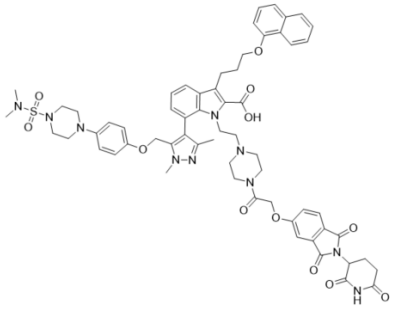
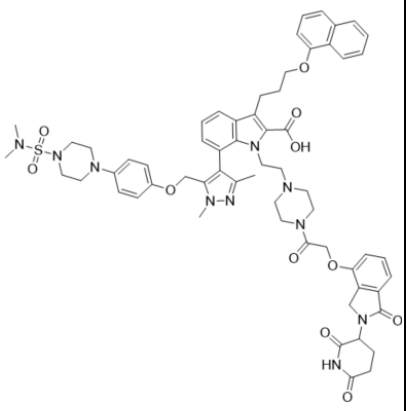
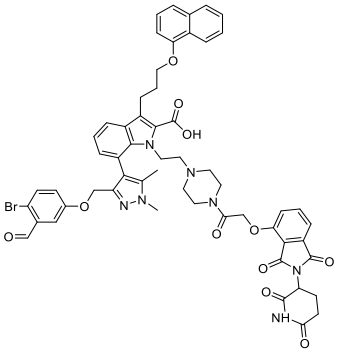
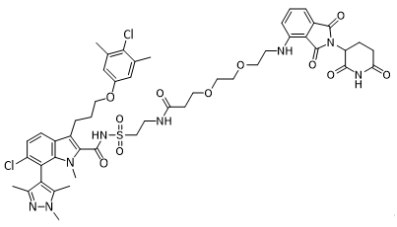
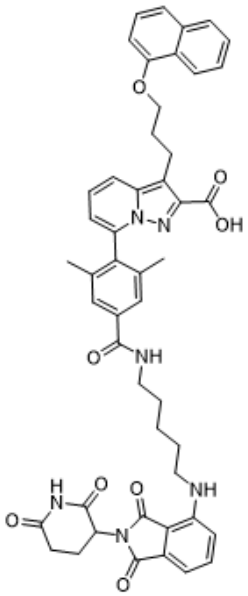
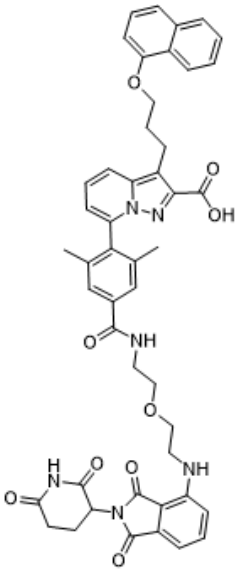
		
213	214	215
		
216	217	218

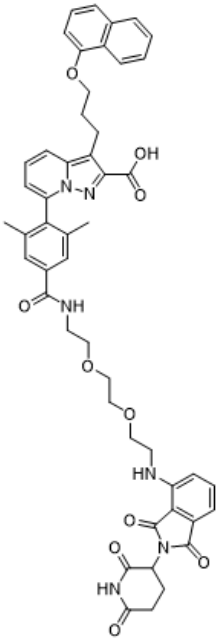
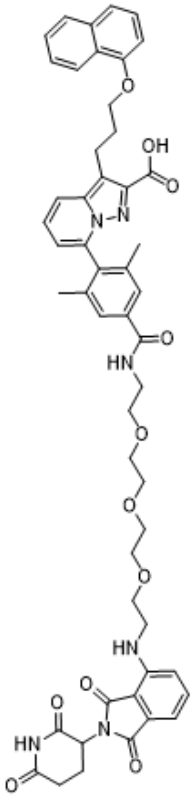
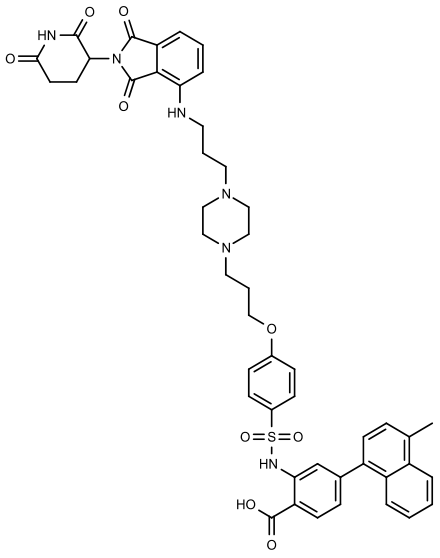
		
219	220	221
		
222	223	224

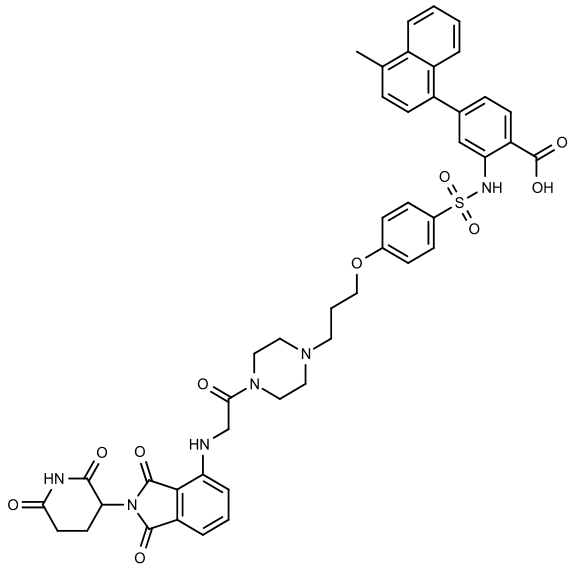
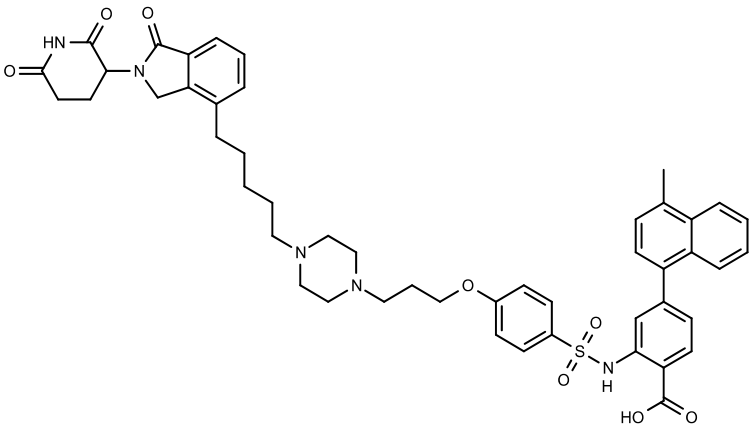
		
225	226	227
		
228	229	230

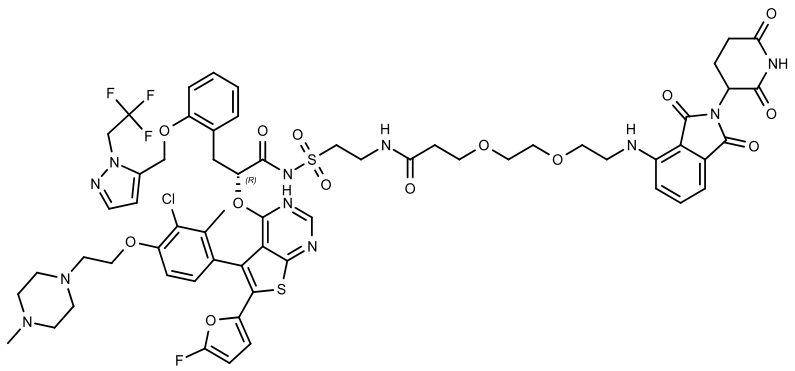
		
231	232	233
		
234	235	236

		
237	238	240
		
241	*242*	*243*

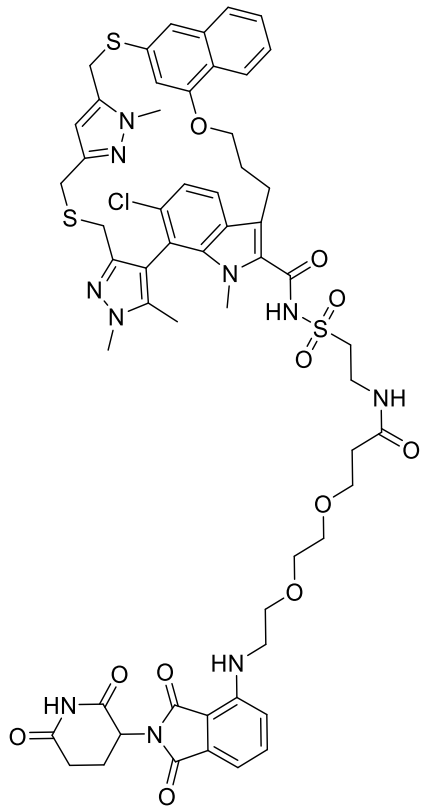
		
244	245	247
		
248	249	251
		

252	253	254
		
255	256	
		
257		


258

259

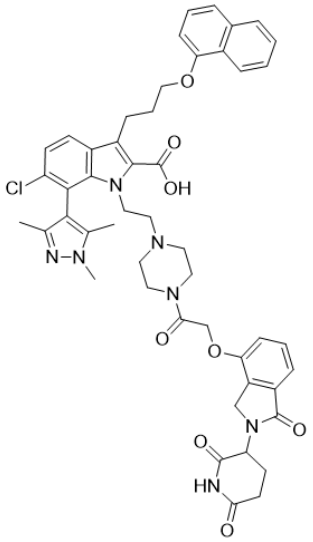
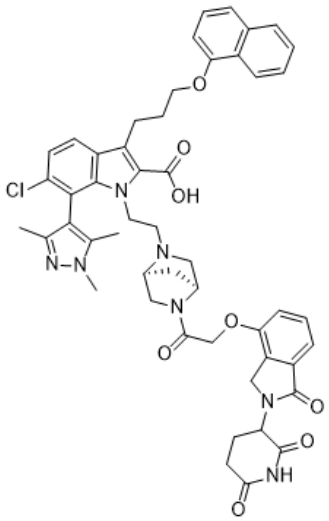
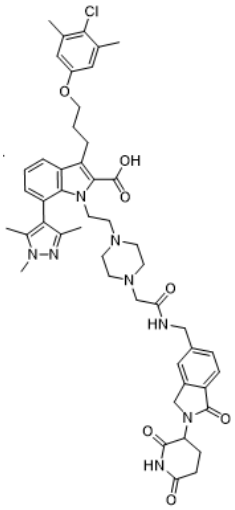
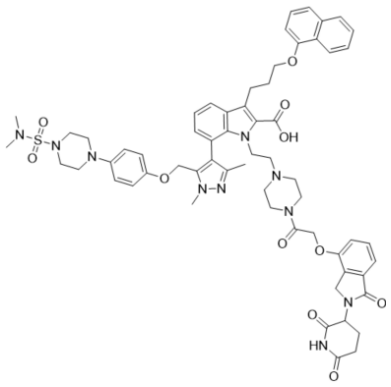
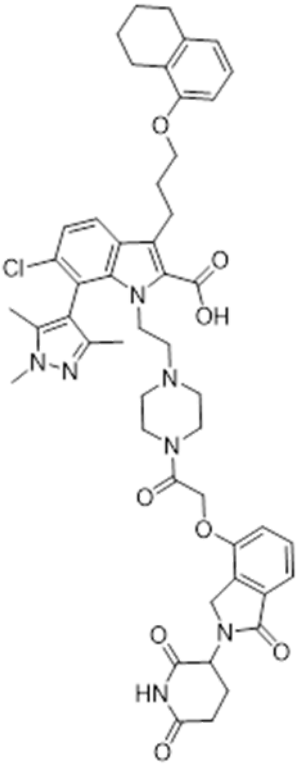
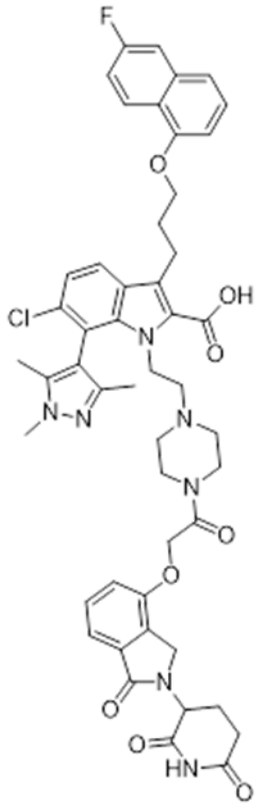


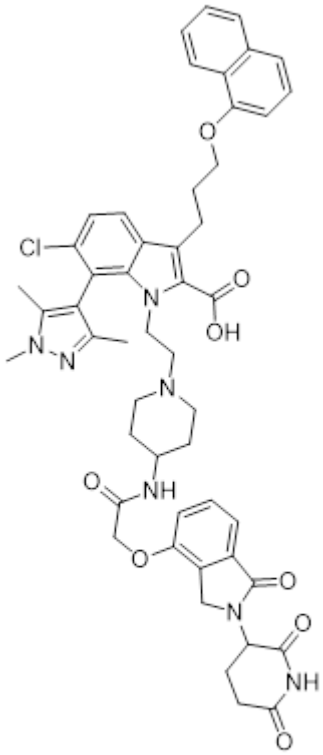
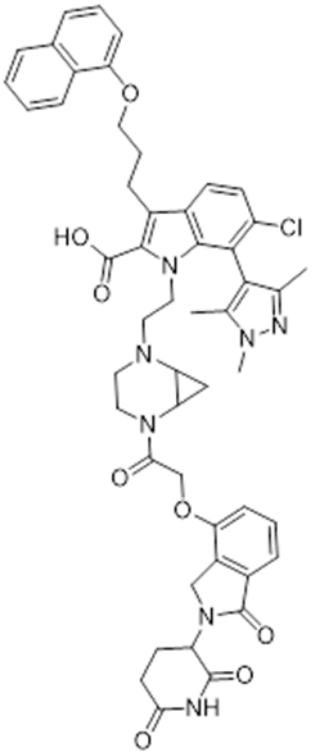
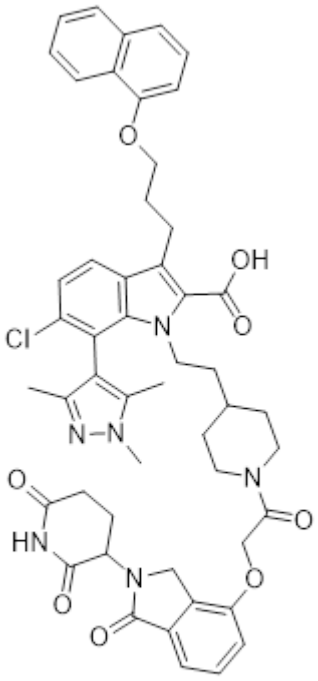
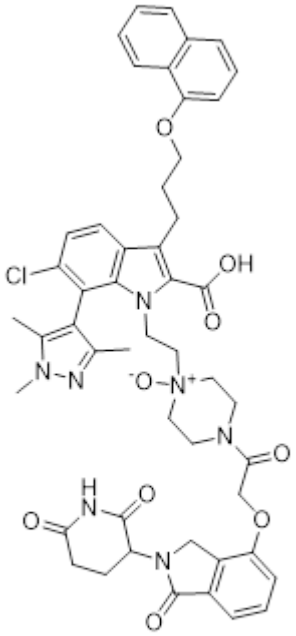
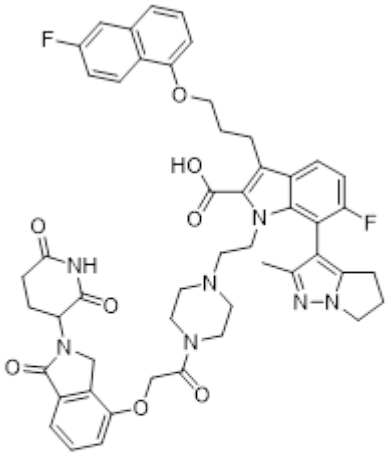
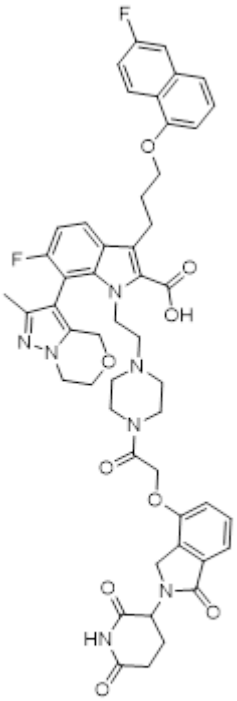
260

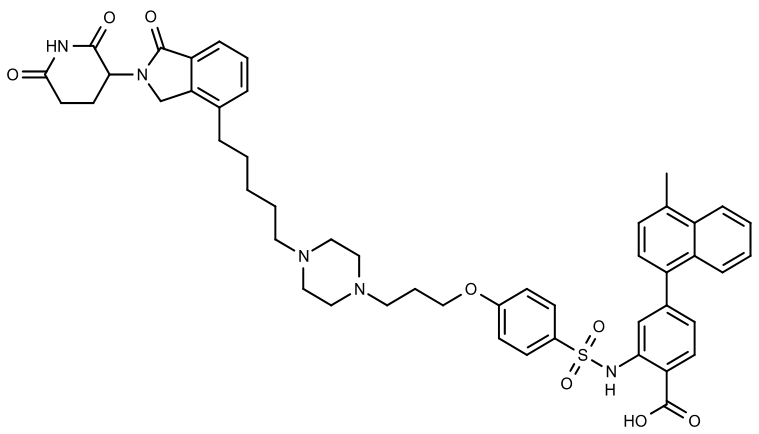


261

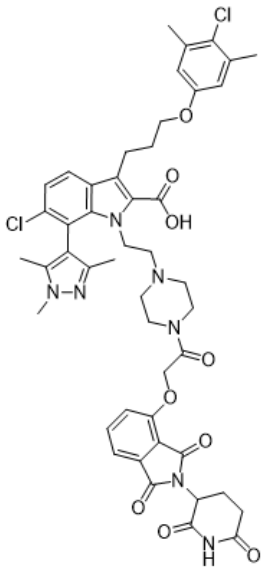
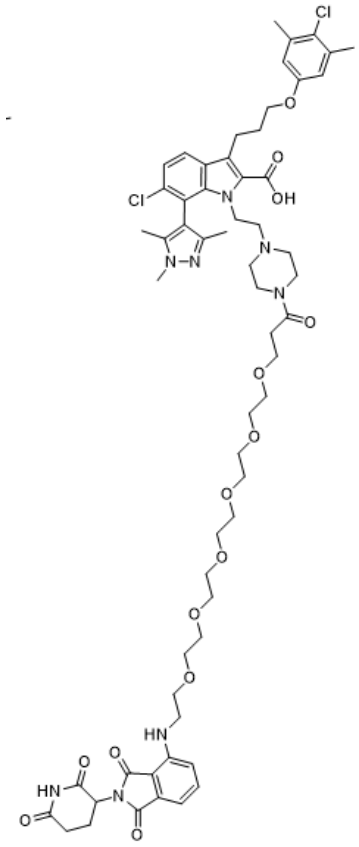
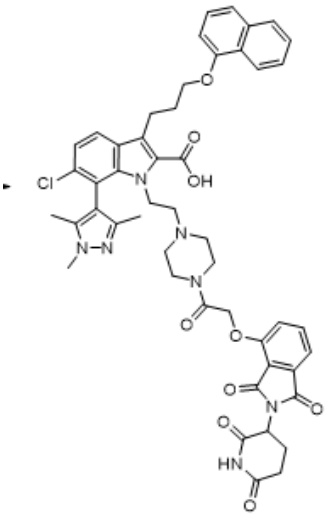
optionally in which the compound is selected from:

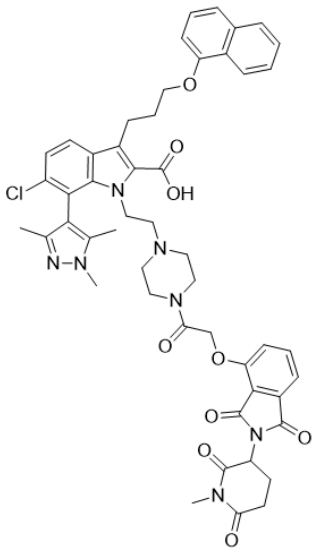
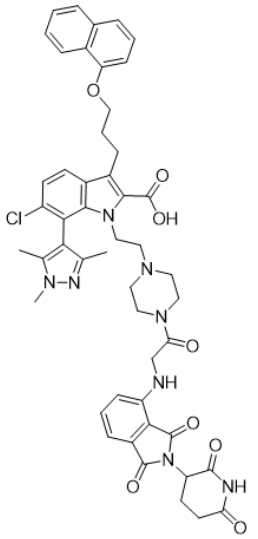
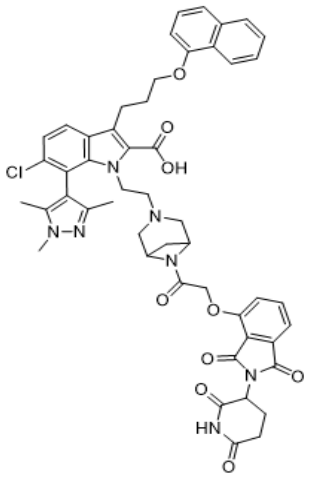
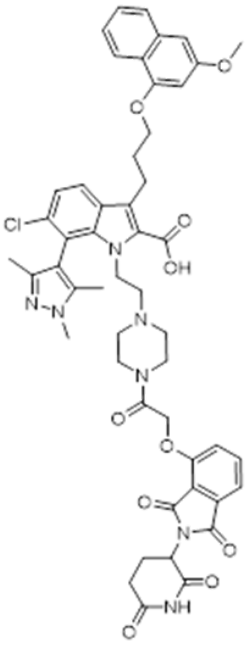
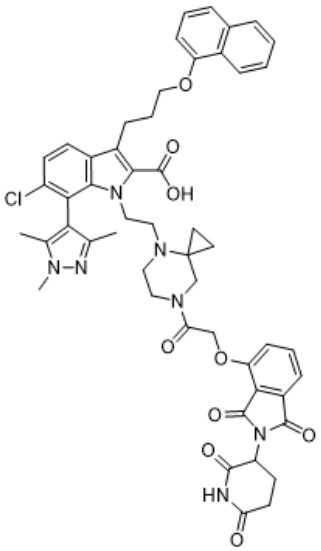
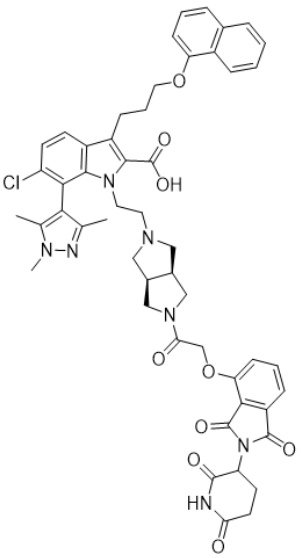
		
206	209	240
		
249	219	220

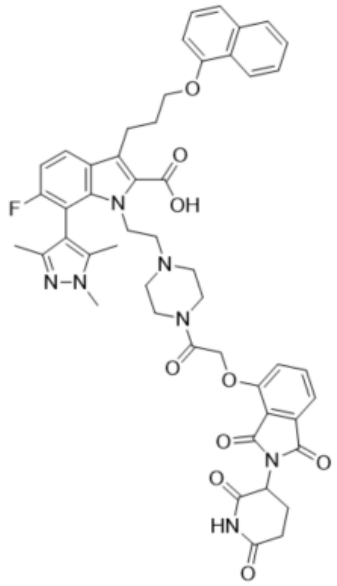
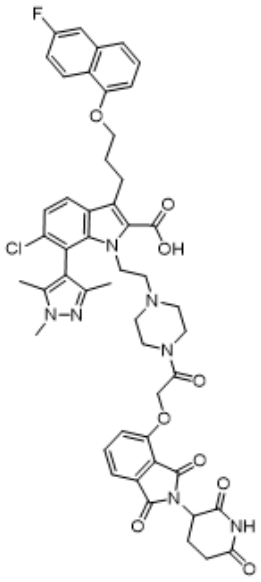
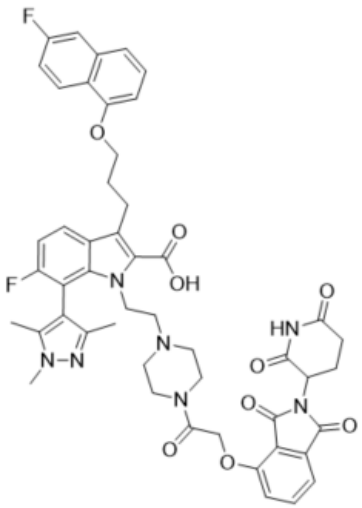
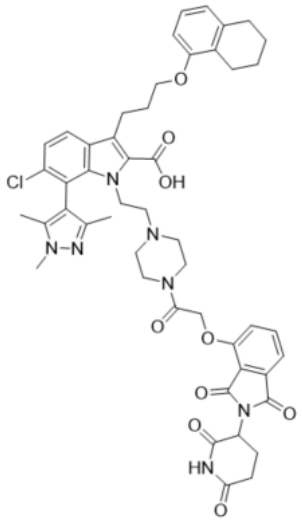
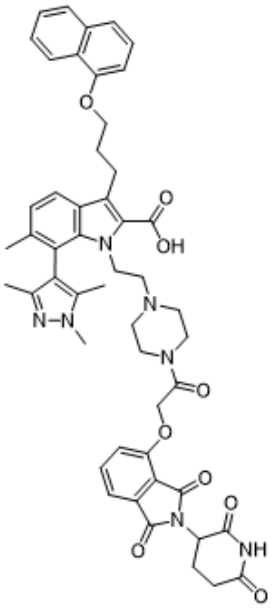
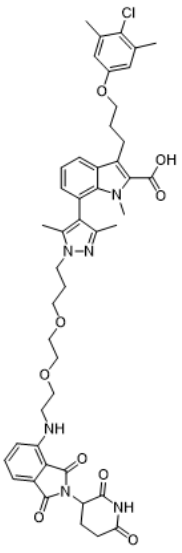
		
221	222	223
		
224	225	226

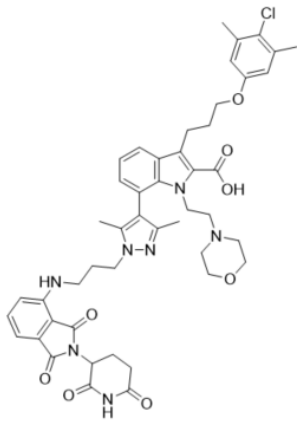
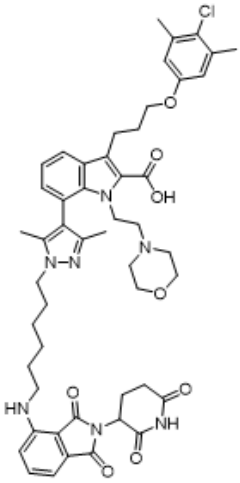
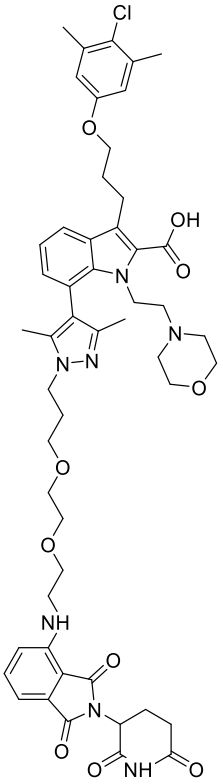
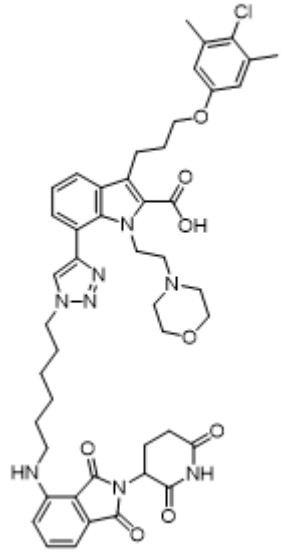
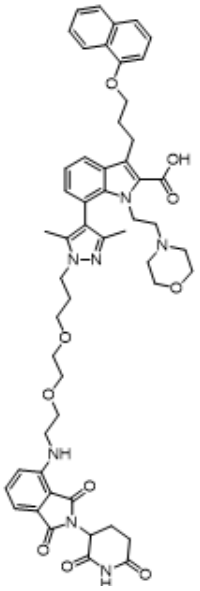
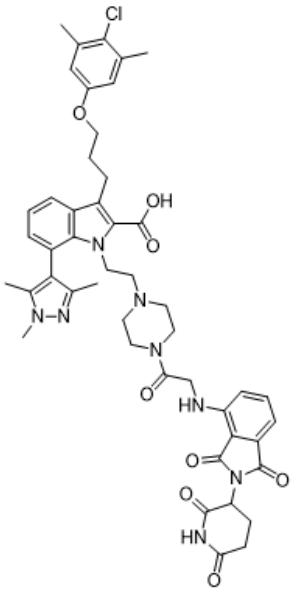

259

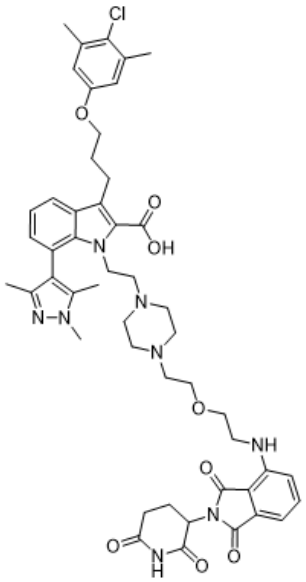
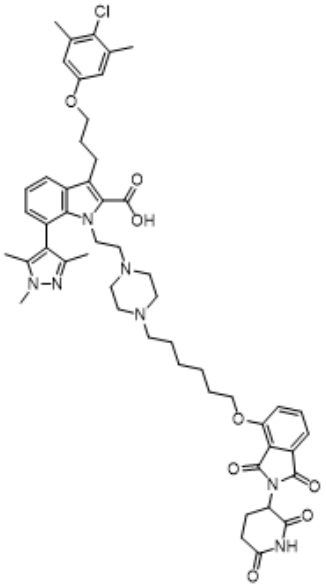
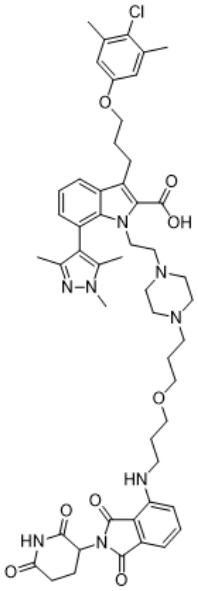
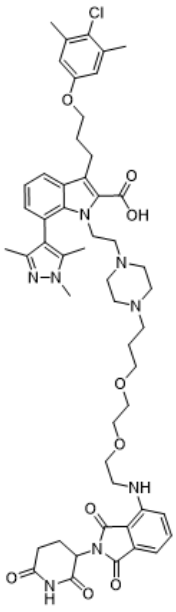
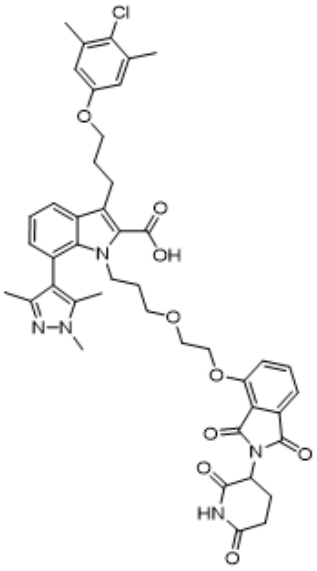
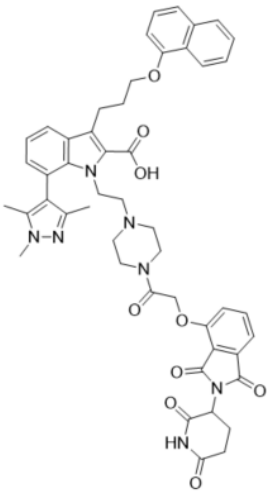
or in which the compound is selected from:

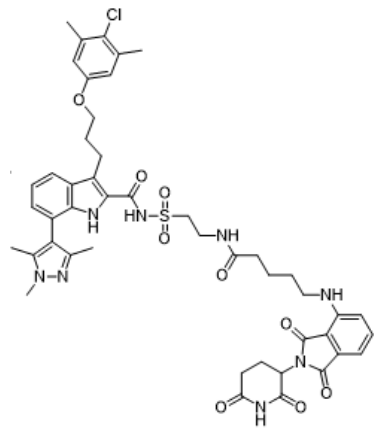
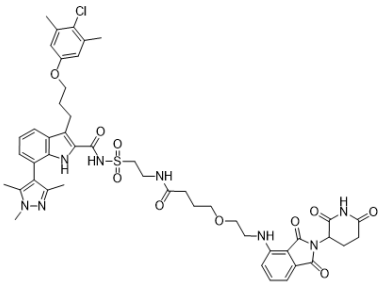
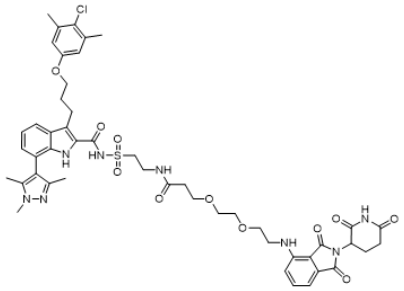
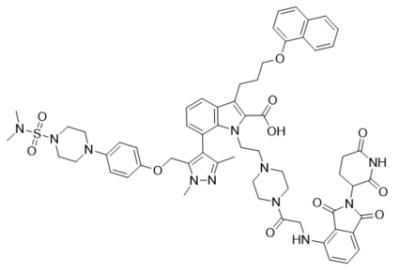
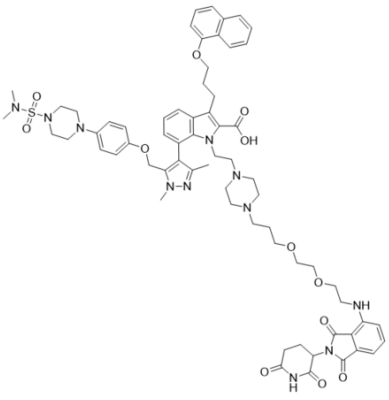
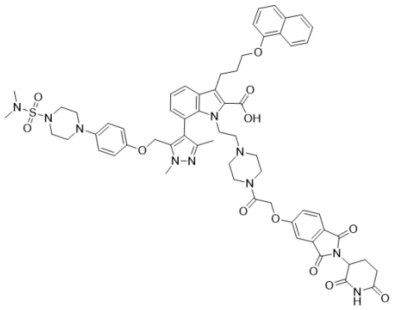
		

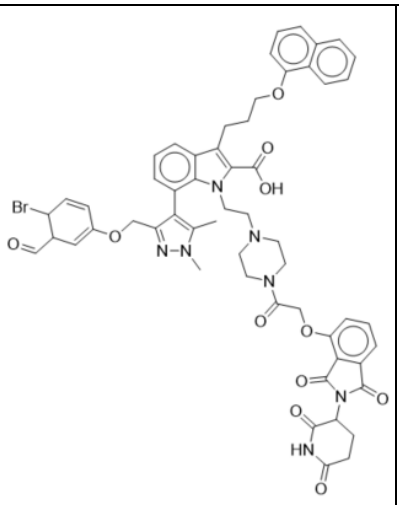
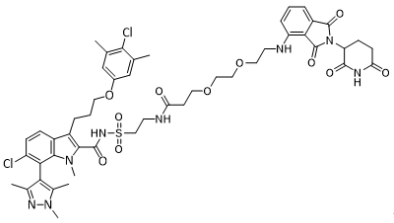
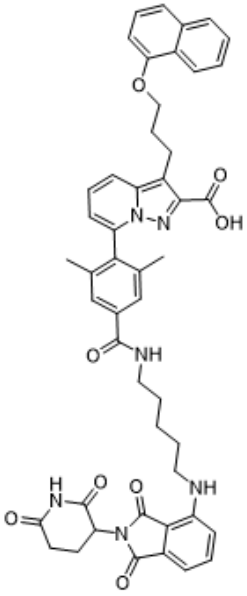
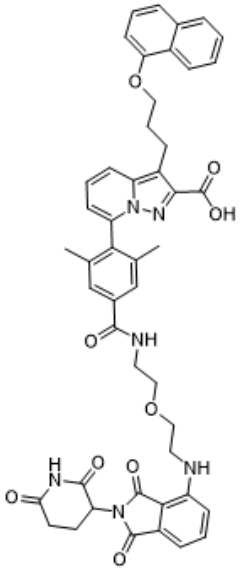
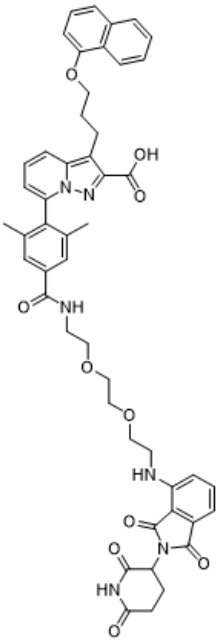
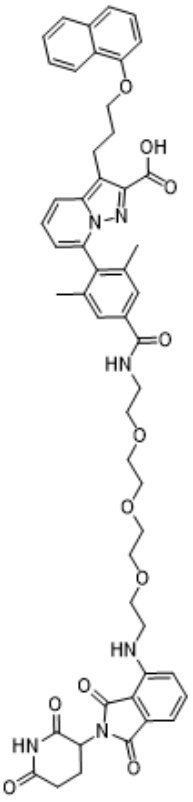
201	203	204
		
205	207	208
		
209	210	211

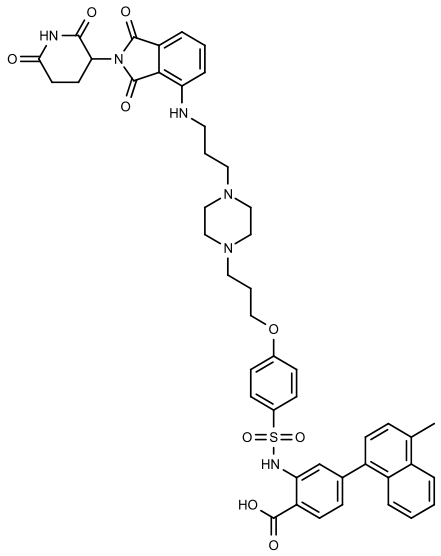
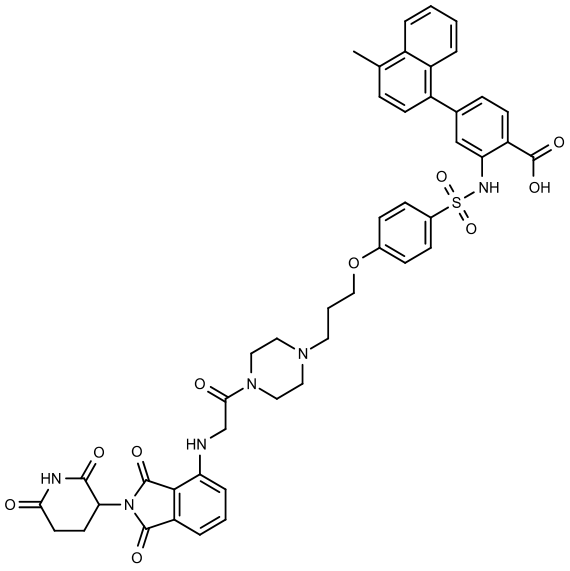
		
213	214	215
		
216	217	227

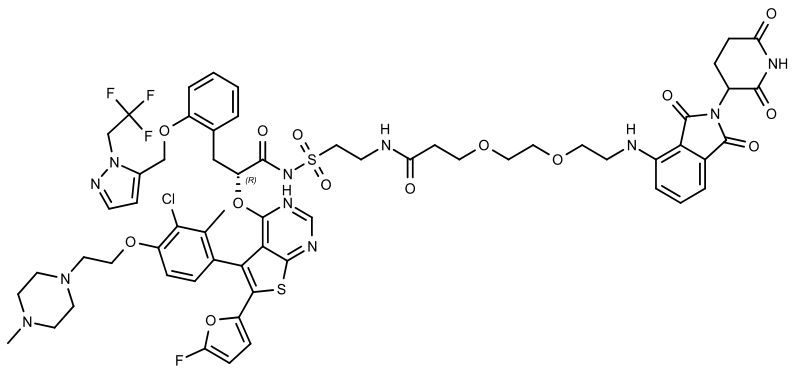
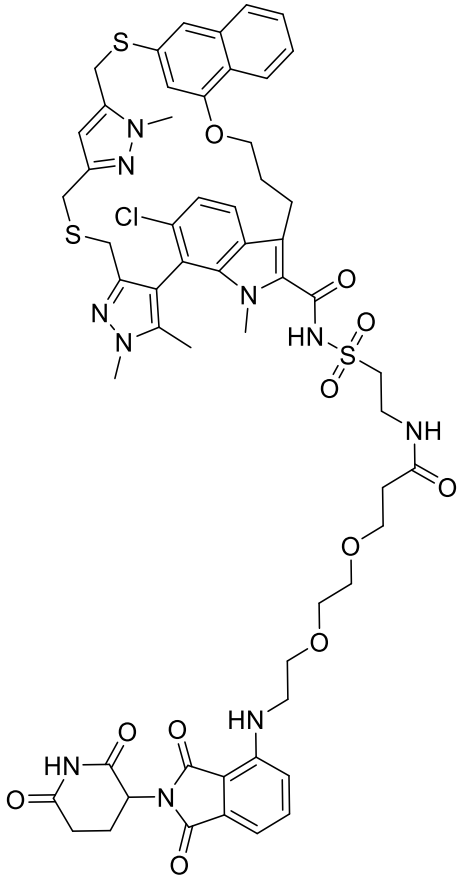
		
228	229	230
		
231	232	233

		
234	235	236
		
237	238	241

		
242	*243*	*244*
		
245	247	248

		
251	*252*	253
		
254	255	256


257

258


260

261

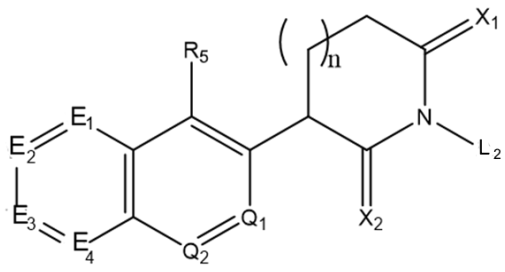
28. A compound of formula (I)

[MCL-1 ligand moiety] – [linker] – [ligase ligand moiety] (I)

or a salt, solvate, hydrate, isomer or prodrug thereof,

in which **[ligase ligand moiety]** is:

(a) Formula (IV)



(IV)

in which:

each of X_1 and X_2 is independently O or S;

each of Q_1 and Q_2 is independently N or CR^5, in which at least one of Q_1 and Q_2 is N;

each of E_1, E_2, E_3 and E_4 is independently N or CR';

n is 0, 1 or 2;

L_2 is hydrogen, alkyl, alkenyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -C(O)R''', -C(O)OR''', -C(O)NH_2, -C(O)NHR''', -C(O)NR'''$_2$, -OR''', -NR'''$_2$, or -$S(O)_2$R''';

each R^5 is independently hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR''', -NR''$_2$, -NR'''C(O)R''', -NR'''C(O)OR''', -NO_2, -CN, -C(O)R''', -C(O)OR''', -C(O)NH_2, -C(O)NHR''', -C(O)NR'''$_2$, -OR''', -OC(O)R''', -OC(O)OR''', -OC(O)NH_2, -OC(O)NHR''', -OC(O)NR'''$_2$, -SR''', -$S(O)_2$R''', -$S(O)_2$OR''', -$S(O)_2NH_2$, -$S(O)_2$NHR''', -$S(O)_2$NR'''$_2$; -O-**R^{21}**, -NH-**R^{21}**, -C(O)-NH-**R^{21}**, or -CH_2-NH-C(O)-**R^{21};**

each R' is independently hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR''', -NR'''$_2$, -NR'''C(O)R''', -NR'''C(O)OR''', -NO_2, -CN, -C(O)R''', -C(O)OR''', -C(O)NH_2, -C(O)NHR''', -C(O)NR'''$_2$, -OR''', -

$OC(O)R'''$,

$-OC(O)OR'''$, $-OC(O)NH_2$, $-OC(O)NHR'''$, $-OC(O)NR'''_2$, $-SR'''$, $-S(O)_2R'''$, $-S(O)_2OR'''$,

$S(O)_2NH_2$, $-S(O)_2NHR'''$, $-S(O)_2NR'''_2$, $-\mathbf{R^{21}}$, $-O-\mathbf{R^{21}}$, $-NH-\mathbf{R^{21}}$, $-C(O)-\mathbf{R^{21}}$, $-C(O)-NH-\mathbf{R^{21}}$, or $-CH_2-NH-C(O)-\mathbf{R^{21}}$;

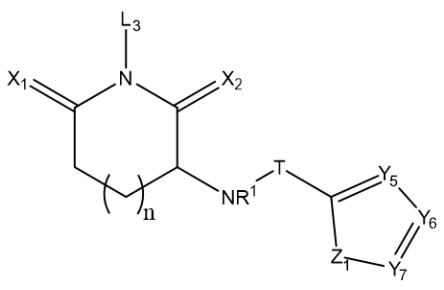
and

each R''' is independently hydrogen, alkyl, alkenyl, aryl, heteroaryl, or benzyl;

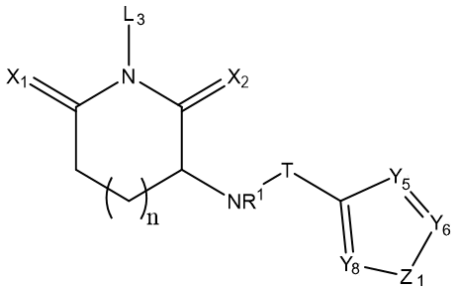
in which $\mathbf{R^{21}}$ is a bond connected to $\mathbf{R^{18}}$ of the linker, and in which Formula (IV) contains a single $\mathbf{R^{21}}$;

or

(b) Formula (Va) or (Vb):



or



(Va) (Vb)

or a pharmaceutically acceptable salt or tautomer thereof,

in which

each of X_1 and X_2 is independently O or S;

Z_1 is O, S or NR^6;

T is is C=O or SO_2;

R^1 is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

each of Y_5, Y_6, Y_7, and Y_8 is independently N or CR^7,

in which at least one of Y_5, Y_6 and Y_7 in Formula (Va) is CR^7, and at least one of Y_5, Y_5 and Y_8 in Formula (Vb) is CR^7;

n is 0, 1 or 2;

L_3 is hydrogen, alkyl, alkenyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -C(O)R'‘‘, -CH_2C(O)OR'‘‘, -C(O)OR'‘‘, -C(O)NH_2, -C(O)NHR'‘‘, -C(O)NR'‘‘$_2$, -OR'‘‘, -NR'‘‘$_2$, or
-$S(O)_2$R'‘‘;

each R^7 is independently hydrogen, halogen, alkyl, cycloalkyl, heterocycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR'‘‘,
-NR'‘‘$_2$, -CH_2NR'‘‘$_2$, -NR'‘‘C(O)R'‘‘, -NR'‘‘C(O)CH_2NR'‘‘$_2$, -NR'‘‘C(O)CH_2-heterocycloalkyl,
-NR'‘‘C(O)CH(OH)R'‘‘, -CH_2NR'‘‘C(O)OR'‘‘, -NR'‘‘C(O)OR'‘‘, -NR'‘‘SO_2R'‘‘, -NO_2, -CN,
-C(O)R'‘‘, -C(O)OR'‘‘, -C(O)NH_2, -C(O)NHR'‘‘, -C(O)NR'‘‘$_2$, -OR'‘‘, -OC(O)R'‘‘, -OC(O)OR'‘‘, -OC(O)NH_2, -OC(O)NHR'‘‘, -OC(O)NR'‘‘$_2$, --NHC(S)NHR'‘‘, SR'‘‘, or -$S(O)_2$R'‘‘,-$S(O)_2$OR'‘‘, -$S(O)_2NH_2$, -$S(O)_2$NHR'‘‘, -$S(O)_2$NR'‘‘$_2$, -O-**R^{21}**, -NH-**R^{21}**, -C(O)-NH-**R^{21}**, or -CH_2-NH-C(O)-**R^{21};**

each R'‘‘‘ is independently hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

R^6 is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR'‘‘, -NR'‘‘$_2$, -NR'‘‘C(O)R'‘‘, -N[C(O)R'‘‘]$_2$, -NR'‘‘C(O)OR'‘‘, -NO_2, -CN, -C(O)R'‘‘, -C(O)OR'‘‘, -C(O)NH_2, -C(O)NHR'‘‘, -C(O)NR'‘‘$_2$, -OR'‘‘, -OC(O)R'‘‘,
-OC(O)OR'‘‘, -OC(O)NH_2, -OC(O)NHR'‘‘, -OC(O)NR'‘‘$_2$, -SR'‘‘, or -$S(O)_2$R'‘‘,-$S(O)_2$OR'‘‘,
-$S(O)_2NH_2$, -$S(O)_2$NHR'‘‘, -$S(O)_2$NR'‘‘$_2$, -**R^{21}**, -C(O)-NH-**R^{21}**, or -CH_2-NH-C(O)-**R^{21};**

in which **R^{21}** is a bond connected to **R^{18}** of the linker, and in which formula (Va) and formula (Vb) each contain a single **R^{21}**;

in which when Z_1 is O, then Y_6 is CR^7 and

in which when the compound is of Formula (Va), then

(i) when each of Y_5, Y_6 and Y_7 is CR^7, then at least one of R^7 is not H;

(ii) when Z_1 is NR^6, then Y_6 and Y_7 are CR^7;

(iii) when Z_1 is S, then Y_5 is not C-OMe and Y_6 is not C-OMe;

(iv) when Z_1 is S and Y_5 is C-NHCOMe, then Y_7 is not C-$CH_2NR'''C(O)OR''''$;

(v) when Z_1 is S and Y_5 is N, then Y_6 is not C-H, C-aryl or C-C(O)OR''''; and

(vi) when Z_1 is S and Y_6 is N, then Y_7 is C-NH_2, C-NHR'''', C-NR''''_2, C-NR''''C(O)OR'''', C-CH_2NR''''C(O)OR'''', C-haloalkyl, C-^{t}Butyl, C-OR'''', C-COOR'''' or C-SR''''; in which when Y_7 is C-NH_2, C-NHR'''' or C-NR''''_2, then Y_5 is C-H;

and when the compound is of Formula (Vb), then:

(vii) when each of Y_5, Y_6 and Y_8 is CR^7, then at least one of R^7 is not H;

(viii) when Z_1 is S, then Y_5 is not C-COOH or C-NHC(O)Me, and Y_8 is not C-Br;

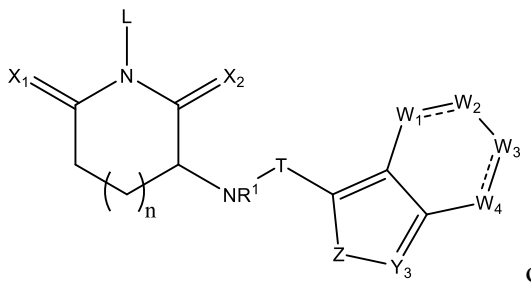
(ix) when Z_1 is S and Y_6 is C-Br, then Y_8 is C-OR''''

(x) when Z_1 is S, Y_5 is N and Y_6 is C-H or C-NH_2, then Y_8 is not C-H

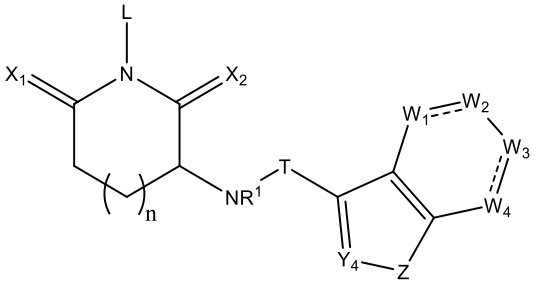
(xi) when Z_1 is S and Y_5 is N, then Y_6 is not C- halogen, C-alkyl, C-cycloalkyl, C-aryl, C-heteroaryl, C-CH_2NH_2, C-COOalkyl, or C-NHC(O)alkyl; (xii) when Z_1 is NR^6, then Y_5, Y_6 and Y_8 are CR^7.

or

(c) Formula (IIa) or (IIb):



or



(IIa) (IIb)

in which

each of X_1 and X_2 is independently O or S;

Z is O, S or NR^2;

T is C=O or SO_2;

Y_3 is N or CR;

Y_4 is N or CR;

 indicates a single or double bond, in which

when each  is a double bond, each of W_1, W_2, W_3 and W_4 is independently N or CR^a, in which at least one of W_1, W_2, W_3 and W_4 is N, and

when each  is a single bond, W_1, W_2, W_3 and W_4 are each CR^a_2 and Y_4 is CR;

n is 0, 1 or 2;

L is hydrogen, alkyl, alkenyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, $-C(O)R^h$, $-C(O)OR^h$, $-C(O)NH_2$, $-C(O)NHR^h$, $-C(O)NR^h_2$, $-OR^h$, $-NR^h_2$, or $-S(O)_2R^h$;

each R is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, $-NH_2$, $-NHR^h$, $-NR^h_2$, $-NR^hC(O)R^h$, $-NR^hC(O)CH_2R^h$, $-NR^hC(O)CH(OH)R^h$, $-NR^hC(O)OR^h$, $-NR^hSO_2R^h$, $-NO_2$, -CN, $-C(O)R^h$, $-C(O)OR^h$, $-C(O)NH_2$, $-C(O)NHR^h$, $-C(O)NR^h_2$, $-OR^h$, $-OC(O)R^h$, $-OC(O)OR^h$, $-OC(O)NH_2$, $-OC(O)NHR^h$, $-OC(O)NR^h_2$, $-SR^h$, or $-S(O)_2R^h$,$-S(O)_2OR^h$, $-S(O)_2NH_2$, $-S(O)_2NHR^h$, or $-S(O)_2NR^h_2$;

each R^a is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, $-NH_2$, $-NHR^h$, $-NR^h_2$, $-NR^hC(O)R^h$, $-NR^hC(O)CH(OH)R^h$, $-NR^hC(O)OR^h$, $-NR^hSO_2R^h$, $-NO_2$, -CN, $-C(O)R^h$, $-C(O)OR^h$, $-C(O)NH_2$, $-C(O)NHR^h$, $-C(O)NR^h_2$, $-OR^h$, $-OC(O)R^h$, $-OC(O)OR^h$, $-OC(O)NH_2$, $-OC(O)NHR^h$, $-OC(O)NR^h_2$, $-SR^h$, $-S(O)_2R^h$, $-S(O)_2OR^h$, $-S(O)_2NH_2$, $-S(O)_2NHR^h$, $-S(O)_2NR^h_2$, -O-**R^{21}**, -NH-**R^{21}**, -C(O)-NH-**R^{21}**, or $-CH_2$-NH-C(O)-**R^{21};**

each R^h is independently hydrogen, alkyl, cycloalkyl, heterocycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

R^2 is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, $-NH_2$, $-NHR^h$, $-NR^h_2$, $-NR^hC(O)R^h$, $-N[C(O)R^h]_2$, $-NR^hC(O)OR^h$, $-NO_2$, -CN, $-C(O)R^h$, $-C(O)OR^h$, $-C(O)NH_2$, $-C(O)NHR^h$, $-C(O)NR^h_2$, $-OR^h$, $-OC(O)R^h$, $-OC(O)OR^h$, $-OC(O)NH_2$, $-OC(O)NHR^h$, $-OC(O)NR^h_2$, $-SR^h$, $-S(O)_2R^h$,$-S(O)_2OR^h$, $-S(O)_2NH_2$, $-S(O)_2NHR^h$, or $-S(O)_2NR^h_2$; and

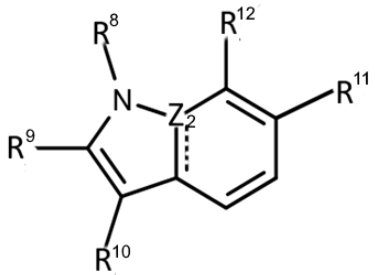
R^1 is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

R^{21} is a bond connected to **R^{18}** of the linker, and in which formula (IIa) and formula (IIb) each contain a single **R^{21}**;

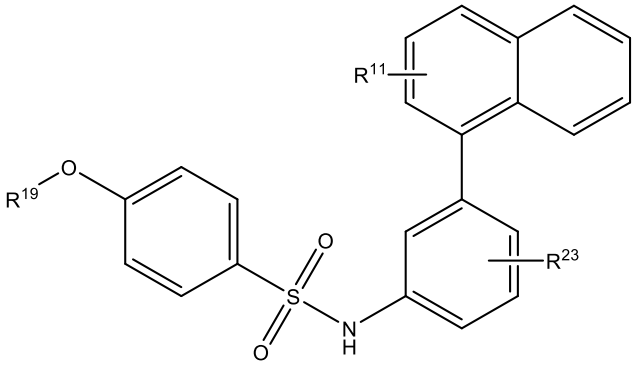
in which when each is a double bond, Z is NR^2, R^2 is hydrogen, and each R^a is hydrogen, then W_4 is CR^a;

in which

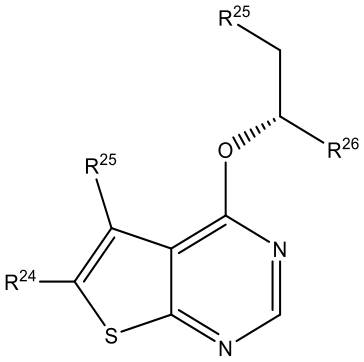
[MCL-1 ligand moiety] is a compound of Formula (A), Formula (B) or Formula (C)



(A)



(B)



(C)

in which

 is a single bond or a double bond;

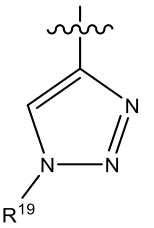
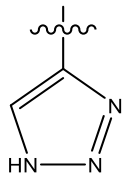
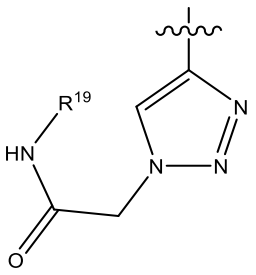
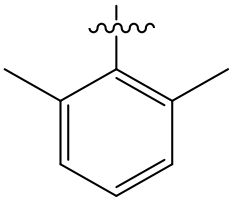
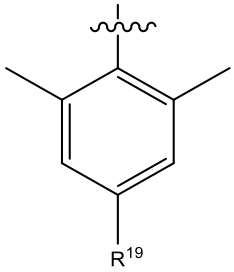
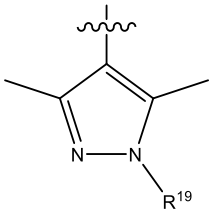
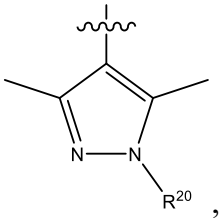
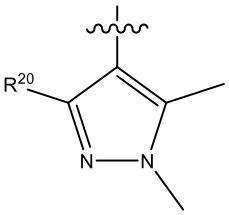
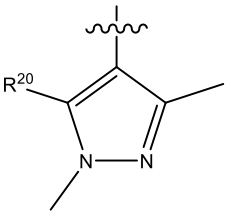
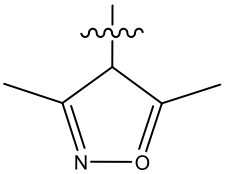
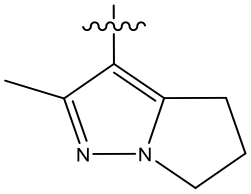
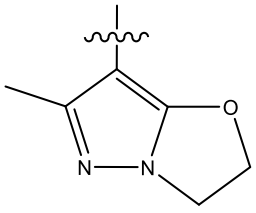
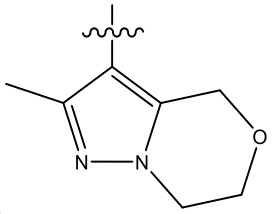
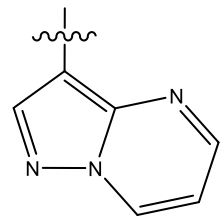
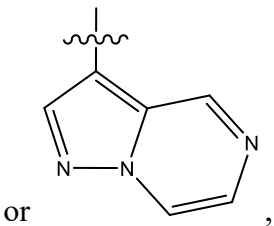
R^8 is H, **R^{19},** or C_1-C_6 alkyl optionally substituted with morpholine;

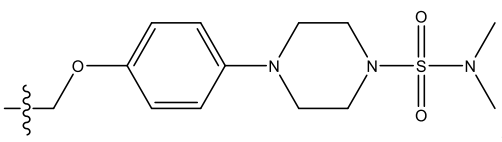
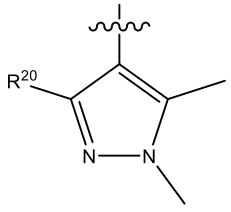
R^9 is -C(O)OH, -C(O)OC_1-C_6alkyl, -C(O)NH_2, -C(O)O**R^{19}** or -C(O)NH**R^{19}**,

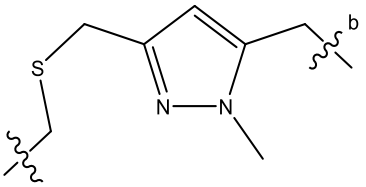
R^{10} is -$C_{2\text{-}5}$alkyl-O-R^{13} or -$C_{2\text{-}5}$alkyl-NMe-R^{13}, in which R^{13} is phenyl, naphthyl or tetraline, in which the phenyl, naphthyl or tetraline is optionally substituted with at least

one substituent selected from halogen, C_1-C_6 alkyl and -O(C_1-C_6 alkyl); or in which the tetraline is optionally substituted with a bridging -CH_2- group; or in which the naphthyl is optionally substituted with -O- or -S-,

R[11] is H, halogen or C_1-C_6 alkyl,

R[12] is H,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , or  ,

in which **R[20]** is Me, -CH_2-OMe, -CH_2-O-bromobenzaldehyde, or  ; or when **R[12]** is  and **R[10]** is -O-

naphthyl substituted with -O- or -S-, then **R[20]** is 

, in which



indicates attachment to -O- or -S- of **R[10]**;

and in which

R[19] is a bond connected to **R[14]** of the linker;

R[23] is -C(O)OH or -C(O)OC_1-C_6alkyl;

Z_2 is N or C, in which when **Z_2** is N, then  is a single bond; and when **Z_2** is C, then  is a double bond,

R[24] is furan optionally substituted with at least one halogen,

each **R[25]** is independently phenyl substituted with -O**R[28]** and optionally further substituted with at least one substituent selected from halogen and C_1-C_6 alkyl;

R[26] is -C(O)O**R[19]** or -C(O)NH**R[19]**; and

each **R[28]** is independently -C_{1-3}alkyl-(N-alkyl piperazine) or -C_{1-3}alkyl-(N-haloalkylpyrazole)

and in which each of Formula (A), Formula (B) and Formula (C) contains a single **R[19];**

and in which **[linker]** has the following formula

R[14]-R[15]-R[16]-R[17]-R[18]

in which

R[14] is -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C_{1-6} alkyl-N(C_{1-6} alkyl)-, -C(O)-, -SO_2- or is absent

R[15] is cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_{1-6} alkyl-NH-, -C_{1-6} alkyl-N(C_{1-6} alkyl)-, -cycloalkyl-NH-, -heterocycloalkyl-NH- or is absent

R[16] is -C_{1-6} alkyl, -C(O)-, -C(O)-NH-, -C(O)O-, -CH_2-C(O)-, -CH_2-C(O)-NH-, -CH_2-C(O)O- or is absent

R[17] is -CH_2(C_2H_4-O)$_y$, (C_2H_4-O)$_x$, (C_3H_6-O)$_x$, or is absent

x is 1-10

y is 2-10

R^{18} is -C_{1-6} alkyl, heterocycloalkyl, or is absent

in which at least one of R^{14}-R^{18} is present.

29. A compound according to Claim 28, in which each R is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR’’’’, -NR’’’’$_2$, -NR’’’’C(O)R’’’’, -NR’’’’C(O)CH(OH)R’’’’, -NR’’’’C(O)OR’’’’, -NR’’’’SO_2R’’’’, -NO_2, -CN,-C(O)R’’’’, -C(O)OR’’’’, -C(O)NH_2, -C(O)NHR’’’’, -C(O)NR’’’’$_2$, -OR’’’’, -OC(O)R’’’’, -OC(O)OR’’’’, -OC(O)NH_2, -OC(O)NHR’’’’, -OC(O)NR’’’’$_2$, -SR’’’’, or -S(O)$_2$R’’’’, -S(O)$_2$OR’’’’, -S(O)$_2$$NH_2$, -S(O)$_2$NHR’’’’, or -S(O)$_2$NR’’’’$_2$, -O-**$R^{21}$**, -NH-**$R^{21}$**, -C(O)-NH-**$R^{21}$**, or -$CH_2$-NH-C(O)-**$R^{21}$**.

30. A compound according to Claim 28 or 29, in which each R’ is independently hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR’’’, -NR’’’$_2$, -NR’’’C(O)R’’’, -NR’’’C(O)OR’’’, -NO_2, -CN, -C(O)R’’’, -C(O)OR’’’, -C(O)NH_2, -C(O)NHR’’’, -C(O)NR’’’$_2$, -OR’’’, -OC(O)R’’’, -OC(O)OR’’’, -OC(O)NH_2, -OC(O)NHR’’’, -OC(O)NR’’’$_2$, -SR’’’, -S(O)$_2$R’’’, -S(O)$_2$OR’’’, S(O)$_2$$NH_2$, -S(O)$_2$NHR’’’, -S(O)$_2$NR’’’$_2$, -O-**$R^{21}$**, -NH-**$R^{21}$**, -C(O)-NH-**$R^{21}$**, or -$CH_2$-NH-C(O)-**$R^{21}$**.

31. A compound according to Claim 28, 29 or30, in which R^1 is hydrogen.

32. A compound according to any of Claims 28 to 31, in which R^6 is hydrogen.

33. A compound according to any of Claims 28 to 32, in which when Z_1 is S in Formula (Vb), then Y_5 is not C- NHC(O)R’’’’ or -C(O)OR’’’’.

34. A compound according to any of Claims 28 to 33, in which Z_1 is NR^6.

35. A compound according to any of Claims 28 to 34, in which:

(a) **[ligase ligand moiety]** is of Formula (Va) and Y_5, Y_6 and Y_7 are each CR^7; optionally in which

Y_5 is -C-NHC(O)R’’’’,

Y_6 is CH, and

Y_7 is CH or CCl;

further optionally in which:

L_3 is hydrogen;

Z_1 is S;

R^1 is hydrogen;

T is C=O; and

Y_7 is CH;

or

(b) **[ligase ligand moiety]** is of Formula (Vb) and Y_5, Y_6 and Y_8 are each CR^7; optionally in which:

(i) L_3 is hydrogen;

Z_1 is S;

R^1 is H;

T is C=O;

Y_5 is CH, C-OR’’’’, CCl, C-CN, or C-NHC(O)R’’’’;

Y_6 is CH, CCl, C-alkyl, C-cycloalkyl, or C-haloalkyl; and

Y_8 is CH, C-OR’’’’, C-NHC(O)R’’’’, C-NHC(O)OR’’’’, C-NHR’’’’, C-NH_2, or C-$NHSO_2$R’’’’;

in which, when Y_5 is CCl, then Y_6 is CH, C-alkyl, C-cycloalkyl, or C-haloalkyl;

optionally in which each R’’’’ is independently alkyl, cycloalkyl, aryl or benzyl; or

(ii) Y_5 is CH;

Y_6 is CH or CCl; and

Y_8 is C-OR’’’’ or C-NH_2, optionally C-OMe or C-NH_2.

36. A compound according to any of Claims 28 to 35, in which Z is NR^2; or in which Z is S.

37. A compound according to any of Claims 28 to 36, in which each  is a double bond.

38. A compound according to any of Claims 28 to 37, in which L is hydrogen.

39. A compound according to Claim 37 or 38, in which:

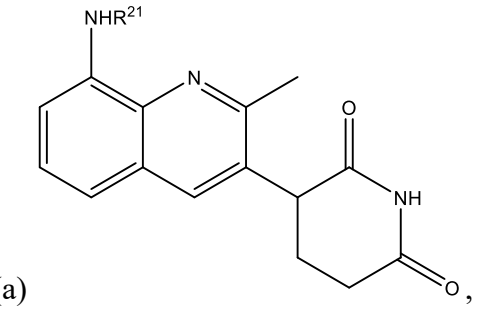
(a) one of W_1, W_2, W_3 and W_4 is N, and the remaining three of W_1, W_2, W_3 and W_4 are each CR^a; optionally in which W_4 is CR^a; or

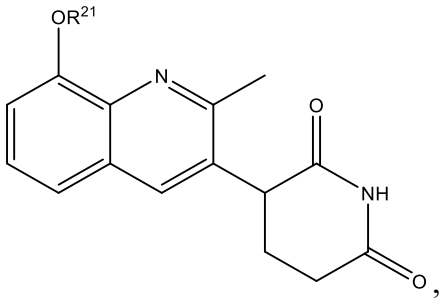
(b) two of W_1, W_2, W_3 and W_4 is N, and the remaining two of W_1, W_2, W_3 and W_4 are each CR^a; or

(c) one of W_1, W_2, W_3 and W_4 is CR^a, and the remaining three of W_1, W_2, W_3 and W_4 are each N.

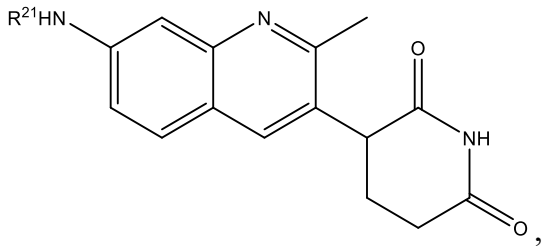
40. A compound according to any of Claims 28 to 39, in which each R is independently hydrogen, halogen or $-NR^hC(O)R^h$.

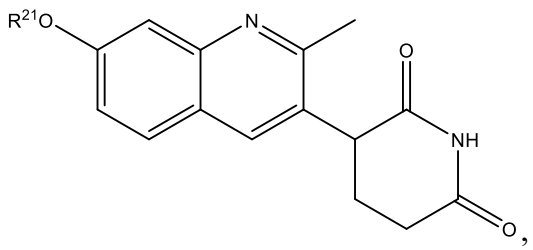
41. A compound according to any of Claims 28 to 40, in which **[ligase ligand moiety]** is:

(a) 

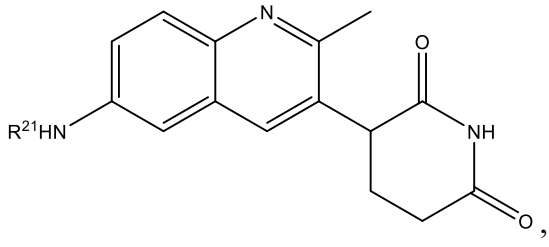
, 

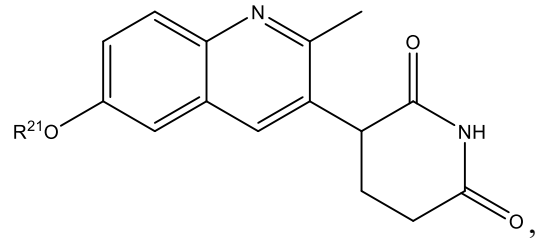
,



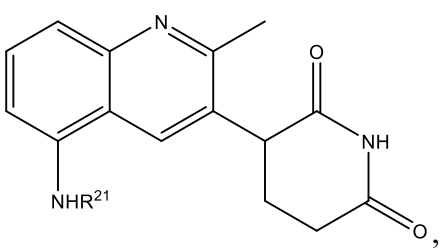
, 

,

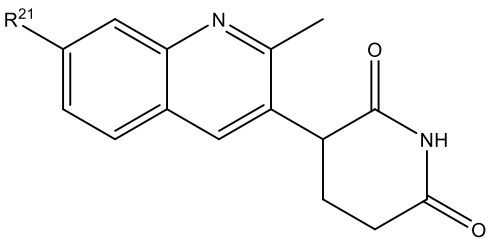


, 

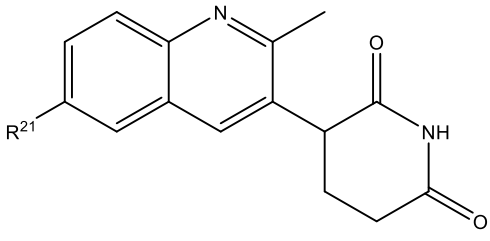
,



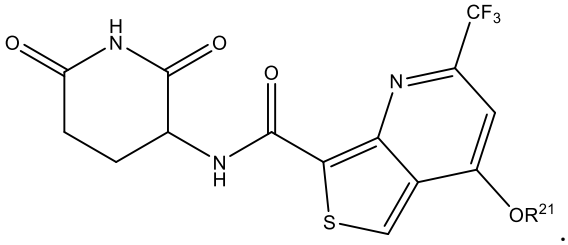
,



or



; or

(b)


.

42. A compound according to any of Claims 28 to 41, in which:

(a) E_1, E_2, E_3 and E_4 are each CR'; or

(b) one of E_1, E_2, E_3 and E_4 is N and the remaining three of E_1, E_2, E_3 and E_4 are each CR'.

43. A compound according to any of Claims 28 to 42, in which Q_1 is CR^5 or in which Q_2 is CR^5.

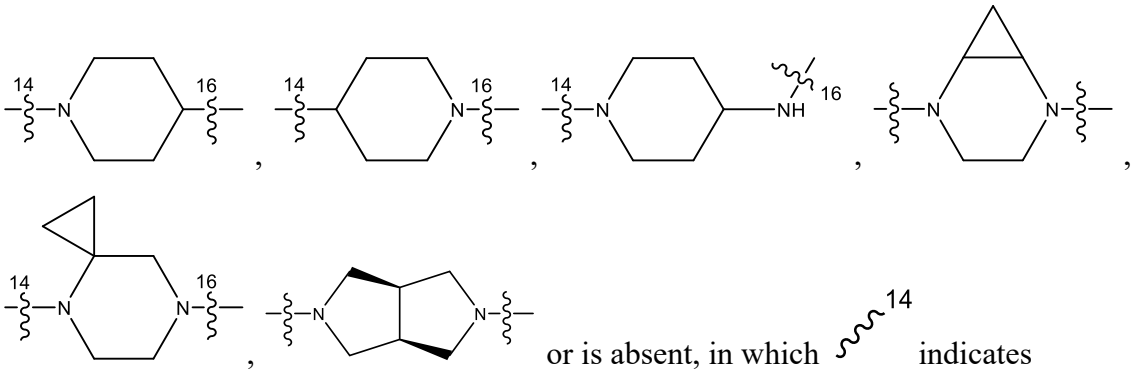
44. A compound according to any of Claims 28 to 43, in which **R^{14}** is -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C(O)-, -SO_2- or is absent.

45. A compound according to any of Claims 28 to 44, in which **R^{15}** is cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_{1-6} alkyl-NH-, -cycloalkyl-NH- or is absent.

46. A compound according to any of Claims 28 to 45, in which

R^{14} is -C_{1-6} alkyl, -SO_2- or is absent

R^{15} is piperazine, bridged piperazine, piperazine N-oxide, piperazine cation, -C_{1-6} alkyl-NH-,



or is absent, in which indicates attachment to **R**[14] and  indicates attachment to **R**[16],

R[16] is -$C_{1\text{-}6}$ alkyl, -C(O)-, -C(O)-NH-, -CH_2-C(O)-NH- or is absent

R[17] is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

x is 1-6

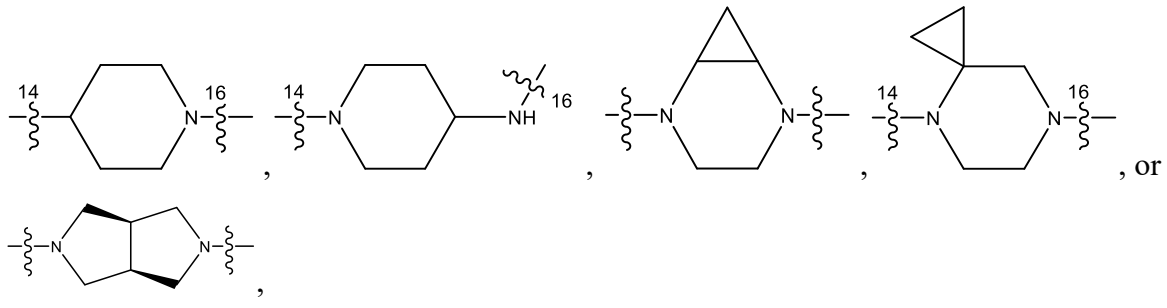
y is 2-6

R[18] is -$C_{1\text{-}6}$ alkyl, piperazine, or is absent

in which at least one of R^{14}-R^{18} is present

47. A compound according to any of Claims 28 to 46, in which **R**[18] is -$C_{1\text{-}6}$ alkyl or is absent.

48. A compound according to any of Claims 28 to 47, in which when **R**[15] is piperazine, bridged piperazine, piperazine N-oxide, piperazine cation, -$C_{1\text{-}6}$ alkyl-NH-,



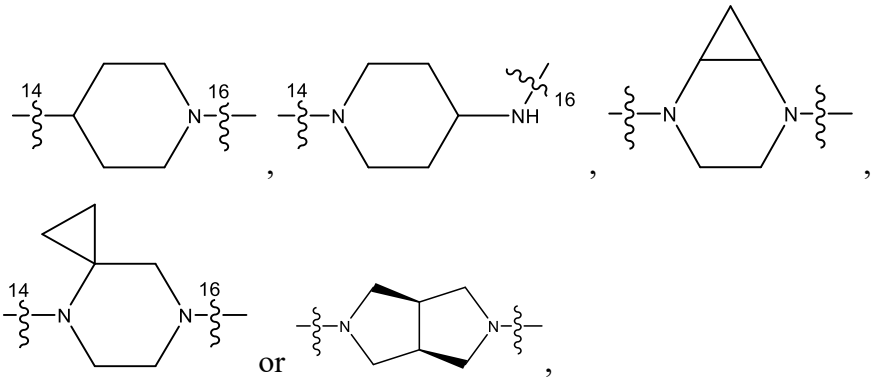
, or

then **R**[14] is -$C_{1\text{-}6}$ alkyl.

49. A compound according to any of Claims 28 to 48, in which

(a) **R**[14] is -$C_{1\text{-}6}$ alkyl,

R[15] is piperazine, bridged piperazine, piperazine N-oxide,



R16 is -C(O)-, -CH_2-C(O)-NH-, or is absent

R17 is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

R18 is -$C_{1\text{-}6}$ alkyl,

in which when **R16** and **R17** are absent, **R18** is -$C_{3\text{-}6}$ alkyl;

optionally in which

R14 is -C_2 alkyl,

x is 1, 2 or 6

y is 2;

or in which

R15 is piperazine,

R16 is -C(O)-,

R17 is absent, optionally in which

R14 is -C_2 alkyl,

R18 is -$C_{1\text{-}2}$ alkyl;

or

(b) when **R14** is -SO_2-, at least two of **R15**-**R18** are present, and at least one of **R15**-**R18** is not $C_{1\text{-}6}$ alkyl; or

(c) **R14** is -SO_2-

R15 is -$C_{1\text{-}6}$ alkyl-NH-

R16 is -C(O)-

$\mathbf{R^{17}}$ is $-CH_2(C_2H_4-O)_y$, $(C_2H_4-O)_x$ or is absent

$\mathbf{R^{18}}$ is $-C_{2-4}$ alkyl;

optionally in which

$\mathbf{R^{15}}$ is $-C_2$alkyl-NH-

x is 1 or 2

y is 1

$\mathbf{R^{18}}$ is $-C_{2-4}$ alkyl

or

(d) $\mathbf{R^{14}}$ is absent

$\mathbf{R^{15}}$ is absent

$\mathbf{R^{16}}$ is -C(O)-NH-, or is absent

$\mathbf{R^{17}}$ is $-CH_2(C_2H_4-O)_y$, $(C_2H_4-O)_x$, $(C_3H_6-O)_x$, or is absent

$\mathbf{R^{18}}$ is $-C_{1-6}$ alkyl.

50. A compound according to any of Claims 28 to 49, in which at least one of $\mathbf{R^{14}}$-$\mathbf{R^{18}}$ is not $-C_{1-6}$ alkyl.

51. A compound according to Claim 49(d) or 50, in which

x is 1, 2 or 3

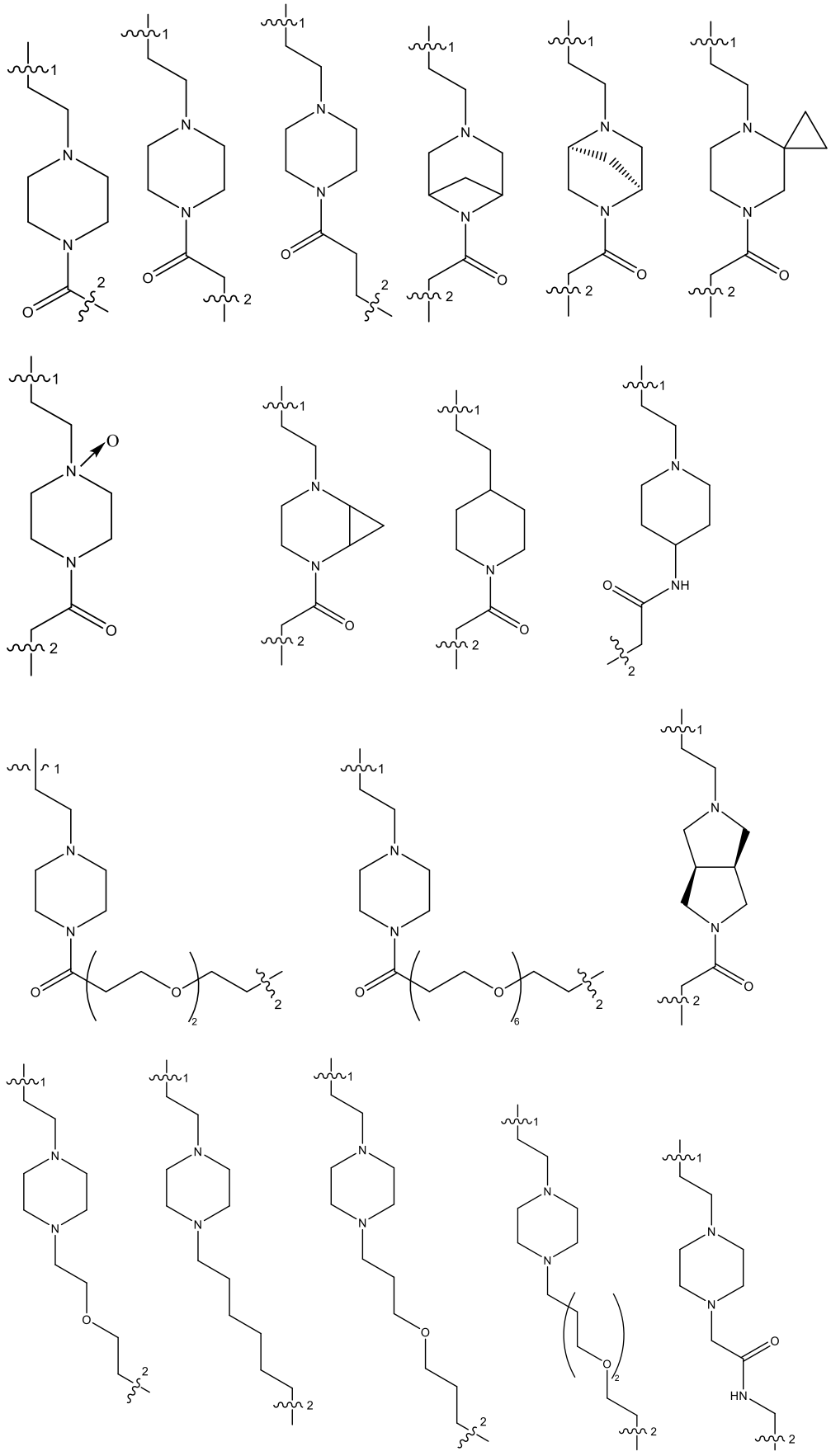
y is 2

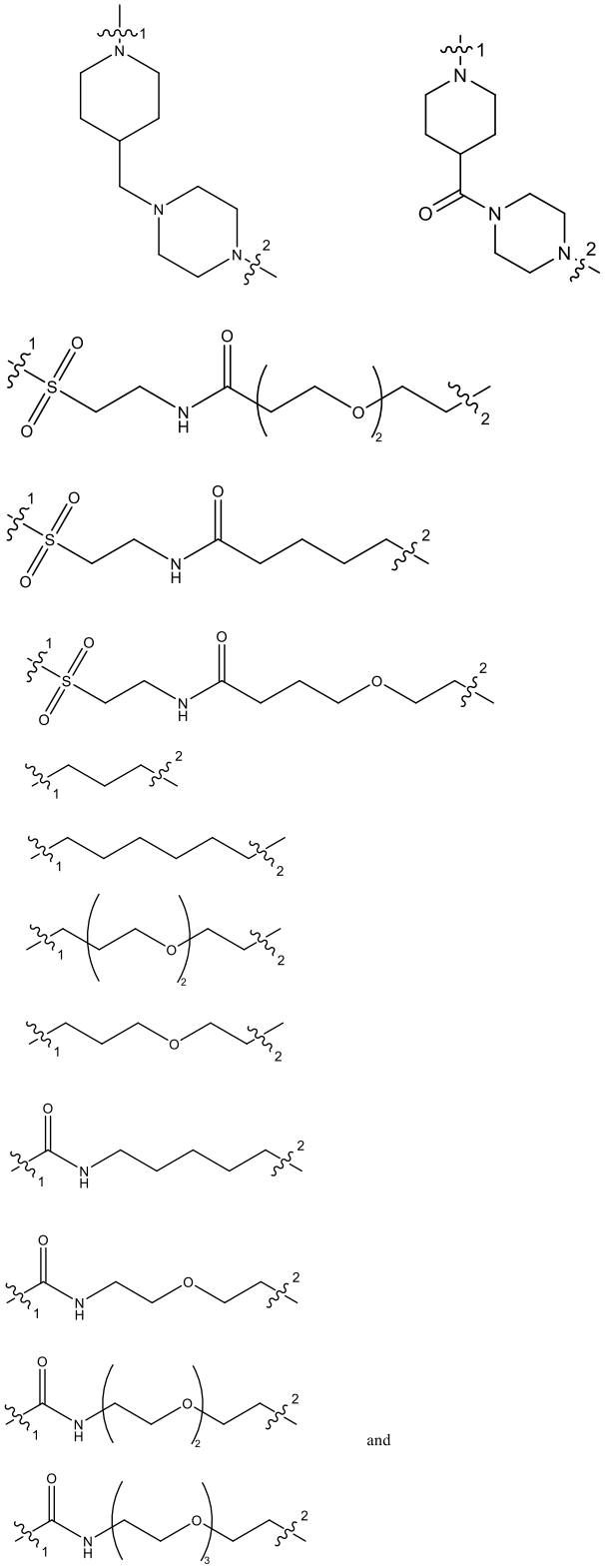
$\mathbf{R^{18}}$ is $-C_{2-6}$ alkyl.

52. A compound according to any of Claims 28 to 51, in which when $\mathbf{R^{15}}$ is $-C_{1-6}$ alkyl-NH-, at least one of $\mathbf{R^{16}}$-$\mathbf{R^{18}}$ is present.

53. A compound according to any of Claims 28 to 52, in which when $\mathbf{R^{17}}$ is $-CH_2(C_2H_4-O)_y$, $(C_2H_4-O)_x$ or $(C_3H_6-O)_x$, at least one of $\mathbf{R^{14}}$-$\mathbf{R^{16}}$ and $\mathbf{R^{18}}$ is present, in which at least one of $\mathbf{R^{14}}$ and $\mathbf{R^{18}}$ is not $-C_{1-6}$ alkyl.

54. A compound according to any of Claims 28 to 53, in which **[linker]** is selected from





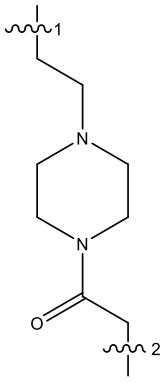
and

in which

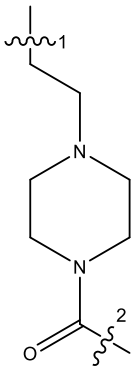
 indicates attachment to **[MCL-1 ligand moiety]** and

 indicates attachment to **[ligase ligand moiety];**

optionally in which **[linker]** is



or



in which



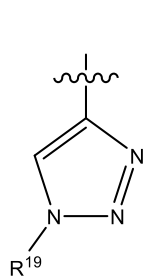
indicates attachment to **[MCL-1 ligand moiety]** and



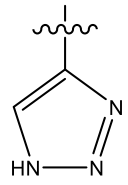
indicates attachment to **[ligase ligand moiety]**.

55. A compound according to any of Claims 28 to 54, in which **R^{10}** is -C_{2-5}alkyl-O-R^{13}, in which R^{13} is phenyl, naphthyl or tetraline, in which the phenyl, naphthyl or tetraline is optionally substituted with at least one substituent selected from halogen, C_1-C_6 alkyl and -O(C_1-C_6 alkyl); or in which the naphthyl is optionally substituted with -O- or -S-.

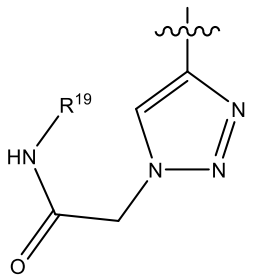
56. A compound according to any of Claims 28 to 55, in which **R^{12}** is H,



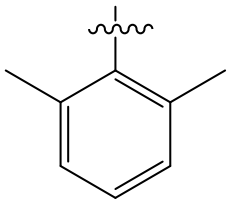
,



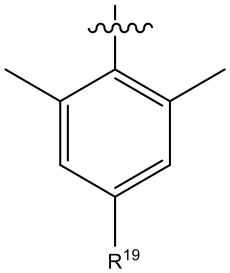
,



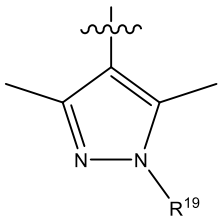
,



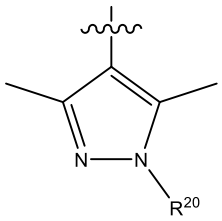
,



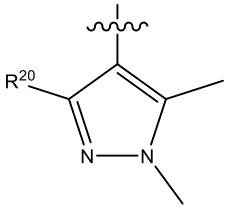
,



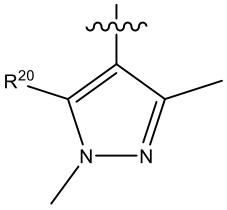
,



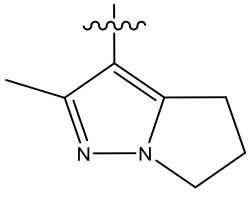
,



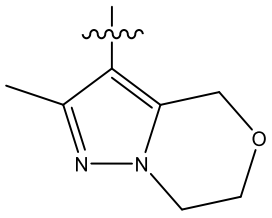
,



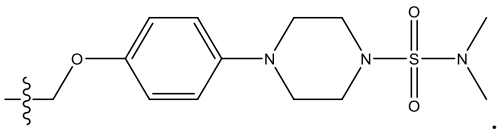
,

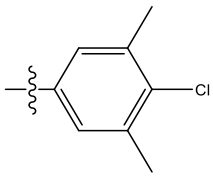


or



.

57. A compound according to any of Claims 28 to 56, in which **R[20]** is Me, -CH_2-O-bromobenzaldehyde, or  .

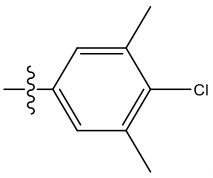
58. A compound according to any of Claims 28 to 57, in which when **R[8]** is H, **R[13]** is  .

59. A compound according to any of Claims 28 to 58, in which

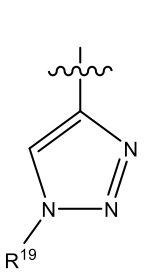
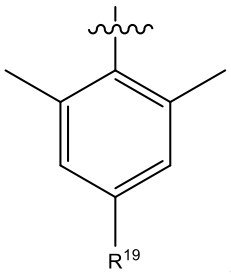
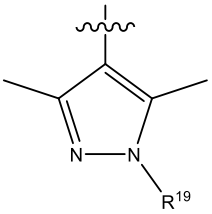
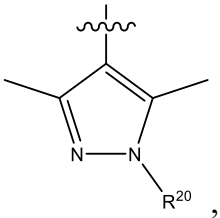
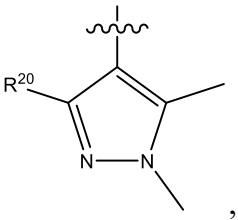
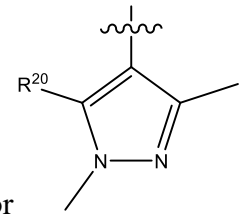
R[8] is H, **R[19]**, methyl, or -CH_2CH_2-morpholine;

R[9] is -C(O)OH or -C(O)NH**R[19]**,

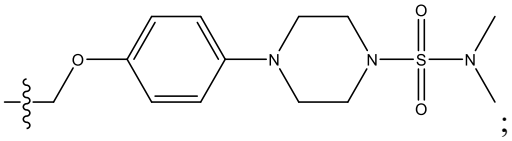
R[10] is -C_3H_6O-R^{13},

in which **R[13]** is  , tetraline, or naphthyl optionally substituted with fluorine;

R[11] is H, Cl, F or methyl,

R[12] is  ,  ,  ,  ,  ,  , or

in which **R[20]** is Me, -CH_2-O-bromobenzaldehyde, or



;

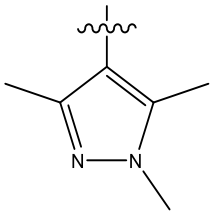
optionally in which

R[8] is **R[19]** or methyl;

R[10] is -C_3H_6O-R^{13}, in which **R[13]** is naphthyl optionally substituted with fluorine;

R[11] is Cl or F,

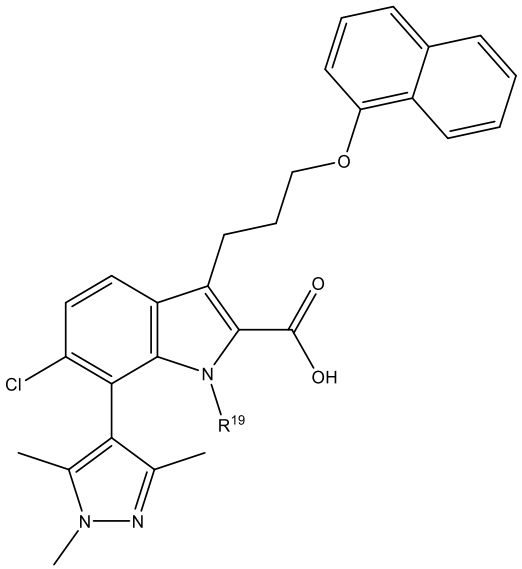
R[12] is



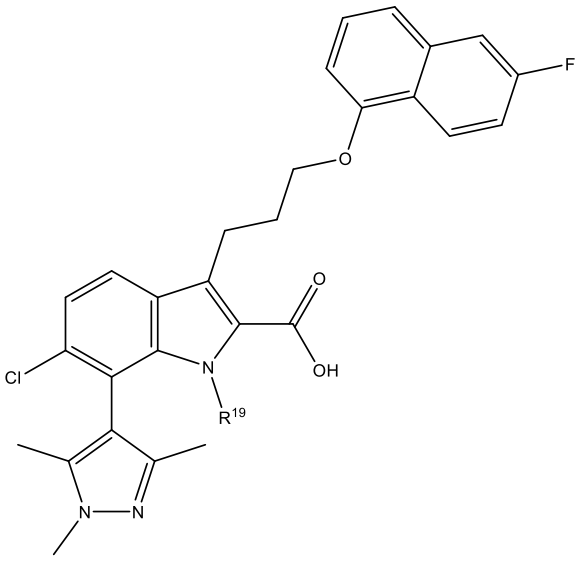
.

60. A compound according to any of Claims 28 to 59, in which **Z_2** is C and  is a double bond.

61. A compound according to any of Claims 28 to 60, in which **[MCL-1 ligand moiety]** is

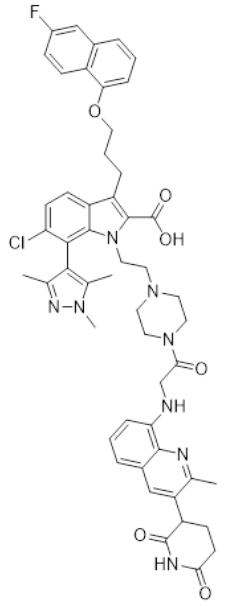
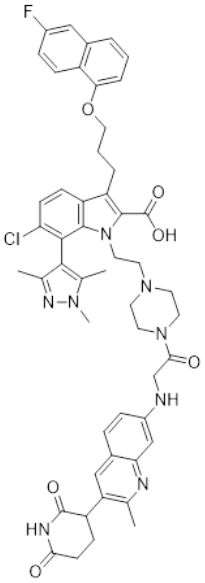
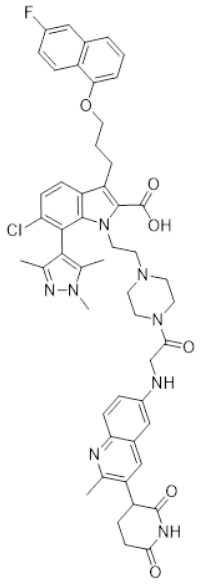
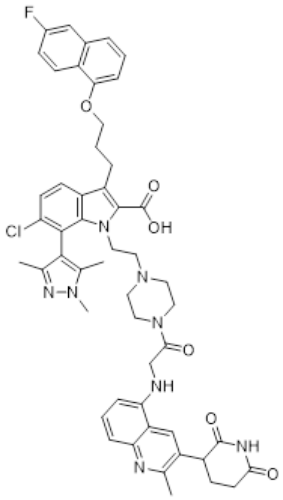
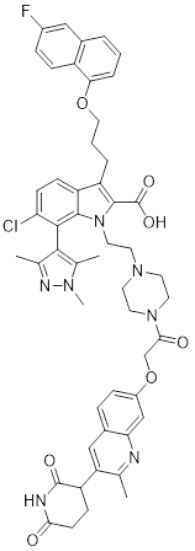
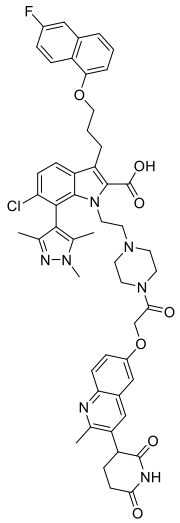


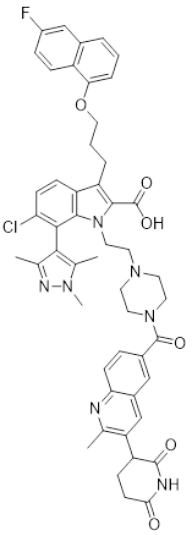
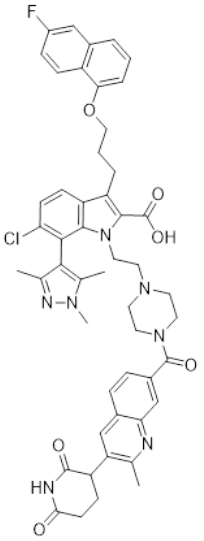
or



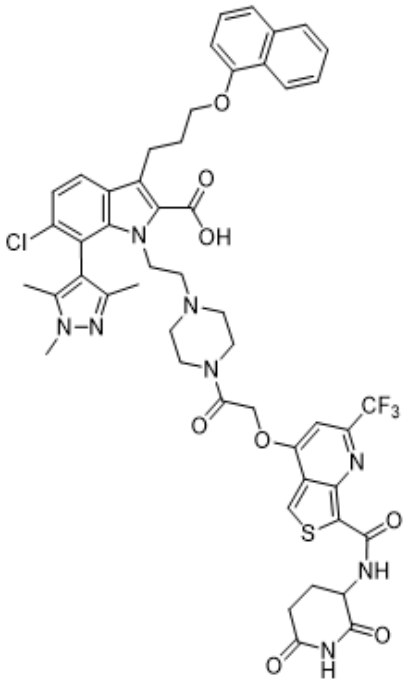
.

62. A compound according to Claim 28, in which the compound is selected from:

 284	 285	 286
 287	 288	 289

		
290	291	

or in which the compound is:



267

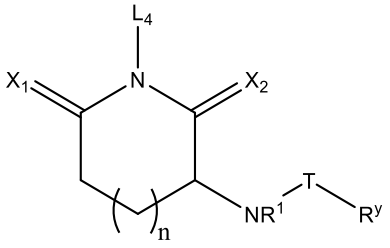
63. A compound of formula (I)

[MCL-1 ligand moiety] – [linker] – [ligase ligand moiety] (I)

or a salt, solvate, hydrate, isomer or prodrug thereof,

in which **[ligase ligand moiety]** is:

(a) Formula (II):



(II)

in which:

each of X_1 and X_2 is independently O or S;

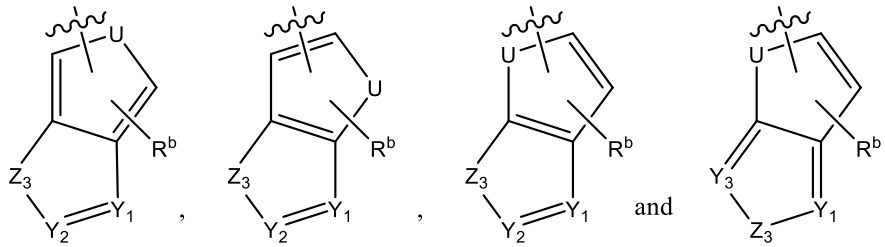
T is C=O or SO_2;

R^1 is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

n is 0, 1 or 2;

L_4 is hydrogen, alkyl, alkenyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -C(O)H, -C(O)R'',-C(O)OH, -C(O)OR'', -C(O)NH_2, -C(O)NHR'', -C(O)NR''_2, -OH, -OR'', -NH_2, -NHR'', -NR''_2, -$S(O)_2$H or -$S(O)_2$R'';

R^y is selected from



in which  indicates attachment to T,

Z_3 is O, S or NR^3;

U is O, S, NR^b or CR^b_2;

each of Y_1, Y_2 and Y_3 is independently N or CR^d;

each R^d is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR'', -NR''_2, -NHC(O)R'', -NR''C(O)R'', NHC(O)CH(OH)R'', -NR''C(O)CH(OH)R'', -NHC(O)OR'', -NR''C(O)OR'', -$NHSO_2$R'', -NR''SO_2R'', -NO_2, -CN, -C(O)H,

C(O)R'', -C(O)OH, -C(O)OR'', -C(O)NH_2, -C(O)NHR'', -C(O)NR''_2,-OH, -OR'', -OC(O)H, -OC(O)R'', -OC(O)OH,-OC(O)OR'', -OC(O)NH_2, -OC(O)NHR'', -OC(O)NR''_2, -SH, -SR'', -$S(O)_2H$, -$S(O)_2R''$, -$S(O)_2OH$, -$S(O)_2OR''$, -$S(O)_2NH_2$, -$S(O)_2NHR''$, -$S(O)_2NR''_2$, -O-**R^{21}**, -NH-**R^{21}**, -C(O)-NH-**R^{21}**, or -CH_2-NH-C(O)-**R^{21};**

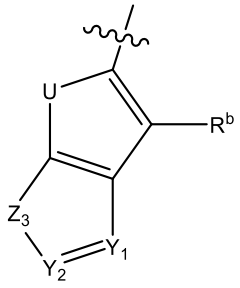
each R^b is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR'', -NR''_2, -NHC(O)R'', -NR''C(O)R'', NHC(O)CH(OH)R'', -NR''C(O)CH(OH)R'', -NHC(O)OR'', -NR''C(O)OR'', -$NHSO_2R''$, -$NR''SO_2R''$, -NO_2, -CN, -C(O)H, C(O)R'', -C(O)OH, -C(O)OR'', -C(O)NH_2, -C(O)NHR'', -C(O)NR''_2,-OH, -OR'', -OC(O)H, -OC(O)R'', -OC(O)OH,-OC(O)OR'', -OC(O)NH_2, -OC(O)NHR'', -OC(O)NR''_2, -SH, -SR'', -$S(O)_2H$, -$S(O)_2R''$, -$S(O)_2OH$, -$S(O)_2OR''$, -$S(O)_2NH_2$, -$S(O)_2NHR''$, or -$S(O)_2NR''_2$**;**

each R^3 is independently hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -NH_2, -NHR'', -NR''_2, -NHC(O)R'', -NR''C(O)R'', NHC(O)CH(OH)R'', -NR''C(O)CH(OH)R'', -NHC(O)OR'', -NR''C(O)OR'', -$NHSO_2R''$, -$NR''SO_2R''$, -NO_2, -CN, -C(O)H, C(O)R'', -C(O)OH, -C(O)OR'', -C(O)NH_2, -C(O)NHR'', -C(O)NR''_2,-OH, -OR'', -OC(O)H, -OC(O)R'', -OC(O)OH,-OC(O)OR'', -OC(O)NH_2, -OC(O)NHR'', -OC(O)NR''_2, -SH, -SR'', -$S(O)_2H$, -$S(O)_2R''$, -$S(O)_2OH$, -$S(O)_2OR''$, -$S(O)_2NH_2$, -$S(O)_2NHR''$, -$S(O)_2NR''_2$, -**R^{21}**, -C(O)-NH-**R^{21}**, or -CH_2-NH-C(O)-**R^{21};**

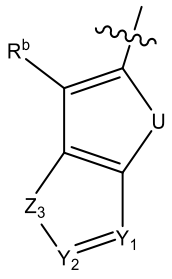
each R'' is independently alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

R^{21} is a bond connected to **R^{18}** of the linker, in which Formula (II) contains a single **R^{21};**

in which,

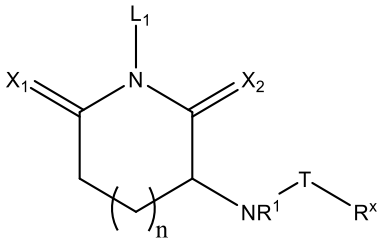
(i) when R^y is 

then Y_2 is CR^d; and

(ii) when R^y is  , then R^b in CR^b_2 is not hydrogen

or

(b) Formula (III):


(III)

in which:

each of X_1 and X_2 is independently O or S;

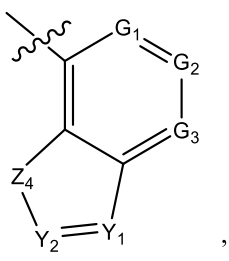
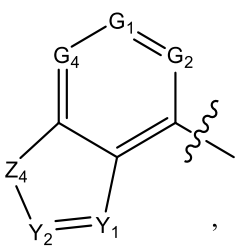
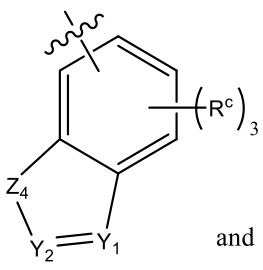
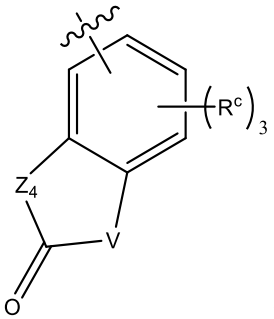
T is C=O or SO_2;

R^1 is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

n is 0, 1 or 2;

L_1 is hydrogen, alkenyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -C(O)H, -C(O)R'',-C(O)OH, -C(O)OR'', $-CH_2C(O)OR''$, $-C(O)NH_2$, -C(O)NHR'', $-C(O)NR''_2$, -OH, -OR'', $-NH_2$, -NHR'', $-NR''_2$, $-S(O)_2H$ or $-S(O)_2R''$;

R^x is selected from


,

,

and

in

which  indicates attachment to T,

Z_4 is O, S or NR^4;

V is CR^f_2, NR^4 or S;

each of G_1, G_2, G_3 and G_4 is independently N or CR^c,

each of Y_1 and Y_2 is independently N or CR^f,

each R^f is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, fused aryl-cycloalkyl, fused aryl-heterocycloalkyl, heteroaryl, heteroaryl substituted with at least one aryl group, benzyl, haloalkyl, haloalkenyl, $-NH_2$, -NHR'', $-NR''_2$, -NHC(O)R'', -NR''C(O)R'', NHC(O)CH(OH)R'', -NR''C(O)CH(OH)R'', -NHC(O)OR'', -NR''C(O)OR'', $-NHSO_2R''$, $-NR''SO_2R''$, $-NO_2$, -CN, -C(O)H, C(O)R'', -C(O)OH, -C(O)OR'', $-C(O)NH_2$, -C(O)NHR'', $-C(O)NR''_2$,-OH, -OR'', -OC(O)H, -OC(O)R'', -OC(O)OH,-OC(O)OR'', $-OC(O)NH_2$, -OC(O)NHR'', $-OC(O)NR''_2$, -SH, -SR'', $-S(O)_2H$, $-S(O)_2R''$, $-S(O)_2OH$, $-S(O)_2OR''$, $-S(O)_2NH_2$, $-S(O)_2NHR''$, $-S(O)_2NR''_2$, - **R^{21}**, -O-**R^{21}**, -NH-**R^{21}**, -C(O)-NH-**R^{21}**, or $-CH_2$-NH-C(O)-**R^{21};** or when Y_1 and Y_2 are CR^f then each R^f, together with the carbon atom to which it is attached, forms a 5- or 6- membered ring;

each R^c is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, aryl substituted with at least one –OR'', heteroaryl, benzyl, haloalkyl, haloalkenyl, $-NH_2$, -NHR'', $-NR''_2$, $-CH_2NH_2$, -NHC(O)R'', -NR''C(O)R'', NHC(O)CH(OH)R'', -NR''C(O)CH(OH)R'', -NHC(O)OR'', -NR''C(O)OR'', $-NHSO_2R''$, $-NR''SO_2R''$, $-NO_2$, -CN, -C(O)H, C(O)R'', -C(O)OR'', $-C(O)NH_2$, -C(O)NHR'', $-C(O)NR''_2$,-OH, -OR'', -OC(O)H, -OC(O)R'', -OC(O)OH,-OC(O)OR'', $-OC(O)NH_2$, -OC(O)NHR'', $-OC(O)NR''_2$, -SH, -SR'', $-S(O)_2H$, $-S(O)_2R''$, $-S(O)_2OH$, $-S(O)_2OR''$, $-S(O)_2NH_2$, $-S(O)_2NHR''$, $-S(O)_2NR''_2$, -O-**R^{21}**, -NH-**R^{21}**, -C(O)-NH-**R^{21}**, or $-CH_2$-NH-C(O)-**R^{21};**

each R^4 is independently hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, benzyl, haloalkyl, haloalkenyl, -C(O)H, C(O)R'', -C(O)OH, -C(O)OR'', $-C(O)NH_2$, -C(O)NHR'', $-C(O)NR''_2$, -OH, -OR'', $-NH_2$, -NHR'', $-NR''_2$, $-S(O)_2H$, $-S(O)_2R''$, - **R^{21}**, -C(O)-NH-**R^{21}**, or $-CH_2$-NH-C(O)-**R^{21};** and

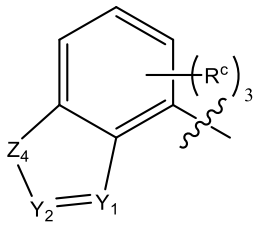
each R'' is independently alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, or benzyl;

R^{21} is a bond connected to **R^{18}** of the linker, in which Formula (III) contains a single **R^{21};**

in which, when n = 2, each R^c is hydrogen, and each of G_1, G_2, G_3 and G_4 is CR^c, then $C=X_1$ may be replaced by CH;

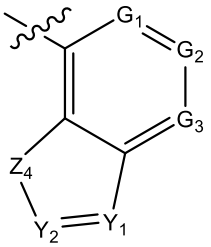
and in which:

(i) when R^x is

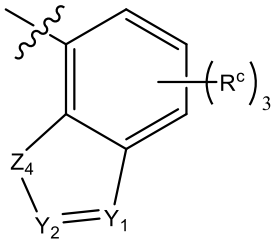


and Z_4 is NH, then L_1 is hydrogen, $-CH_2C(O)OR''$, or $-OR''$;

(ii) when R^x is

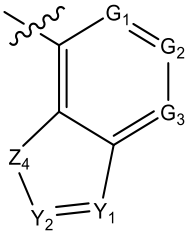


or



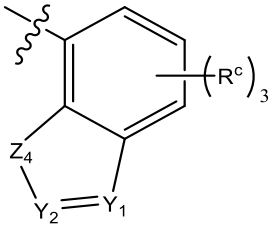
, Z_4 is NR^4, Y_1 is CR^f, and Y_2 is N, then R^4 is not alkyl and at least one of R^2 and R is not H;

(iii) when R^x is



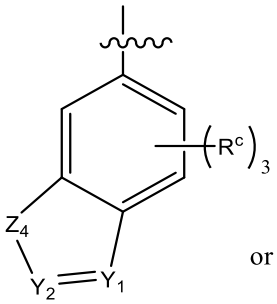
, Z_4 is NR^4, and Y_1 and Y_2 are CR^f, then at least one of G_1, G_2 and G_3 is N;

(iv) when Z_4 is NR^4, and Y_1 and Y_2 are CR^f, then R^x is not

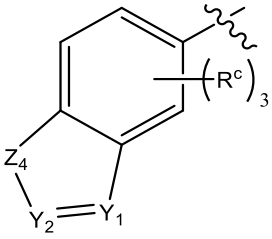


;

(v) when R^x is

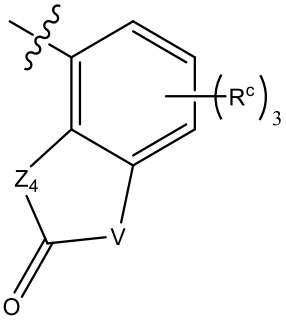


or

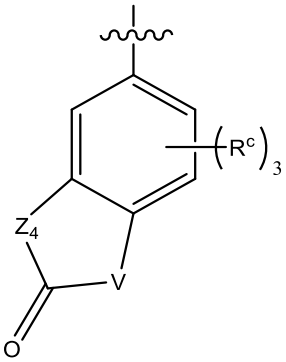


, Z_4 is NR^4, and Y_1 or Y_2 is N, then R^4 is not alkyl;

(vi) when R^x is

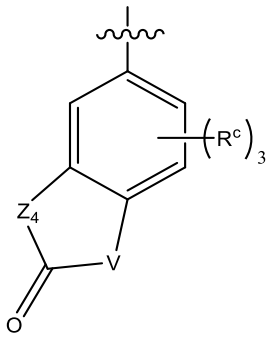


or

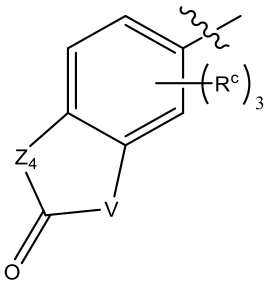


, then n = 1 or 2; and

(vii) when R^x is



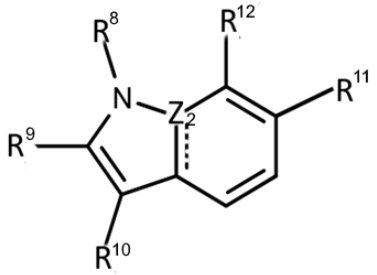
or

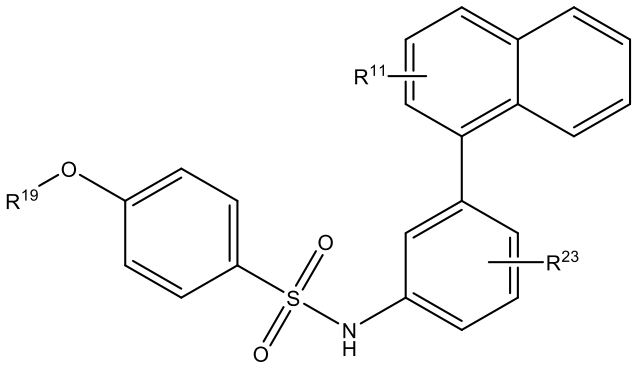


, then Z_4 = O or S

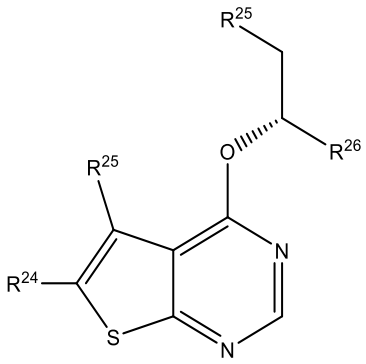
in which

[MCL-1 ligand moiety] is a compound of Formula (A), Formula (B) or Formula (C)





(A) (B)



(C)

in which

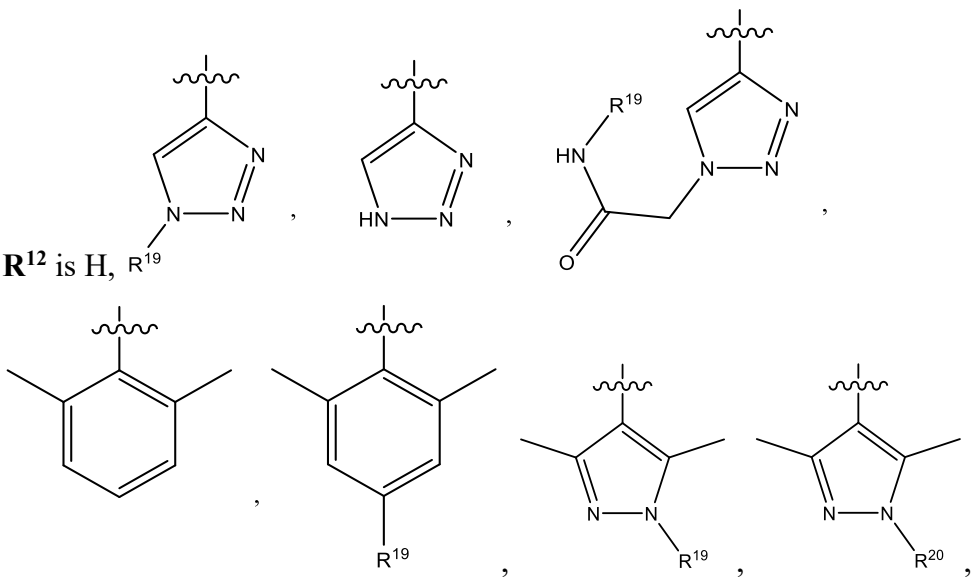
 is a single bond or a double bond;

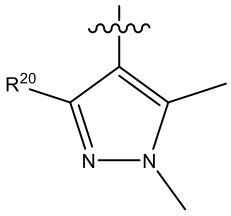
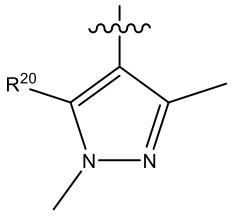
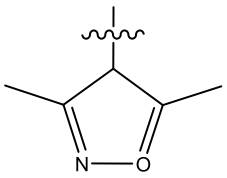
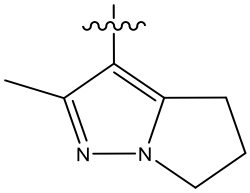
R[8] is H, **R[19]**, or C_1-C_6 alkyl optionally substituted with morpholine;

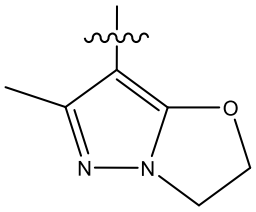
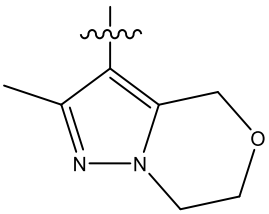
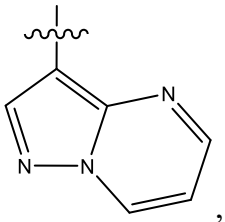
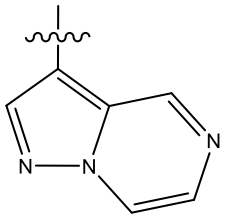
R[9] is -C(O)OH, -C(O)OC_1-C_6alkyl; -C(O)NH_2; -C(O)O**R[19]** or -C(O)NH**R[19]**,

R[10] is -C_{2-5}alkyl-O-R^{13} or -C_{2-5}alkyl-NMe-R^{13}, in which R^{13} is phenyl, naphthyl or tetraline, in which the phenyl, naphthyl or tetraline is optionally substituted with at least one substituent selected from halogen, C_1-C_6 alkyl and -O(C_1-C_6 alkyl); or in which the tetraline is optionally substituted with a bridging -CH_2- group; or in which the naphthyl is optionally substituted with -O- or -S-,

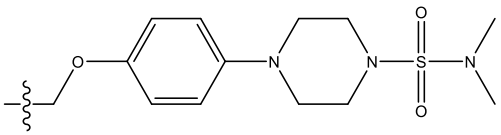
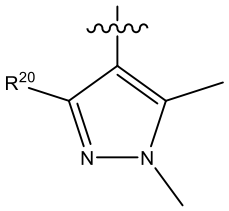
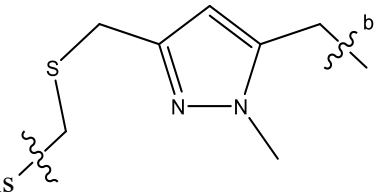
R[11] is H, halogen or C_1-C_6 alkyl,

R[12] is H, 

 ,  ,  ,  ,

 ,  ,  , or  ,

in which $\mathbf{R^{20}}$ is Me, $-CH_2-OMe$, $-CH_2-O$-bromobenzaldehyde, or

 ;or when $\mathbf{R^{12}}$ is  and $\mathbf{R^{10}}$ is -O-naphthyl substituted with -O- or -S-, then $\mathbf{R^{20}}$ is  , in which  indicates attachment to -O- or -S- of $\mathbf{R^{10}}$;

and in which

$\mathbf{R^{19}}$ is a bond connected to $\mathbf{R^{14}}$ of the linker;

$\mathbf{R^{23}}$ is -C(O)OH or $-C(O)OC_1-C_6$alkyl;

$\mathbf{Z_2}$ is N or C, in which when $\mathbf{Z_2}$ is N, then  is a single bond; and when $\mathbf{Z_2}$ is C, then  is a double bond,

$\mathbf{R^{24}}$ is furan optionally substituted with at least one halogen,

each $\mathbf{R^{25}}$ is independently phenyl substituted with $-O\mathbf{R^{28}}$ and optionally further substituted with at least one substituent selected from halogen and C_1-C_6 alkyl;

$\mathbf{R^{26}}$ is $-C(O)O\mathbf{R^{19}}$ or $-C(O)NH\mathbf{R^{19}}$; and

each $\mathbf{R^{28}}$ is independently $-C_{1-3}$alkyl-(N-alkyl piperazine) or $-C_{1-3}$alkyl-(N-haloalkylpyrazole)

and in which each of Formula (A), Formula (B) and Formula (C) contains a single **R^{19};**

and in which **[linker]** has the following formula

R^{14}-R^{15}-R^{16}-R^{17}-R^{18}

in which

R^{14} is -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, C_{1-6} alkyl-N(C_{1-6} alkyl)-, -C(O)-, -SO_2- or is absent

R^{15} is cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_{1-6} alkyl-NH-, -C_{1-6} alkyl-N(C_{1-6} alkyl)-, -cycloalkyl-NH-, -heterocycloalkyl-NH- or is absent

R^{16} is -C_{1-6} alkyl, -C(O)-, -C(O)-NH-, -C(O)O-, -CH_2-C(O)-, -CH_2-C(O)-NH-, -CH_2-C(O)O- or is absent

R^{17} is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

x is 1-10

y is 2-10

R^{18} is -C_{1-6} alkyl, heterocycloalkyl, or is absent

in which at least one of R^{14}-R^{18} is present

64. A compound according to Claim 63, in which in Formula (III):

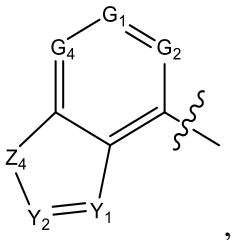
each of X_1 and X_2 is O;

T is C=O;

R^1 is hydrogen,

L_1 is hydrogen,

R^x is



,

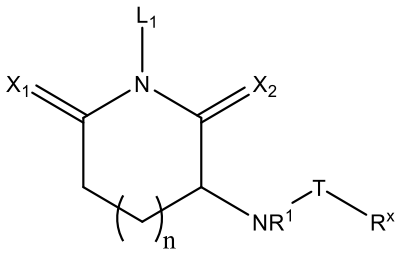
Z_4 is NR^4;

each of G_1, G_2 and G_4 is CR^c,

Y_1 is N, and

Y_2 is CR^f, in which R^f is not hydrogen.

65. A compound according to Claim 63 or 64, in which **[ligase ligand moiety]** is Formula (III):



(III)

66. A compound according to Claim 63, 64 or 65, in which one of R^c is -O-**R21**, -NH-**R21**, -C(O)-NH-**R21**, or -CH_2-NH-C(O)-**R21**.

67. A compound according to any of Claims 63 to 66, in which G_1 is C-O-**R21**, C-NH-**R21**, C-C(O)-NH-**R21**, or C-CH_2-NH-C(O)-**R21**; or in which G_2 is C-O-**R21**, C-NH-**R21**, C-C(O)-NH-**R21**, or C-CH_2-NH-C(O)-**R21**.

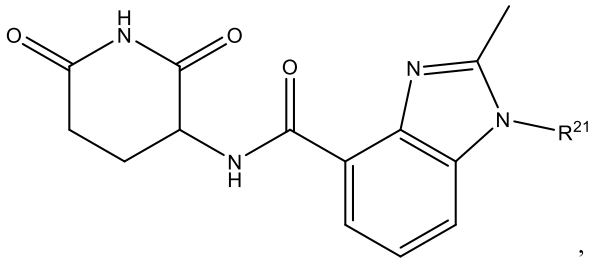
68. A compound according to Claim 63, 64 or 65, in which:

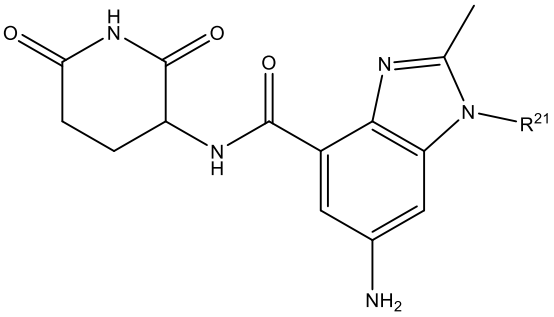
(a) R^4 is **R21**, -C(O)-NH-**R21**, or -CH_2-NH-C(O)-**R21**;

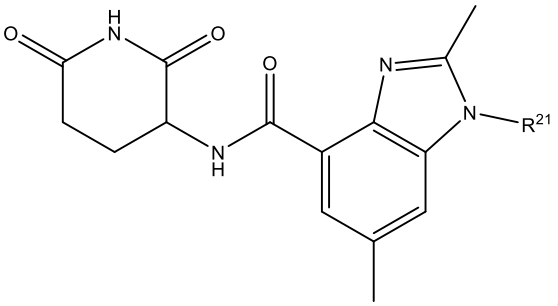
(b) one of R^f is - **R21**, -O-**R21**, -NH-**R21**, -C(O)-NH-**R21**, or -CH_2-NH-C(O)-**R21**;

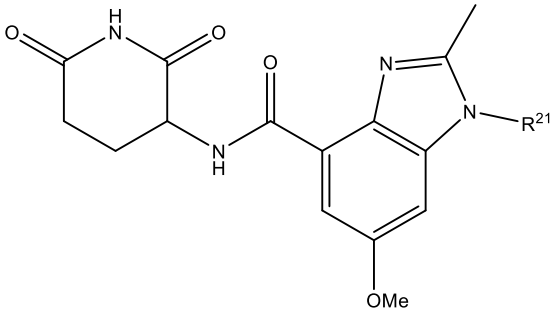
optionally in which Y_2 is C-**R21**, CO-**R21**, C-NH-**R21**, C-C(O)-NH-**R21**, or C-CH_2-NH-C(O)-**R21**.

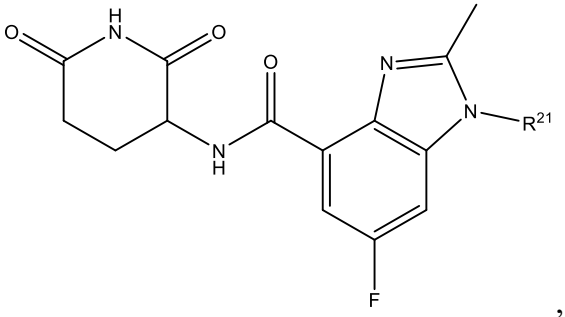
69. A compound according to any of Claims 63 to 68, in which **[ligase ligand moiety]** is selected from

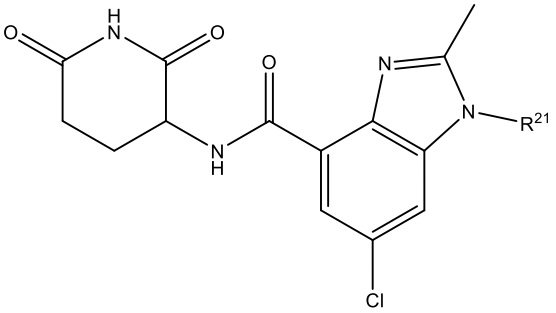

,

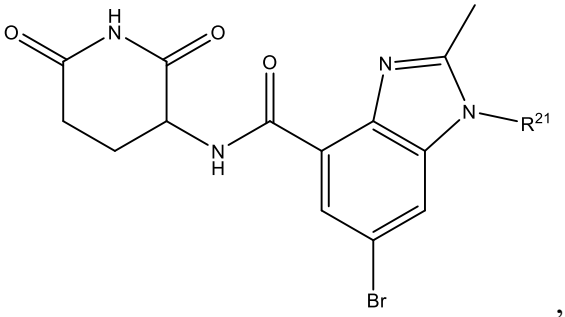

,

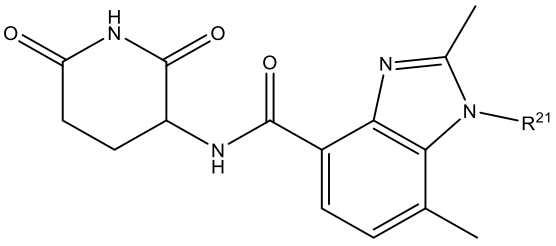

,

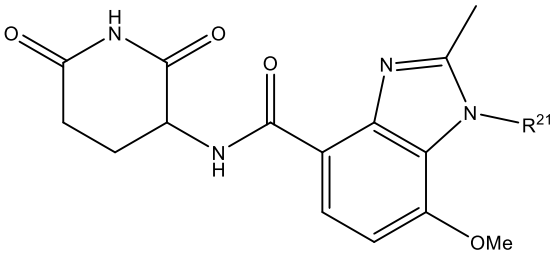

,

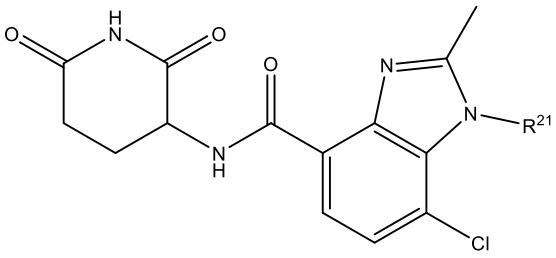

,

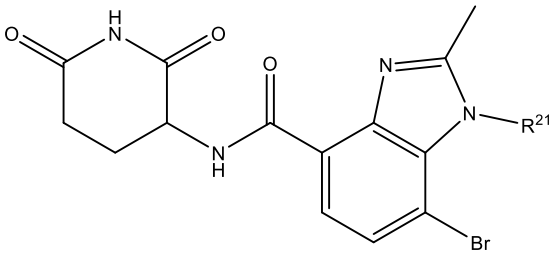

,

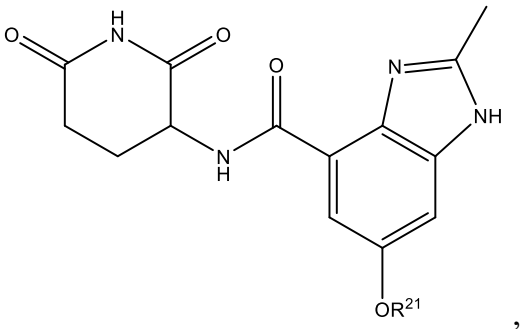

,

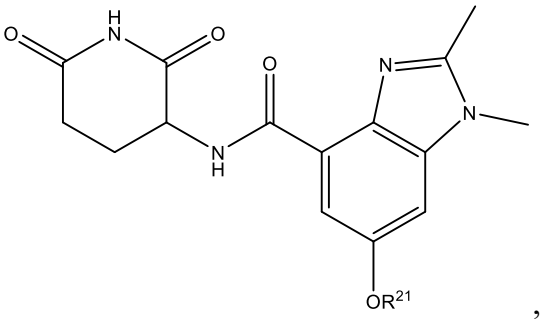

,

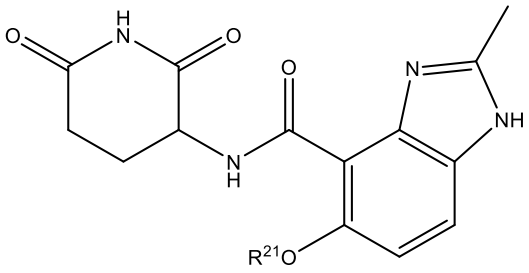


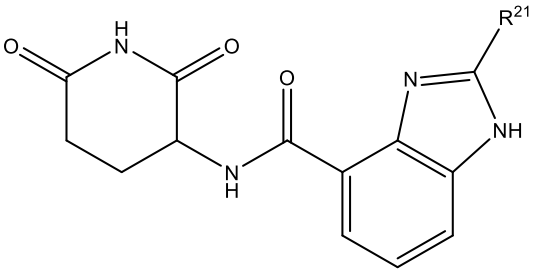
,


,


,


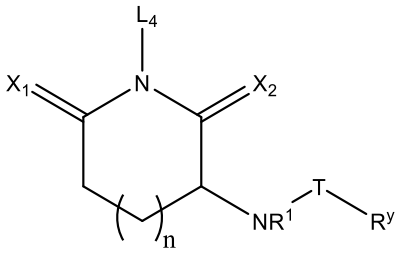
,


,


and


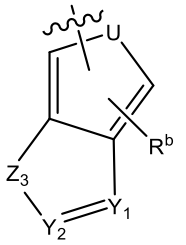
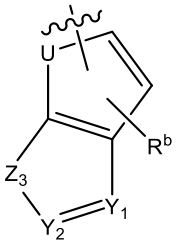
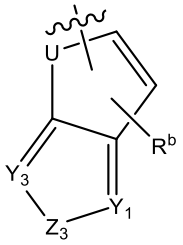
,

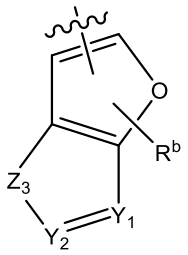
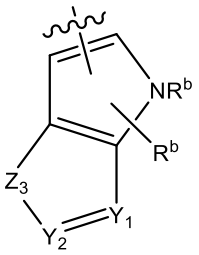
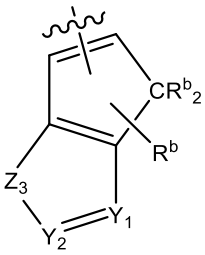
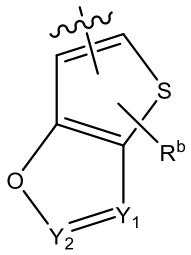
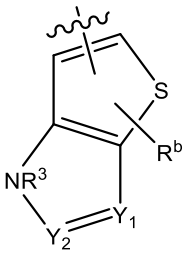
70. A compound according to Claim 63, in which **[ligase ligand moiety]** is of Formula (II):



(II)

71. A compound according to Claim 63 or 70, in which R^y is selected from


,

,

,


,

,

,

and


72. A compound according to any of Claims 63, 70 or 71, in which

Z_3 is S or NR^3;

U is O or S;

each of Y_1, Y_2 and Y_3 is independently N or CR^d.

73. A compound according to any of Claims 63 or 70 to 72, in which R^b is hydrogen or alkyl.

74. A compound according to any of Claims 63 and 70 to 73, in which R^3 is hydrogen, alkyl, cycloalkyl, -**R**^{21}, -C(O)-NH-**R**^{21}, or -CH_2-NH-C(O)-**R**^{21}.

75. A compound according to any of Claims 63 and 70 to 74, in which each R^d is independently hydrogen, alkyl, -O-**R**^{21}, -NH-**R**^{21}, -C(O)-NH-**R**^{21}, or -CH_2-NH-C(O)-**R**^{21}.

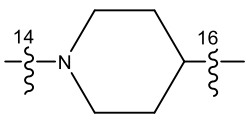
76. A compound according to any of Claims 63 to 75, in which **R**^{14} is -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C(O)-, -SO_2- or is absent.

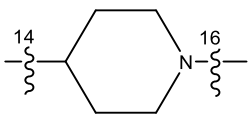
77. A compound according to any of Claims 63 to 76, in which **R[15]** is cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_{1-6} alkyl-NH-, -cycloalkyl-NH- or is absent.

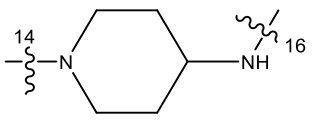
78. A compound according to any of Claims 63 to 77, in which

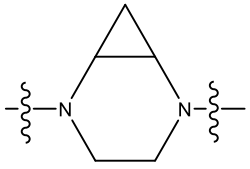
R[14] is -C_{1-6} alkyl, -SO_2- or is absent

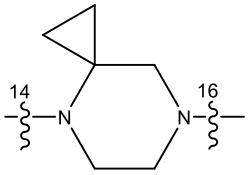
R[15] is piperazine, bridged piperazine, piperazine N-oxide, piperazine cation, -C_{1-6} alkyl-NH-,

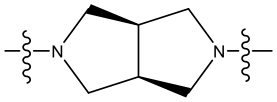


,


,


,


,


,


or is absent, in which 

indicates attachment to **R[14]** and 

indicates attachment to **R[16]**,

R[16] is -C_{1-6} alkyl, -C(O)-, -C(O)-NH-, -CH_2-C(O)-NH- or is absent

R[17] is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

x is 1-6

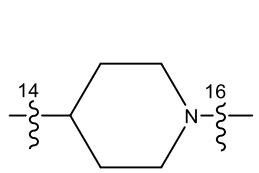
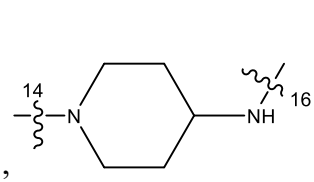
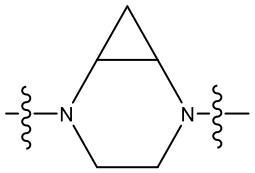
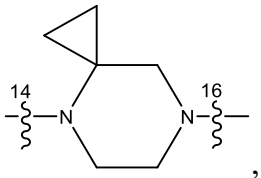
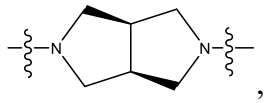
y is 2-6

R[18] is -C_{1-6} alkyl, piperazine, or is absent

in which at least one of R^{14}-R^{18} is present.

79. A compound according to any of Claims 63 to 78, in which **R[18]** is -C_{1-6} alkyl or is absent.

80. A compound according to any of Claims 63 to 79, in which when **R[15]** is piperazine, bridged piperazine, piperazine N-oxide, piperazine cation, -C_{1-6} alkyl-NH-,

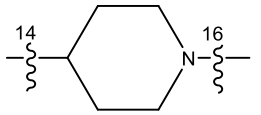
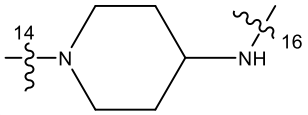
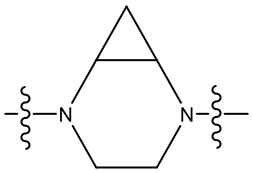
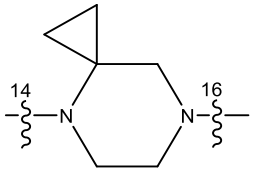
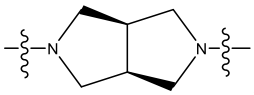




, or

,

then **R**^{14} is -C_{1-6} alkyl.

81. A compound according to any of Claims 63 to 80, in which

(a) **R**^{14} is -C_{1-6} alkyl,

R^{15} is piperazine, bridged piperazine, piperazine N-oxide,





or

,

R^{16} is -C(O)-, -CH_2-C(O)-NH-, or is absent

R^{17} is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

R^{18} is -C_{1-6} alkyl.

in which when **R**^{16} and **R**^{17} are absent, **R**^{18} is -C_{3-6} alkyl;

optionally in which:

(i) **R**^{14} is -C_2 alkyl,

x is 1, 2 or 6

y is 2; or

(ii) **R**^{15} is piperazine,

R^{16} is -C(O)-,

R^{17} is – absent;

optionally in which

$\mathbf{R^{14}}$ is -C_2 alkyl,

$\mathbf{R^{18}}$ is -$C_{1\text{-}2}$ alkyl;

or

(b) when $\mathbf{R^{14}}$ is -SO_2-, at least two of $\mathbf{R^{15}}$-$\mathbf{R^{18}}$ are present, and at least one of $\mathbf{R^{15}}$-$\mathbf{R^{18}}$ is not $C_{1\text{-}6}$ alkyl;

or

(c) $\mathbf{R^{14}}$ is -SO_2-

$\mathbf{R^{15}}$ is -$C_{1\text{-}6}$ alkyl-NH-

$\mathbf{R^{16}}$ is -C(O)-

$\mathbf{R^{17}}$ is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$ or is absent

$\mathbf{R^{18}}$ is -$C_{2\text{-}4}$ alkyl;

optionally in which

$\mathbf{R^{15}}$ is -C_2alkyl-NH-

x is 1 or 2

y is 1

$\mathbf{R^{18}}$ is -$C_{2\text{-}4}$ alkyl;

or

(d) $\mathbf{R^{14}}$ is absent

$\mathbf{R^{15}}$ is absent

$\mathbf{R^{16}}$ is -C(O)-NH-, or is absent

$\mathbf{R^{17}}$ is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$, $(C_3H_6\text{-}O)_x$, or is absent

$\mathbf{R^{18}}$ is -$C_{1\text{-}6}$ alkyl.

82. A compound according to any of Claims 63 to 81, in which at least one of $\mathbf{R^{14}}$-$\mathbf{R^{18}}$ is not -$C_{1\text{-}6}$ alkyl.

83. A compound according to Claim 81(d) or 82, in which

x is 1, 2 or 3

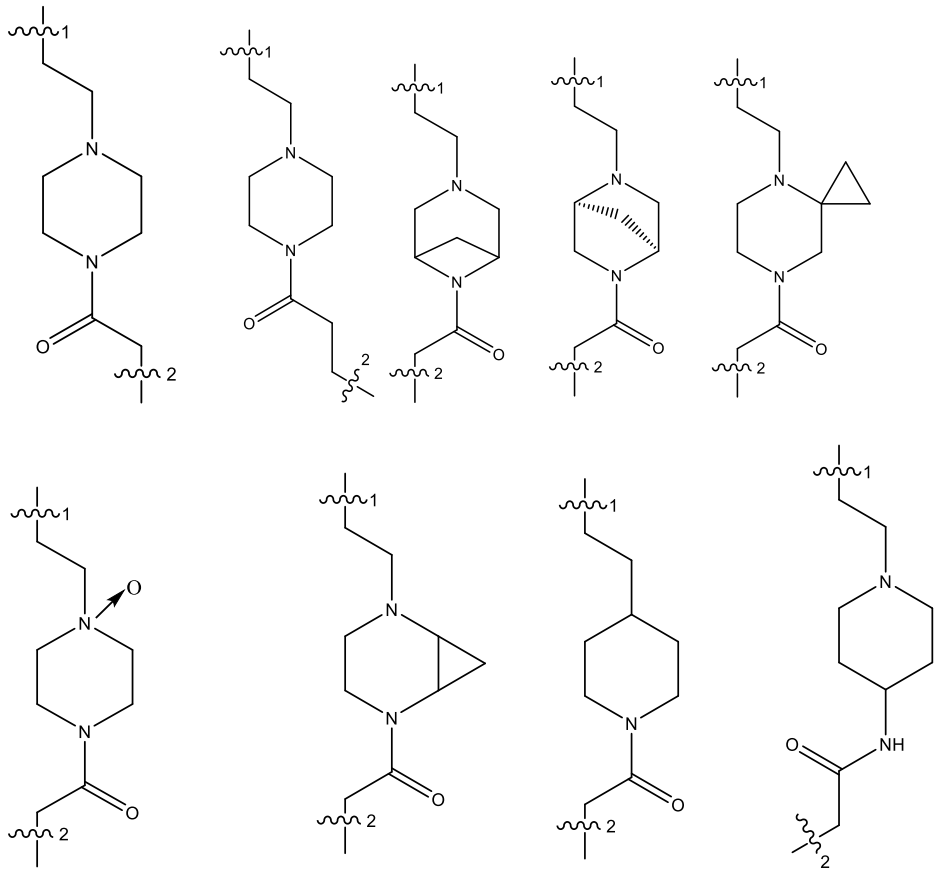
y is 2

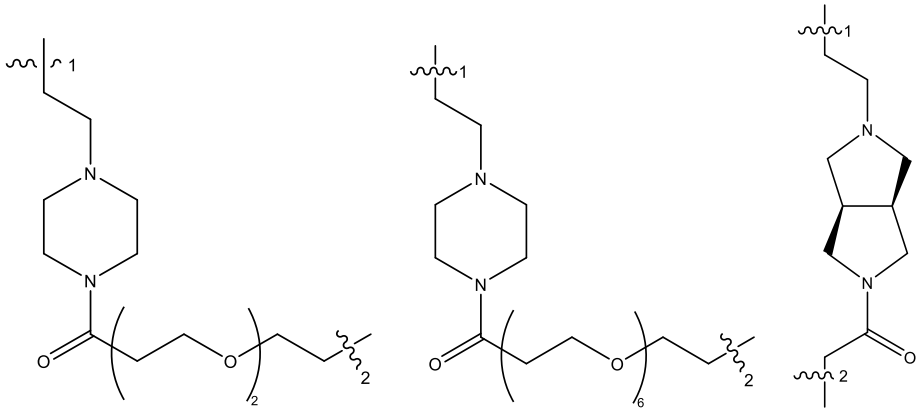
R[18] is -C_{2-6} alkyl.

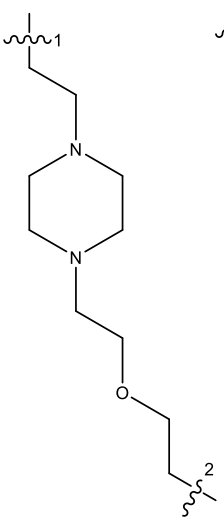
84. A compound according to any of Claims 63 to 83, in which when **R[15]** is -C_{1-6} alkyl-NH-, at least one of **R[16]-R[18]** is present.

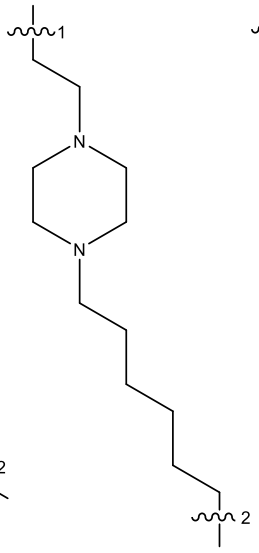
85. A compound according to any of Claims 63 to 84, in which when **R[17]** is -$CH_2(C_2H_4\text{-}O)_y$, $(C_2H_4\text{-}O)_x$ or $(C_3H_6\text{-}O)_x$, at least one of **R[14]-R[16]** and **R[18]** is present, in which at least one of **R[14]** and **R[18]** is not -C_{1-6} alkyl.

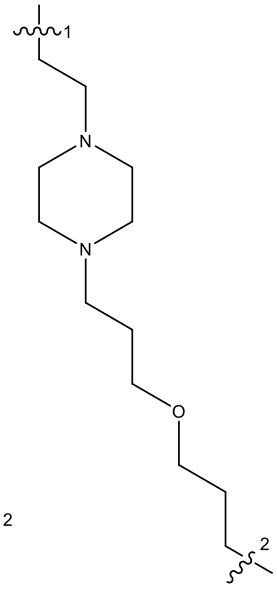
86. A compound according to any of Claims 63 to 85, in which **[linker]** is selected from

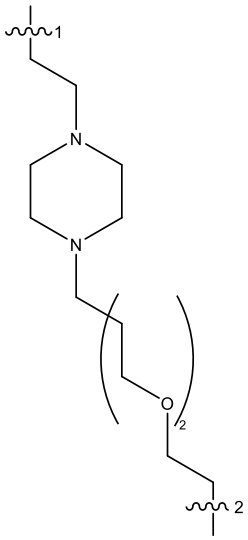


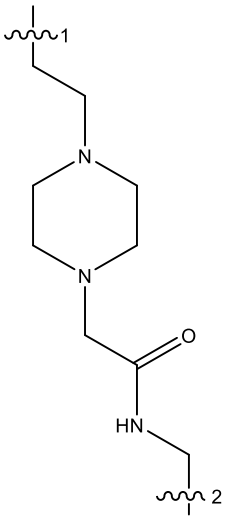


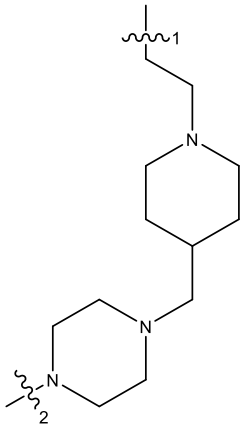


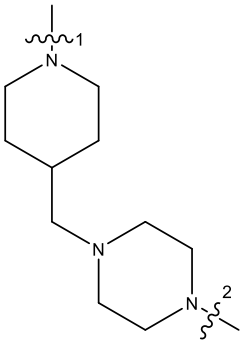


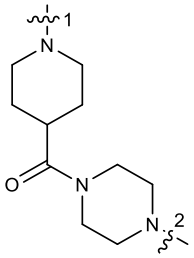


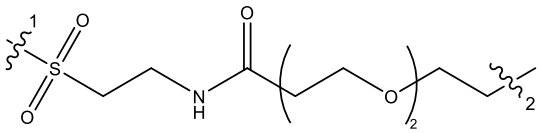


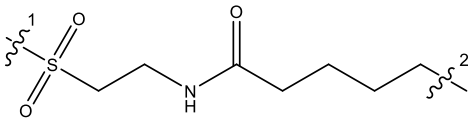


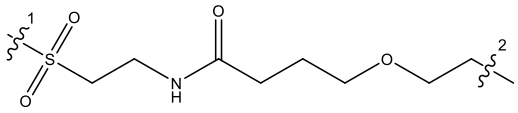


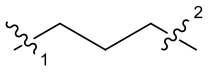


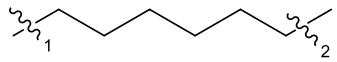


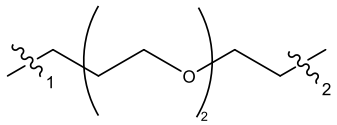


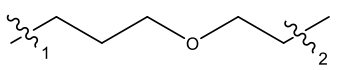


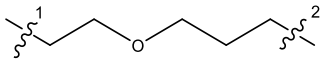


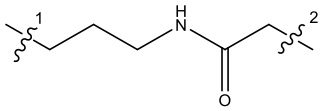


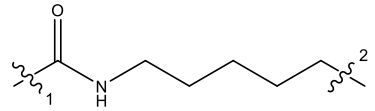


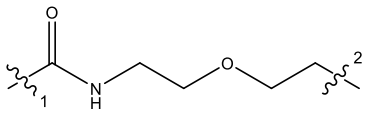


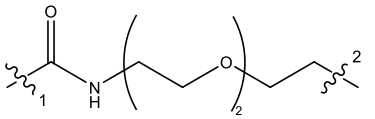




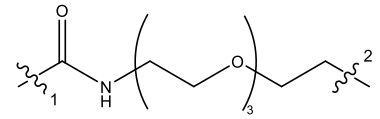








and



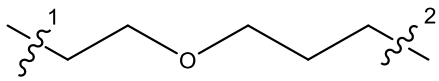
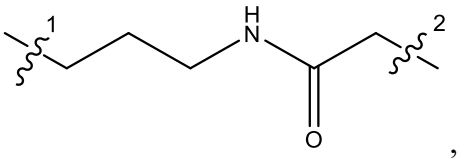
in which

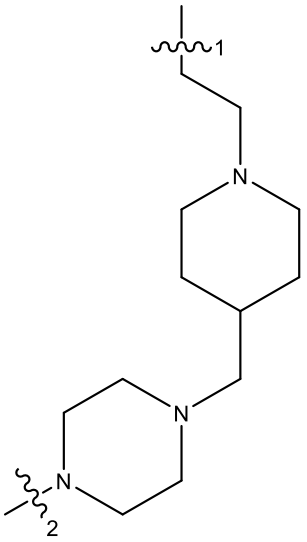
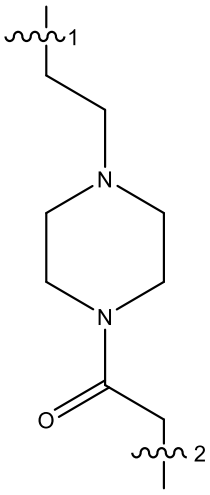
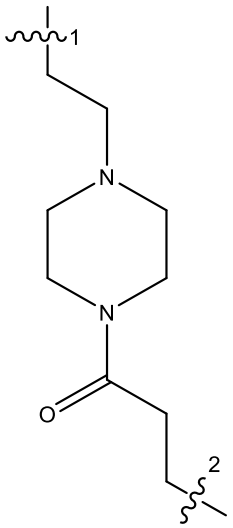
 indicates attachment to **[MCL-1 ligand moiety]** and

 indicates attachment to **[ligase ligand moiety]**;

optionally in which

[linker] is selected from


,

,


,

and


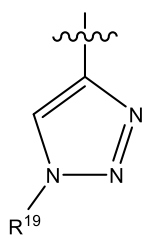
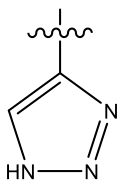
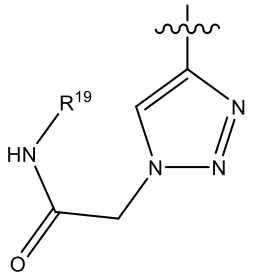
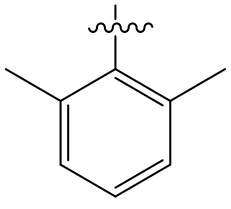
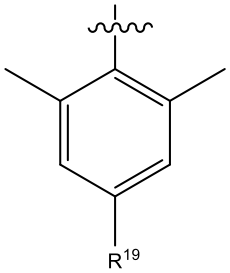
in which

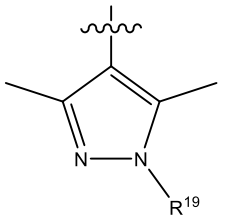
 indicates attachment to [MCL-1 ligand moiety] and

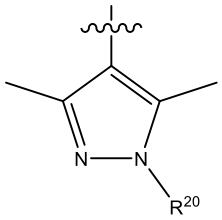
 indicates attachment to [ligase ligand moiety].

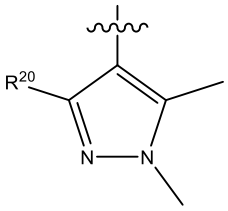
87. A compound according to any of Claims 63 to 86, in which $\mathbf{R^{10}}$ is -C_{2-5}alkyl-O-R^{13}, in which R^{13} is phenyl, naphthyl or tetraline, in which the phenyl, naphthyl or tetraline is optionally substituted with at least one substituent selected from halogen, C_1-C_6 alkyl and -O(C_1-C_6 alkyl); or in which the naphthyl is optionally substituted with -O- or -S-.

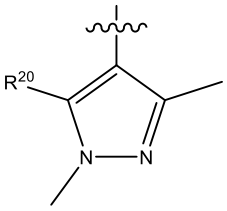
88. A compound according to any of Claims 63 to 87, in which $\mathbf{R^{12}}$ is H,


,

,

,

,

,

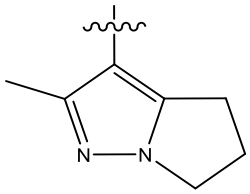


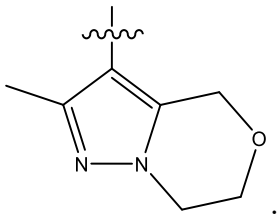
,


,


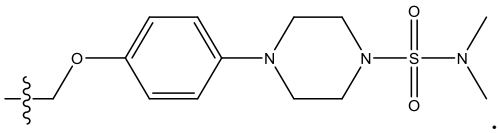
,


,

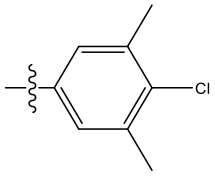


or


.

89. A compound according to any of Claims 63 to 88, in which $\mathbf{R^{20}}$ is Me, $-CH_2-O-$ bromobenzaldehyde, or 

.

90. A compound according to any of Claims 63 to 89, in which when $\mathbf{R^8}$ is H, $\mathbf{R^{13}}$ is 

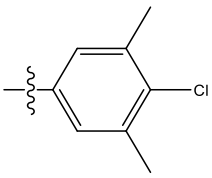
.

91. A compound according to any of Claims 63 to 90, in which

$\mathbf{R^8}$ is H, $\mathbf{R^{19}}$, methyl, or $-CH_2CH_2$-morpholine;

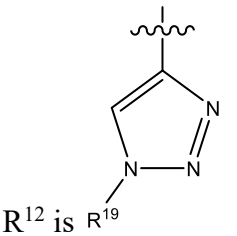
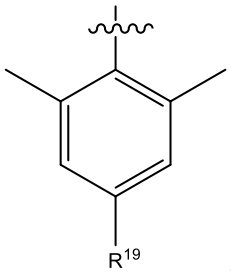
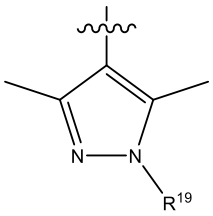
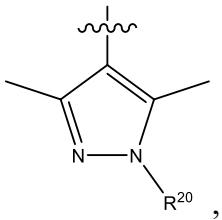
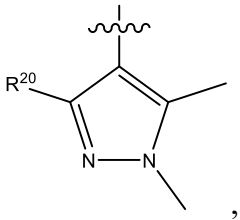
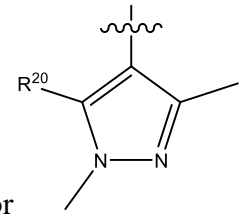
$\mathbf{R^9}$ is -C(O)OH or -C(O)NH$\mathbf{R^{19}}$,

$\mathbf{R^{10}}$ is $-C_3H_6O-R^{13}$,

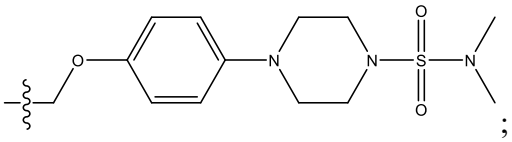
in which $\mathbf{R^{13}}$ is 

, tetraline or naphthyl optionally substituted with fluorine;

$\mathbf{R^{11}}$ is H, Cl, F or methyl,

R^{12} is  ,  ,  ,  ,  ,  , or

in which **R^{20}** is Me, -CH_2-O-bromobenzaldehyde, or

 ;

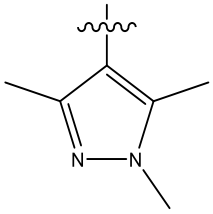
optionally in which

R^8 is **R^{19}** or methyl;

R^{10} is -C_3H_6O-R^{13}, in which **R^{13}** is naphthyl optionally substituted with fluorine;

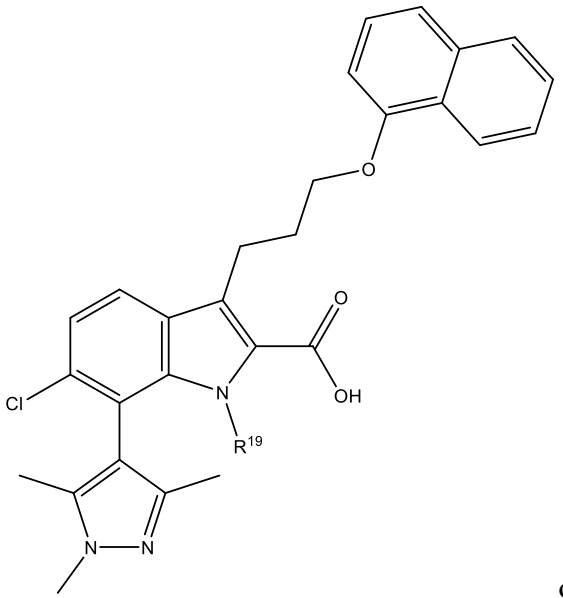
R^{11} is Cl or F,

R^{12} is

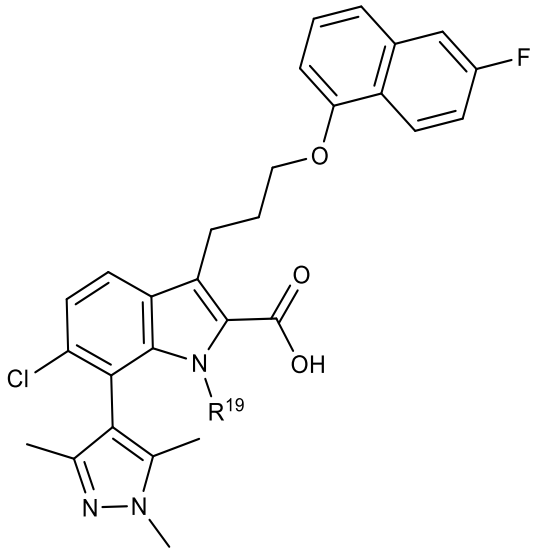
 .

92. A compound according to any of Claims 63 to 91, in which **Z_2** is C and is a double bond.

93. A compound according to any of Claims 63 to 92, in which **[MCL-1 ligand moiety]** is

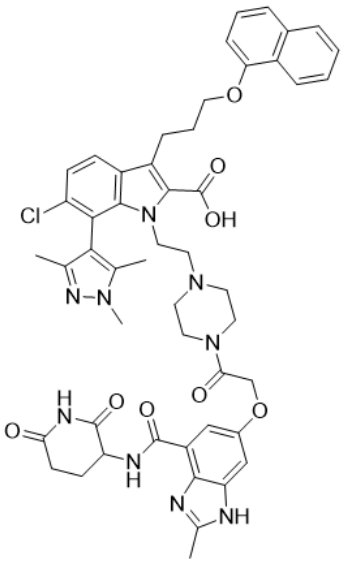
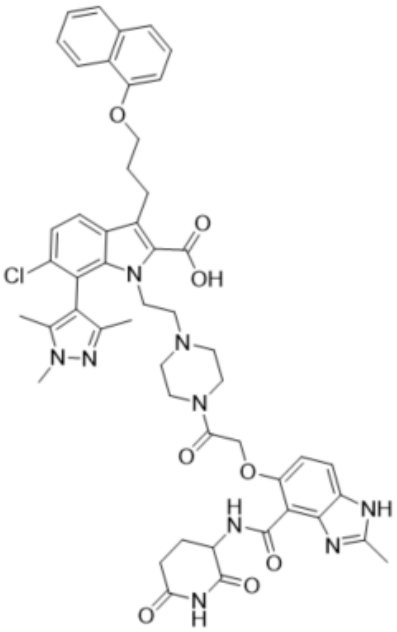
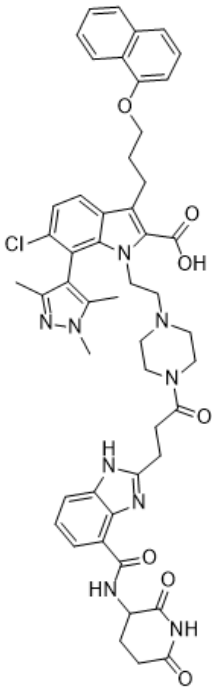


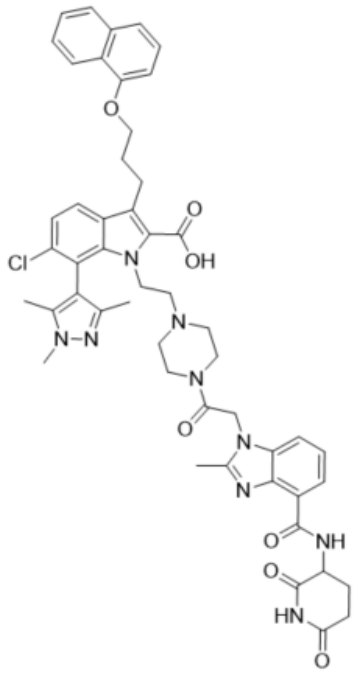
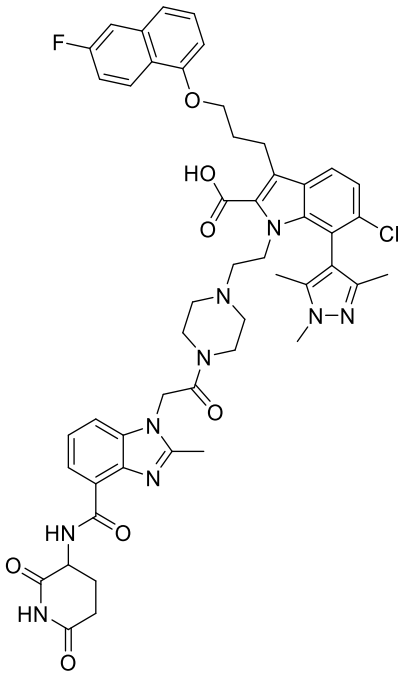
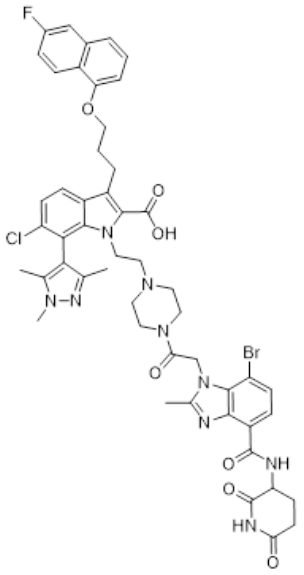
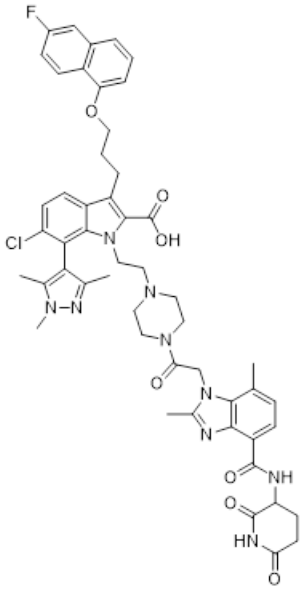
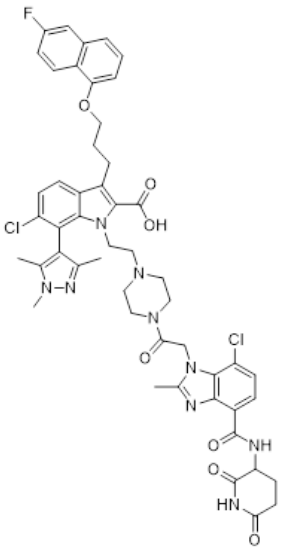
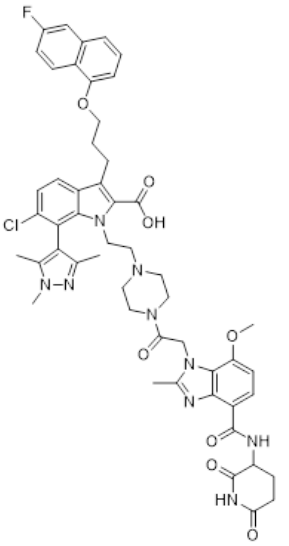
or

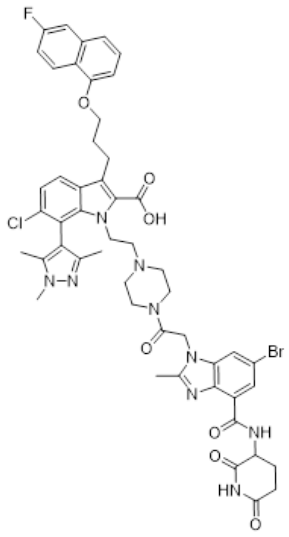
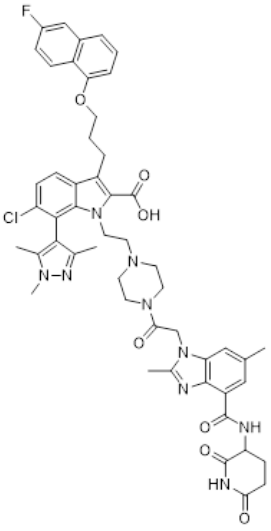
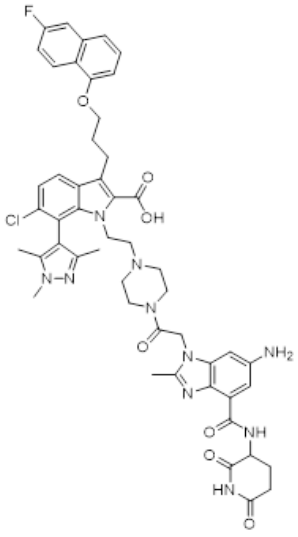
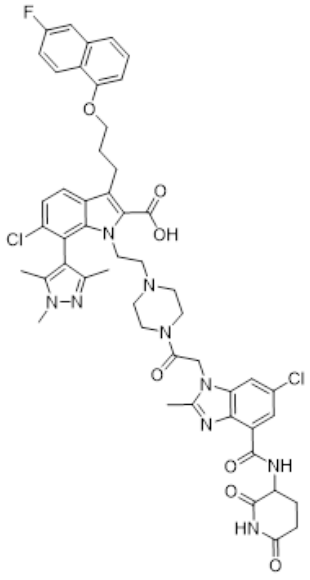
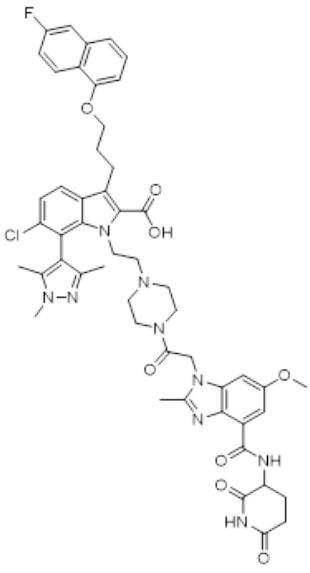
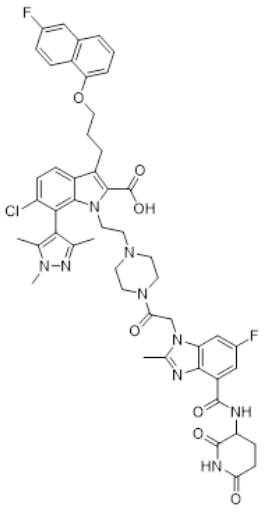


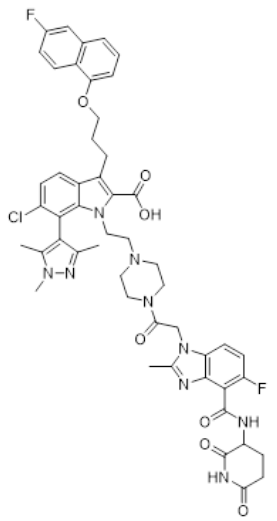
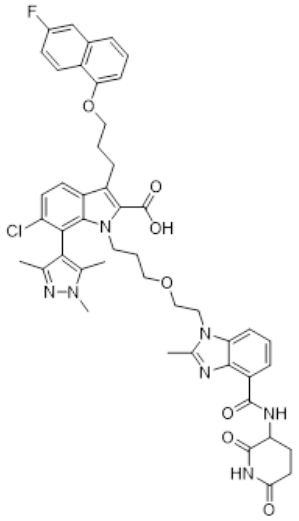
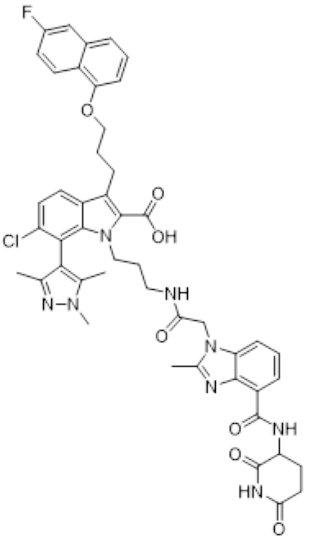
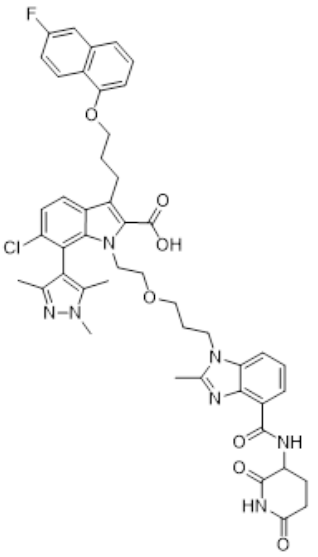
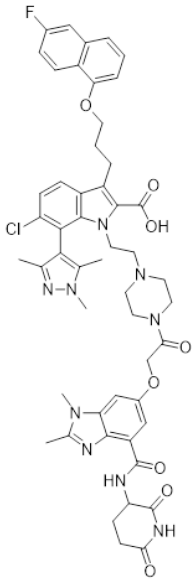
.

optionally in which the compound is selected from

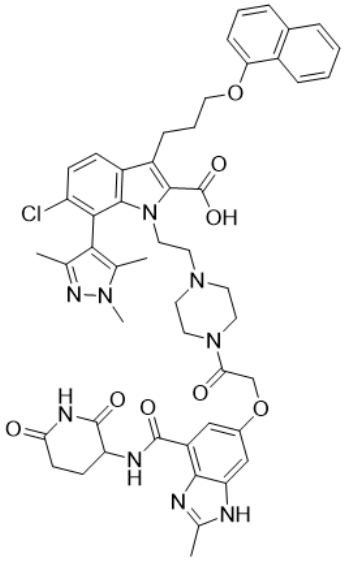
		
263	264	265

		
266	268	269
		
270	271	272

 273	 274	 275
 276	 277	 278

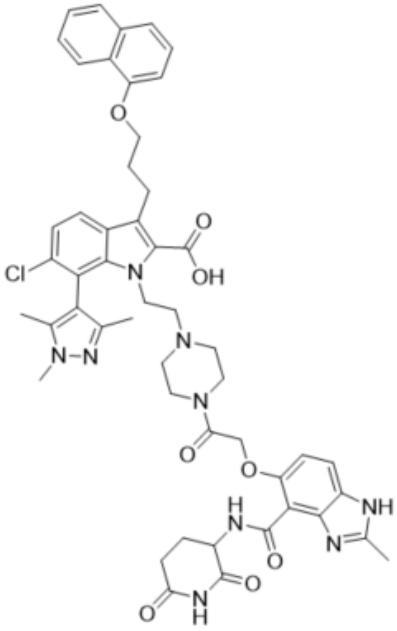
 279	 280	 281
 282	 283	

further optionally in which the compound is selected from:



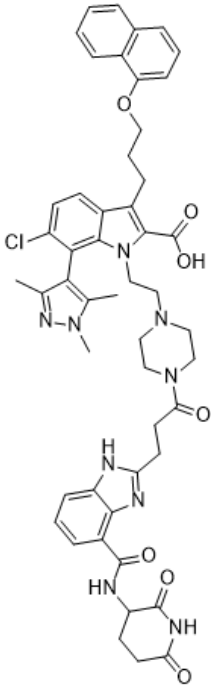
,

263



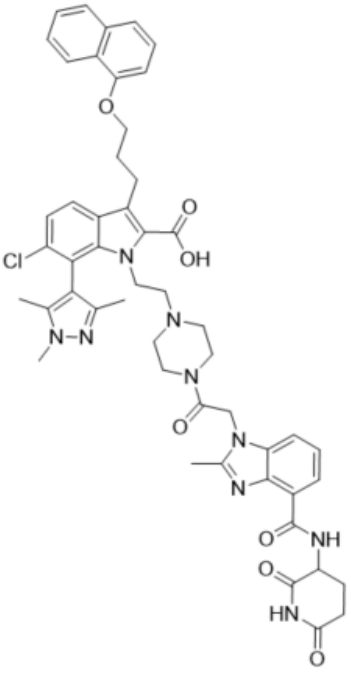
,

264



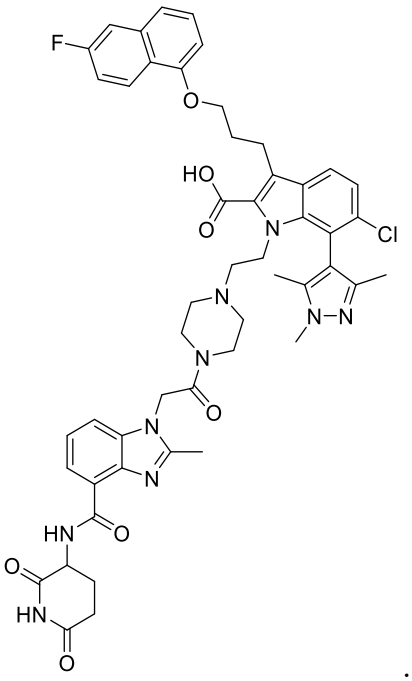
,

265



and

266



.

268

94. A compound according to any preceding claim, in which each alkyl, alkenyl, alkynyl, aryl, heteroaryl and benzyl is unsubstituted.

95. A compound according to any preceding claim, in which:

(a) T is C=O; or

(b) T is SO_2.

96. A compound according to preceding claim, in which:

(a) X_1 and X_2 are O;

(b) X_1 is O and X_2 is S;

(c) X_1 is S and X_2 is O; or

(d) X_1 and X_2 are S.

97. A compound according to any preceding claim, in which n is:

(a) 0;

(b) 1 or 2;

(c) 1; or

(d) 2.

98. A compound according to any preceding claim, in which **[MCL-1 ligand moiety]** is a compound of Formula (A), and in which $\mathbf{R^{10}}$ is $-C_{2\text{-}5}alkyl\text{-}O\text{-}R^{13}$,

99. A compound according to any preceding claim, in which $\mathbf{R^{10}}$ is $-C_3H_6\text{-}O\text{-}R^{13}$,

100. A pharmaceutical composition comprising a compound of any one of claims 1-161.

101. Use of a compound according to any of Claims 1 to 99 in the preparation of a medicament.

102. Use of a compound of any of Claims 1 to 99 in the preparation of a medicament for the treatment of cancer.

103. Use according to Claim 102, in which the cancer is selected from breast cancer, triple negative breast cancer, colorectal cancer, pancreatic cancer, skin cancer, melanoma, ovarian cancer, kidney cancer, lung cancer, small-cell lung cancer, non-small-cell lung cancer, lymphoma, non-Hodgkin's lymphoma, multiple myeloma, cervical cancer, leukaemia, chronic lymphocytic leukaemia (CLL), acute myeloid leukaemia (AML), chronic myelogenous leukaemia (CML), acute lymphoblastic leukaemia (ALL), bladder cancer, and prostate cancer; optionally in which the cancer is multiple myeloma or acute myeloid leukaemia.

104. A compound of formula (X):

[MCL-1 inhibitor] – L – [cereblon binding moiety] (X)

in which L is a bond or a linker compound.

105. A method of reducing the cardiac cytotoxicity of an MCL-1 inhibitor, comprising coupling a cereblon binding moiety to the MCL-1 inhibitor.

106. A compound according to Claim 104 or a method according to Claim 105, in which the cereblon binding moiety is a **[ligase ligand moiety]** as defined in any of Claims 1 to 97, the MCL-1 inhibitor is an **[MCL-1 ligand moiety]** as defined in any of Claims 1 to 97, and in which the cereblon binding moiety is coupled to the MCL-1 inhibitor by a linker compound, in which the linker compound is covalently attached to the cereblon binding moiety and the MCL-1 inhibitor and is a **[linker]** as defined in any of Claims 1 to 97.