

genes for survival. Beroukhim et al. Mcl-1 is a relevant target for the re-iniation of apoptosis in numerous cancer cells. See G. Lessene, P. Czabotar and P. Colman, Nat. Rev. Drug. Discov., 2008, 7, 989–1000; C. Akgul Cell. Mol. Life Sci. Vol. 66, 2009; and Arthur M. Mandelin II, Richard M. Pope, Expert Opin.

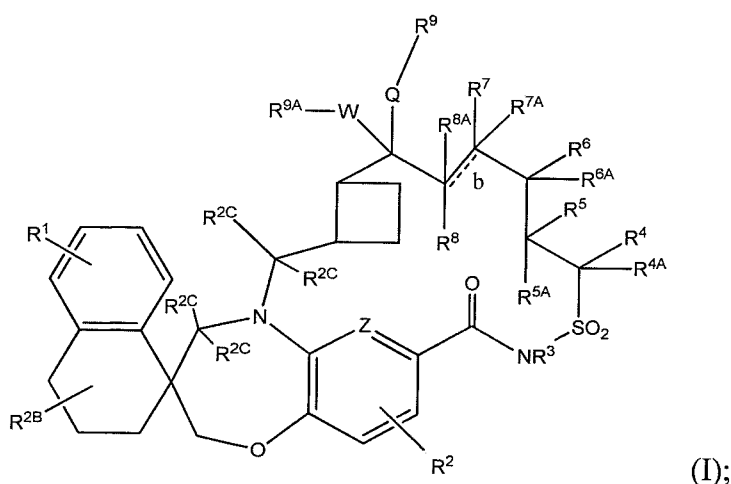
5 Ther. Targets (2007) 11(3):363-373.

New compositions and methods for preparing and formulating Mcl-1 inhibitors would be useful.

SUMMARY

In one example, the present disclosure comprises a compound of Formula

10 I:



a stereoisomer thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable salt of the stereoisomer thereof, wherein:

15 Z is C or N;

Q is O, S, $\text{CR}^{\text{WA}}\text{R}^{\text{WB}}$, or $\text{NR}^{\text{a}}\text{R}^{\text{b}}$;

W is $\text{CR}^{\text{WA}}\text{R}^{\text{WB}}$, $-\text{C}=\text{O}$, or is absent;

R^{WA} and R^{WB} are independently selected from H, $-\text{C}_{1-3}\text{alkyl}$, $-\text{C}_{2-3}\text{alkenyl}$, $-\text{C}_{2-3}\text{alkynyl}$, halo, $-\text{OH}$, or $-\text{O}-\text{C}_{1-3}\text{alkyl}$;

20 b, represented by the symbol ----- , is a single or double chemical bond which may be cis or trans;

R^1 is independently selected from H, halo, C_{1-6} alkylhalo, C_{1-6} alkyl, C_{2-6} alkenyl, $-(CH_2CH_2O)_nR^a$, $-SO_2R^a$, $-C(=O)R^a$, $-C(=O)OR^a$, or $-C(=O)NR^aR^b$; R^2 is selected from H, halo, C_{1-6} haloalkyl, C_{1-6} alkyl, $O-C_{1-6}$ alkyl, C_{2-6} alkenyl, C_{1-6} alkenylene, $-C_{1-6}$ alkyl- $O-C_{1-6}$ alkyl, $-(CH_2CH_2O)_nR^a$, $-SO_2R^a$, $-C(=O)R^a$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)NR^aR^b$, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, or a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl or heterocycloalkyl group have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl, and heterocycloalkyl groups may include a S=O or SO_2 ;

R^3 is selected from H, $-C_{1-6}$ alkylhalo, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-(CH_2CH_2O)_nR^a$, $-C(=O)R^a$, $-C(=O)OR^a$, or $-C(=O)NR^aR^b$; each of R^{2B} , R^{2C} , R^4 , R^5 , R^6 , R^7 , and R^8 is independently selected from H, halo, $-C_{1-6}$ haloalkyl, $-C_{1-6}$ alkyl, $-O-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{1-6}$ alkyl- $O-C_{1-6}$ alkyl, $-(CH_2CH_2O)_nR^a$, $-SO_2R^a$, $-C(=O)R^a$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)NR^aR^b$, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO_2 ;

alternatively R^3 and R^4 together with the atoms to which they are bonded may form a 5- to 12-membered ring, optionally containing a heteroatom selected from a N, O or S atom, in addition to the S and N atoms present in the ring, wherein the ring may optionally contain at least one double bond; and the ring may be substituted with 0, 1, 2, or 3 R^{3A} substituents;

wherein R^{3A} is selected from H, halo, -OH, C_{1-6} haloalkyl, C_{1-6} alkyl, O- C_{1-6} alkyl, C_{2-6} alkenyl, - C_{1-6} alkyl-O- C_{1-6} alkyl, $-(CH_2CH_2O)_nR^a$, $-SO_2R^a$, $-C(=O)R^a$, $-C(=O)OR^a$, $-OC(=O)R^a$, or $-C(=O)NR^aR^b$;

each of R^{4A} , R^{5A} , R^{6A} , R^{7A} , and R^{8A} is independently selected from H, OH, halo, or - C_{1-6} alkyl;

R^{7A} and R^{8A} are absent when b is a double chemical bond;

alternatively R^7 and R^8 together with the atoms to which they are bonded may form a 3- to 12-membered ring, wherein the ring may optionally contain at least one double bond;

R^9 is independently selected from H, OH, $-(=O)$, $-C_{1-6}$ haloalkyl, $-C_{1-6}$ alkyl, $-C_{1-6}$ alkenylene, $-(CH_2CH_2O)_nR^a$, $-C(=O)R^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^b$, $-C_{1-6}$ alkyl-O- C_{1-6} alkyl, cyano, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl or heterocycloalkyl groups have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, and the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl group may include a C=O group, and further wherein the spiroheterocycloalkyl, and heterocycloalkyl groups may include a S=O or SO_2 ;

R^{9A} is independently selected from H, -OH, halo, cyano, $-C_{1-6}$ haloalkyl, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-C_{1-6}$ alkenylene, $-(CH_2CH_2O)_nR^a$, $-P(=O)OR^aOR^b$, $-CSR^a$, $-CS(=O)R^a$, $-SR^a$, $-SOR^a$, $-OSO_2R^a$, $-SO_2R^a$, $-(CH_2CH_2O)_nCH_3$, $-(=O)$, $-C(=O)$, $-C(=O)R^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^b$, $-CH_2NR^aR^b$, $-NR^aR^b$, $-C_{1-6}$ alkyl-O- C_{1-6} alkyl, $-OC_{1-6}$ alkyl, $-O-C_{1-6}$ alkyl-O- C_{1-6} alkyl, phenyl, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl,

spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may contain a double bond and may contain a C=O group, and further wherein the spiroheterocycloalkyl, and heterocycloalkyl groups may include a S=O or SO₂;

wherein R^{9A} is not H when W is absent;

5 wherein the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, spirocycloalkyl and spiroheterocycloalkyl groups of the R^{9A} substituent can be unsubstituted or substituted with 1, 2, 3 or 4 R¹⁰ substituents independently selected from OH, halo, -NR^cR^d, -C₁₋₆alkyl, -C₂-C₆ alkenyl, -C₂-C₆alkynyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -CN, -
10 C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and
15 heterocycloalkyl groups have 0, 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

alternatively R⁷ and R^{9A} together with the atoms to which they are bonded
20 may form a 3- to 12-membered ring, wherein the ring may optionally contain at least one double bond;

alternatively R⁹ and R^{9A} together with Q, W, and the C to which W and Q are bonded, may form a 3- to 12-membered monocyclic or bicyclic ring, optionally containing a heteroatom in addition to Q that is selected from N, O or
25 S, wherein the ring may contain a double bond, wherein the ring may optionally include a C=O group, and further wherein the ring optionally may be substituted by 1, 2, or 3 R¹¹ substituents;

R¹¹ is independently selected from H, -OH, halo, -C₁₋₆alkyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, -C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -

CN, $-NR^cR^d$, $-C(=O)NR^cR^d$, $-C(=O)R^c$, $-OC(=O)R^c$, $-C(=O)OR^c$, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl groups have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl group may include a double bond, and wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl group may include a C=O group, and further wherein the spiroheterocycloalkyl, and heterocycloalkyl groups may include a S=O or SO₂;

wherein the C₁₋₆alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl and the -OC₁₋₆alkyl of any of the R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R^{4A}, R^{5A}, R^{6A}, R^{7A}, R^{8A}, R^{9A}, R^{WA} and R^{WB} substituents is unsubstituted or substituted by 1, 2 or 3 R¹² substituents independently selected from OH, -OC₁₋₆alkyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, halo, -O-haloC₁₋₆alkyl, -CN, -NR^aR^b, -(NR^aR^bR^c)_n, -OSO₂R^a, -SO₂R^a, -(CH₂CH₂O)_nCH₃, -(=O), -C(=O), -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^a, -C(=O)NR^aR^b, -O-SiR^aR^bR^c, -SiR^aR^bR^c, -O-(3- to 10-membered heterocycloalkyl), a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl, and heterocycloalkyl groups may include a S=O or SO₂;

wherein the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, spirocycloalkyl and spiroheterocycloalkyl group of any of the R², R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R^{9A}, R¹⁰, R¹¹, R¹², R^{WA} and R^{WB} substituents can be unsubstituted or substituted with 1, 2, 3 or 4 R¹³ substituents independently selected from OH, halo, -NR^cR^d, -C₁₋₆alkyl, -

OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl groups of R¹³ have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, and spiroheterocycloalkyl groups of R¹³ or the heterocycloalkyl group of R¹³ may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

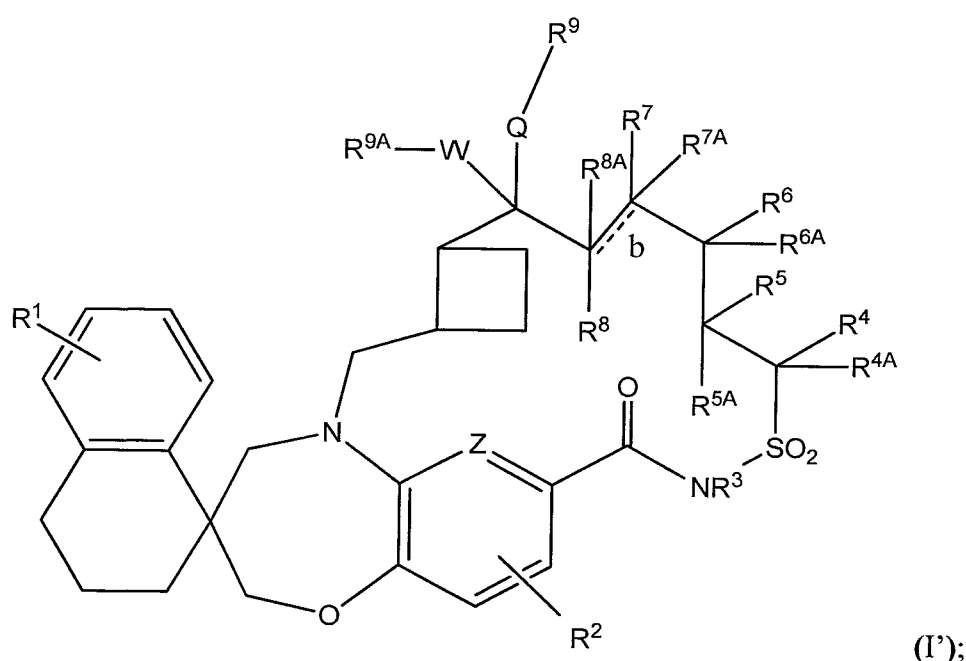
wherein each R^a, R^b, R^c, and R^d is independently hydrogen, OH, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₁₋₆alkyl-NR¹⁴R¹⁴, -NR¹⁴R¹⁴, -SO₂R¹⁴, -(CH₂CH₂O)_nCH₃, -(=O), -C(=O)R¹⁴, -OC(=O)R¹⁴, -C(=O)OR¹⁴, -C(=O)NR¹⁴R¹⁴, -C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, benzyl, phenyl, -C₁₋₆alkyl-C(=O)OH, -C₁₋₆alkyl-C(=O)-O-C₁₋₆alkyl, -C₁₋₆alkyl-cycloalkyl, -C₁₋₆alkyl-heterocycloalkyl, -C₁₋₆alkyl-6- to 10-membered aryl, -C₁₋₆alkyl-6- to 10-membered heteroaryl, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, or a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, where the heteroaryl, spiroheterocycloalkyl, heterocycloalkyl group or the -C₁₋₆alkyl-heterocycloalkyl groups have 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, and the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, heterocycloalkyl, group of R^a, R^b, R^c, and R^d or the heterocycloalkyl group or the -C₁₋₆alkyl-heterocycloalkyl group may include a double bond and may contain a C=O group, and the spiroheterocycloalkyl, or heterocycloalkyl may include a S=O or SO₂;

the alkyl, aryl, heteroaryl, spirocycloalkyl, spiroheterocycloalkyl, cycloalkyl, or heterocycloalkyl group of R^a, R^b, R^c, and R^d and the

heterocycloalkyl group of the -C₁₋₆alkyl-heterocycloalkyl group of R^a, R^b, R^c, and R^d can be unsubstituted or substituted with 1, 2, 3, or 4 R¹⁴ substituents, wherein each R¹⁴ is independently selected from H, -OH, -N=N=N, halo, -C₁₋₆alkyl, -C₁₋₆haloalkyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, phenyl, tolyl, -C(=O)C₁₋₆alkyl, -C(=O)O-C₁₋₆alkyl, N(CH₃)₂ or -SO₂-N(CH₃)₂; and

wherein n is independently in each instance an integer of 1, 2, 3 or 4.

In one aspect, the present disclosure comprises a compound of Formula I':



a stereoisomer thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable salt of the stereoisomer thereof, wherein:

Z is C or N;

Q is O or S;

W is CR^{WA}R^{WB} or C=O;

R^{WA} and R^{WB} are independently selected from H, C₁₋₃alkyl, halo, -OH, or -O-C₁₋₃alkyl;

b, represented by the symbol ----- is a single or double chemical bond which may be cis or trans;

R¹ is independently selected from H, halo, C₁₋₆alkylhalo, C₁₋₆alkyl, -
(CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a, or -C(=O)NR^aR^b;

R² is selected from H, halo, -C₁₋₆haloalkyl, -C₁₋₆alkyl, -O-C₁₋₆alkyl, -C₂₋₆
alkenyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a,
5 -OC(=O)R^a, or -C(=O)NR^aR^b,

R³ is independently selected from H, -C₁₋₆alkylhalo, -C₁₋₆alkyl, -C₂₋₆
alkenyl, -(CH₂CH₂O)_nR^a, -C(=O)R^a, -C(=O)OR^a, or -C(=O)NR^aR^b;

each of R⁴, R⁵, R⁶, R⁷, and R⁸ is independently selected from H, halo, -C₁₋₆
haloalkyl, -C₁₋₆alkyl, -O-C₁₋₆alkyl, -C₂₋₆alkenyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -
10 (CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a, -OC(=O)R^a, -C(=O)NR^aR^b, a 6-
to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or
spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered
monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic
heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and
15 heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected
from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl,
and heterocycloalkyl groups may include a C=O group, and further wherein the
spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

alternatively R³ and R⁴ together with the atoms to which they are bonded
20 may form a 5- to 12-membered ring, optionally containing a heteroatom selected
from a N, O or S atom, in addition to the S and N atoms present in the ring,
wherein the ring may optionally contain at least one double bond; and the ring
may be substituted with 0, 1, 2, or 3 R^{3A} substituents;

R^{3A} is independently selected from H, halo, -OH, C₁₋₆haloalkyl, C₁₋₆alkyl,
25 O-C₁₋₆alkyl, C₂₋₆alkenyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -
C(=O)R^a, -C(=O)OR^a, -OC(=O)R^a, -C(=O)NR^aR^b;

each of R^{4A}, R^{5A}, R^{6A}, R^{7A}, and R^{8A} is independently selected from H, OH,
halo, -C₁₋₆alkyl;

R^{7A} and R^{8A} are absent when b is a double chemical bond;

30 R⁹ is independently selected from H, -C₁₋₆haloalkyl, -C₁₋₆alkyl, -C₂₋₆
alkenyl, -C₂₋₆alkynyl, -(CH₂CH₂O)_nR^a, -C(=O)R^a, -C(=O)OR^a, -C(=O)NR^aR^b, -

C_{1-6} alkyl-O- C_{1-6} alkyl, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the

5 heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

10 R^{9A} is independently selected from H, C_{1-6} haloalkyl, C_{1-6} alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a, -C(=O)NR^aR^b, -NR^aR^b, -N=N=N, -C₁₋₆alkyl-O- C_{1-6} alkyl, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered

15 monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the

20 spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

wherein the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, spirocycloalkyl and spiroheterocycloalkyl groups of the R^{9A} substituent can be unsubstituted or substituted with 1, 2, 3 or 4 R^{10} substituents independently selected from OH, halo, -NR^cR^d, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-

25 OH, -C₁₋₆alkyl-O- C_{1-6} alkyl, C_{1-6} haloalkyl, -O-halo C_{1-6} alkyl, -SO₂R^c, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic

30 heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and

heterocycloalkyl groups have 0, 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

5 alternatively R⁹ and R^{9A} together with Q, W, and the C to which W and Q are bonded, may form a 3- to 12-membered monocyclic or bicyclic ring, optionally containing a heteroatom in addition to Q that is selected from N, O or S, wherein the ring may contain a double bond, wherein the ring may optionally include a C=O group, and further wherein the ring optionally may be substituted
10 by 1, 2, or 3 R¹¹ substituents;

R¹¹ is independently selected from OH, halo, -NR^cR^d, -C₁₋₆alkyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, a 6- to 12-membered aryl or heteroaryl, a 6- to 12-membered spirocycloalkyl or
15 spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl group have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and
20 heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

wherein the -C₁₋₆alkyl of any of the R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R^{4A}, R^{5A}, R^{6A}, R^{7A}, R^{8A}, and R^{9A} substituents is unsubstituted or substituted by 1, 2 or 3 R¹² substituents independently selected from OH, -OC₁₋₆alkyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, halo, -O-haloC₁₋₆alkyl, -CN, -NR^aR^b, -(NR^aR^bR^c)_n, -SO₂R^a, -
25 (CH₂CH₂O)_nCH₃, (=O), -C(=O), -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^a, -C(=O)NR^aR^b, -O-SiR^aR^bR^c, -O-(3- to 12-membered heterocycloalkyl), phenyl, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered

monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

wherein the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, spirocycloalkyl and spiroheterocycloalkyl groups of any of the R², R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹ and R¹² substituents can be unsubstituted or substituted with 1, 2, 3 or 4 R¹³ substituents independently selected from OH, halo, -C₁₋₆alkyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -NR^cR^d, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, -B(OH)₂, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

wherein each R^a, R^b, R^c, and R^d is independently H, OH, -C₁₋₆alkyl, -C₁₋₆alkenyl, -C₂₋₆alkynyl, -C₁₋₆alkyl-NR¹⁴R¹⁴, NR¹⁴R¹⁴, -SO₂R¹⁴, -(CH₂CH₂O)_nCH₃, (=O), -C(=O)R¹⁴, -OC(=O)R¹⁴, -C(=O)OR¹⁴, -C(=O)NR¹⁴R¹⁴, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -C₁₋₆alkyl-OH, benzyl, phenyl, a -C₁₋₆alkyl-3- to 12-membered heterocycloalkyl, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl groups and the heterocycloalkyl group of the -C₁₋₆alkyl-heterocycloalkyl group have 1, 2, 3, or 4

pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

In another aspect, the present disclosure refers to the use of a compound as described herein in the preparation of a medicament for treating cancer.

5 Another example of the present disclosure provides a method of treating cancer. Such methods include: administering to a patient in need thereof a therapeutically effective amount of the compound of any of the examples or a pharmaceutically acceptable salt thereof. In some such methods, the cancer is a hematologic malignancy. In some such methods, the cancer is selected from the
10 group consisting of breast cancer, colorectal cancer, skin cancer, melanoma, ovarian cancer, kidney cancer, lung cancer, non-small cell lung cancer, lymphoma, non-Hodgkin's lymphoma, myeloma, multiple myeloma, leukemia, and acute myelogenous leukemia. In some other such methods, the cancer is multiple myeloma. In some other such methods, the cancer is acute myelogenous
15 leukemia. In some other such methods, the cancer is non-Hodgkin's lymphoma. In another example, the method further includes administering to a patient in need thereof a therapeutically effective amount of an additional pharmaceutically active compound. For example, in some such methods the additional pharmaceutically active compound is carfilzomib. In others, the additional pharmaceutically active
20 compound is venetoclax. In still other such methods, the additional pharmaceutically active compound is cytarabine.

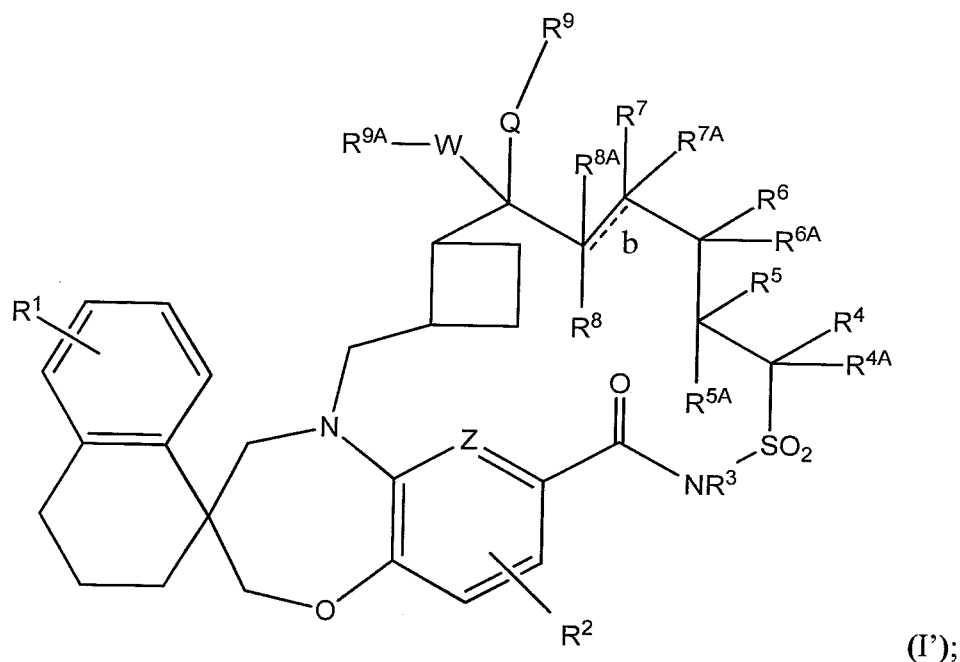
Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Methods and materials are described herein for
25 use in the present disclosure; other, suitable methods and materials known in the art can also be used. The materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent applications, patents, sequences, database entries, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present

specification, including definitions, will control.

Other features and advantages of the disclosure will be apparent from the following detailed description and figures, and from the Claims.

Claims

1. A compound of Formula I':



or a stereoisomer thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable salt of the stereoisomer thereof,

wherein:

Z is C or N;

Q is O or S;

W is CR^{WA}R^{WB} or C=O;

R^{WA} and R^{WB} are independently selected from H, C₁₋₃alkyl, halo, -OH, or -O-C₁₋₃alkyl;

b, represented by the symbol ----- is a single or double chemical bond which may be cis or trans;

R¹ is independently selected from H, halo, C₁₋₆alkylhalo, C₁₋₆alkyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a, or -C(=O)NR^aR^b;

R² is selected from H, halo, -C₁₋₆haloalkyl, -C₁₋₆alkyl, -O-C₁₋₆alkyl, -C₂₋₆alkenyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a, -OC(=O)R^a, or -C(=O)NR^aR^b;

R³ is independently selected from H, -C₁₋₆alkylhalo, -C₁₋₆alkyl, -C₂₋₆alkenyl, -(CH₂CH₂O)_nR^a, -C(=O)R^a, -C(=O)OR^a, or -C(=O)NR^aR^b;

each of R⁴, R⁵, R⁶, R⁷, and R⁸ is independently selected from H, halo, -C₁₋₆haloalkyl, -C₁₋₆alkyl, -O-C₁₋₆alkyl, -C₂₋₆alkenyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -

C(=O)R^a, -C(=O)OR^a, -OC(=O)R^a, -C(=O)NR^aR^b, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

alternatively R³ and R⁴ together with the atoms to which they are bonded may form a 5- to 12-membered ring, optionally containing a heteroatom selected from a N, O or S atom, in addition to the S and N atoms present in the ring, wherein the ring may optionally contain at least one double bond; and the ring may be substituted with 0, 1, 2, or 3 R^{3A} substituents;

R^{3A} is independently selected from H, halo, -OH, C₁₋₆haloalkyl, C₁₋₆alkyl, O-C₁₋₆alkyl, C₂₋₆alkenyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a, -OC(=O)R^a, -C(=O)NR^aR^b;

each of R^{4A}, R^{5A}, R^{6A}, R^{7A}, and R^{8A} is independently selected from H, OH, halo, or -C₁₋₆alkyl;

R^{7A} and R^{8A} are absent when b is a double chemical bond;

R⁹ is independently selected from H, -C₁₋₆haloalkyl, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -(CH₂CH₂O)_nR^a, -C(=O)R^a, -C(=O)OR^a, -C(=O)NR^aR^b, -C₁₋₆alkyl-O-C₁₋₆alkyl, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

R^{9A} is independently selected from H, C₁₋₆haloalkyl, C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -(CH₂CH₂O)_nR^a, -SO₂R^a, -C(=O)R^a, -C(=O)OR^a, -C(=O)NR^aR^b, -NR^aR^b, -N=N=N, -C₁₋₆alkyl-O-C₁₋₆alkyl, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3-

to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

wherein the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, spirocycloalkyl and spiroheterocycloalkyl groups of the R^{9A} substituent can be unsubstituted or substituted with 1, 2, 3 or 4 R¹⁰ substituents independently selected from OH, halo, -NR^cR^d, -C₁₋₆alkyl, -C₂-C₆alkenyl, -C₂-C₆alkynyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl groups have 0, 1, 2, 3 or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

alternatively R⁹ and R^{9A} together with Q, W, and the C to which W and Q are bonded, may form a 3- to 12-membered monocyclic or bicyclic ring, optionally containing a heteroatom in addition to Q that is selected from N, O or S, wherein the ring may contain a double bond, wherein the ring may optionally include a C=O group, and further wherein the ring optionally may be substituted by 1, 2, or 3 R¹¹ substituents;

R¹¹ is independently selected from OH, halo, -NR^cR^d, -C₁₋₆alkyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl group have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl,

spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

wherein the -C₁₋₆alkyl of any of the R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R^{4A}, R^{5A}, R^{6A}, R^{7A}, R^{8A}, and R^{9A} substituents is unsubstituted or substituted by 1, 2 or 3 R¹² substituents independently selected from OH, -OC₁₋₆alkyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, halo, -O-haloC₁₋₆alkyl, -CN, -NR^aR^b, -(NR^aR^bR^c)_n, -SO₂R^a, -(CH₂CH₂O)_nCH₃, (=O), -C(=O), -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^a, -C(=O)NR^aR^b, -O-SiR^aR^bR^c, -O-(3- to 12-membered heterocycloalkyl), phenyl, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

wherein the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, spirocycloalkyl and spiroheterocycloalkyl groups of any of the R², R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹ and R¹² substituents can be unsubstituted or substituted with 1, 2, 3 or 4 R¹³ substituents independently selected from OH, halo, -C₁₋₆alkyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -NR^cR^d, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, -B(OH)₂, a 6- to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

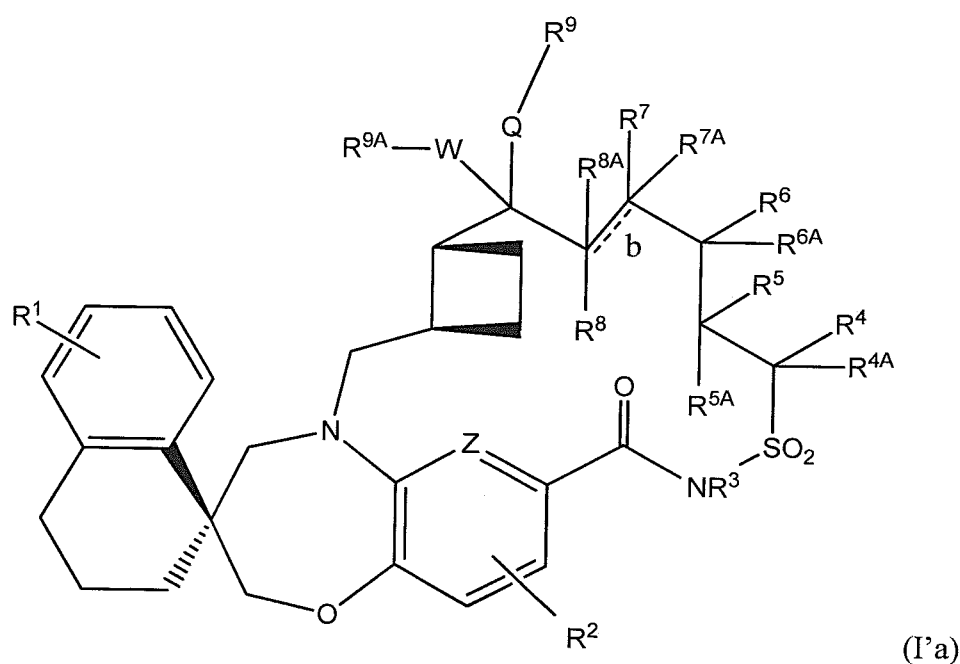
wherein each R^a, R^b, R^c, and R^d is independently H, OH, -C₁₋₆alkyl, -C₁₋₆alkenyl, -C₂₋₆alkynyl, -C₁₋₆alkyl-NR¹⁴R¹⁴, NR¹⁴R¹⁴, -SO₂R¹⁴, -(CH₂CH₂O)_nCH₃, (=O), -C(=O)R¹⁴, -OC(=O)R¹⁴, -C(=O)OR¹⁴, -C(=O)NR¹⁴R¹⁴, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -C₁₋₆alkyl-O-C₁₋₆alkyl, -C₁₋₆alkyl-OH, benzyl, phenyl, a -C₁₋₆alkyl-3- to 12-membered heterocycloalkyl, a 6-

to 12-membered aryl or heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, and heterocycloalkyl groups and the heterocycloalkyl group of the $-C_{1-6}$ alkyl–heterocycloalkyl group have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, heterocycloalkyl, and the heterocycloalkyl groups of the $-C_{1-6}$ alkyl–heterocycloalkyl group may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂;

the alkyl, aryl, heteroaryl, spirocycloalkyl, spiroheterocycloalkyl, cycloalkyl, heterocycloalkyl and the heterocycloalkyl groups of the $-C_{1-6}$ alkyl–heterocycloalkyl groups of R^a, R^b, R^c, and R^d can be unsubstituted or substituted with 1, 2, 3, or 4 R¹⁴ substituents independently selected from H, OH, -N=N=N, halo, $-C_{1-6}$ alkyl, $-OC_{1-6}$ alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, phenyl, tolyl, -C(O)C₁₋₆alkyl, -C(O)OCH₃, SO₂-phenyl, or -SO₂-N(CH₃)₂; and

n is independently, in each instance, an integer of 1, 2, 3 or 4.

2. The compound of Claim 1, wherein the compound of Formula I' has the Formula I'a:



or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof.

3. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein b is a double bond.
4. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein Z is C.
5. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein Q is O.
6. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein W is $CR^{WA}R^{WB}$ and R^{WA} and R^{WB} are both H.
7. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^1 is halo.
8. The compound of Claim 7, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^1 is Cl.
9. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^2 is H and R^3 is H.
10. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^4 selected from H, $-C_{1-6}alkyl$, $-C_{1-6}alkylhalo$, $-C_{1-6}alkyl-O-C_{1-6}alkyl$, or $-(CH_2CH_2O)_nR^a$, wherein the $-C_{1-6}alkyl$ is unsubstituted or substituted with $-OH$, $(=O)$, phenyl, $-O-SiR^aR^bR^c$, $-NR^aR^b$, a 3- to 12-membered cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl having 1, 2, 3, or 4 heteroatoms independently selected from O, N or S.

11. The compound of Claim 10, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^4 is H or $-C_{1-6}$ alkyl.

12. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^5 is H or $-C_{1-6}$ alkyl.

13. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^6 is H or $-C_{1-6}$ alkyl.

14. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein each of R^{4A} , R^{5A} , R^{6A} , R^{7A} and R^{8A} is independently selected from H, OH, halo, or $-C_{1-6}$ alkyl.

15. The compound of Claim 14, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein each of R^{4A} , R^{5A} , R^{6A} , R^{7A} and R^{8A} is H.

16. The compound of Claim 1, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^9 is independently selected from H, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, or $-C_{1-6}$ alkyl- $O-C_{1-6}$ alkyl or $-C_{1-6}$ haloalkyl.

17. The compound of Claim 16, or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^9 is H, $-CH_3$, or $-CH_2CH_3$.

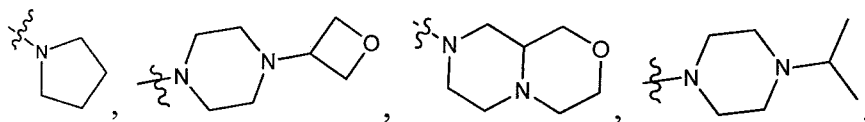
18. The compound of Claim 1 or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R^{9A} is selected from H, C_{1-6} haloalkyl, C_{1-6} alkyl, $-C_{2-6}$ alkenyl $-(CH_2CH_2O)_nR^a$, $-SO_2R^a$, $-C(=O)R^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^b$, $-NR^aR^b$, $-N=N=N$, $-C_{1-6}$ alkyl- $O-C_{1-6}$ alkyl, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic

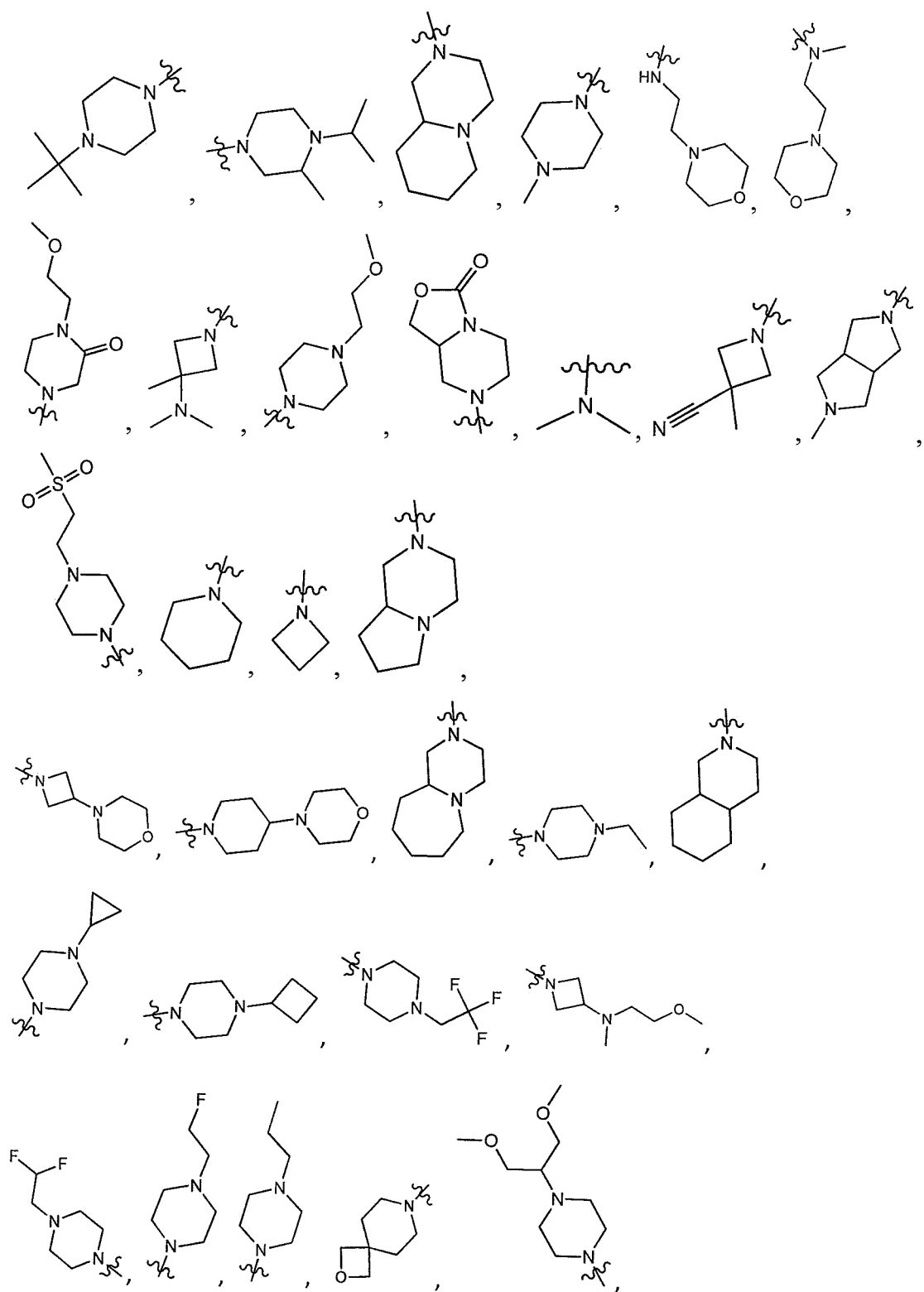
heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl and heterocycloalkyl groups have 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂.

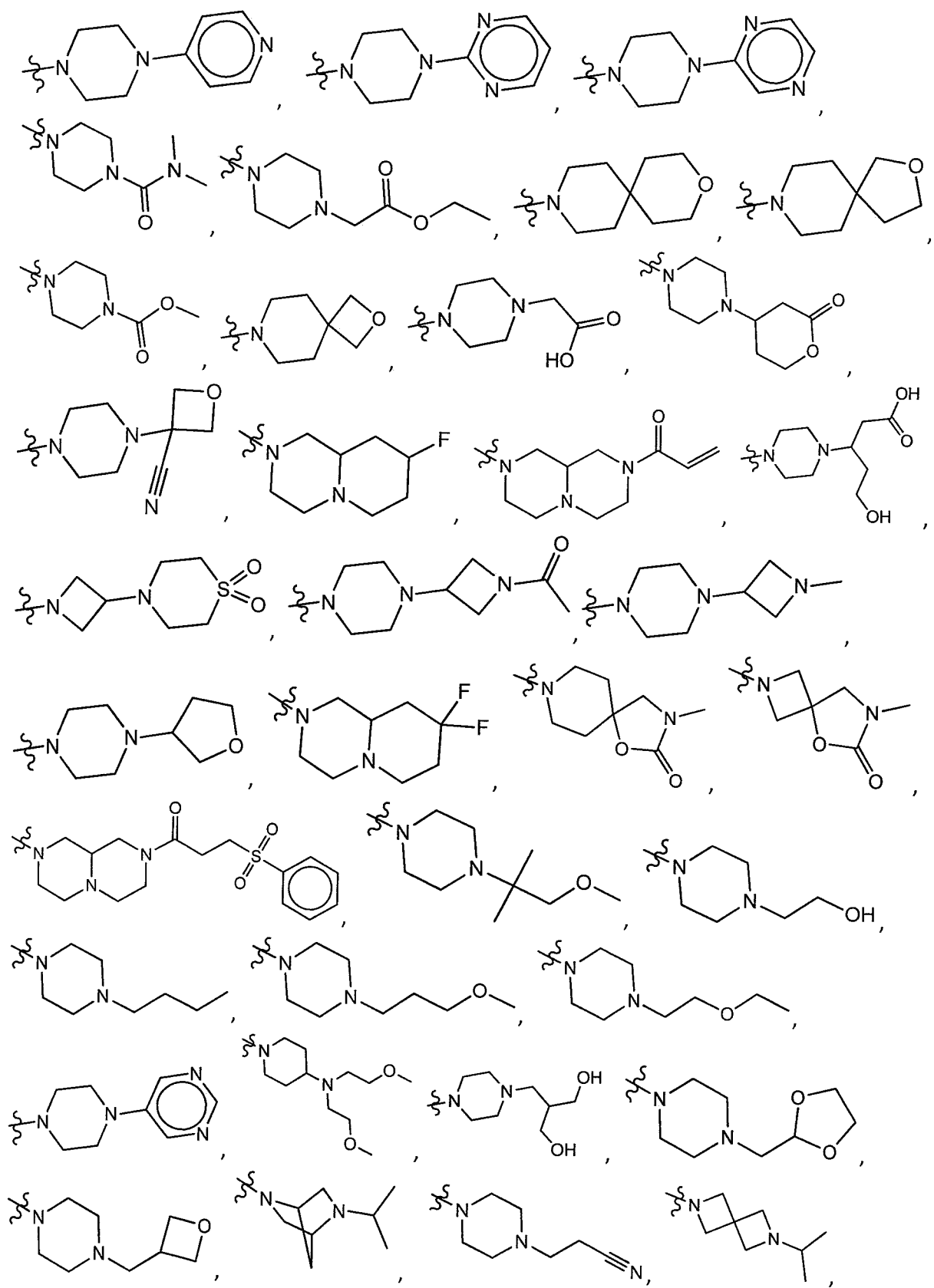
19. The compound of Claim 18 or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein the 3- to 12-membered monocyclic heterocycloalkyl R^{9A} group can be unsubstituted or substituted with 1, 2, 3 or 4 R¹⁰ substituents independently selected from OH, halo, -NR^cR^d, -C₁₋₆alkyl, -C₂₋₆ alkenyl, -C₂₋₆alkynyl, -OC₁₋₆alkyl, -C₁₋₆alkyl-OH, -C₁₋₆alkyl-O-C₁₋₆alkyl, C₁₋₆haloalkyl, -O-haloC₁₋₆alkyl, -SO₂R^c, -CN, -C(=O)NR^cR^d, -C(=O)R^c, -OC(=O)R^a, -C(=O)OR^c, a 6- to 12-membered aryl, a 6- to 12-membered heteroaryl, a 5- to 12-membered spirocycloalkyl or spiroheterocycloalkyl, a 3- to 12-membered cycloalkenyl, a 3- to 12-membered monocyclic or bicyclic cycloalkyl, or a 3- to 12-membered monocyclic or bicyclic heterocycloalkyl group, wherein the heteroaryl, spiroheterocycloalkyl, or heterocycloalkyl group have from 1, 2, 3, or 4 heteroatoms independently selected from O, N or S, wherein the cycloalkyl, spirocycloalkyl, spiroheterocycloalkyl, and heterocycloalkyl groups may include a C=O group, and further wherein the spiroheterocycloalkyl and heterocycloalkyl groups may include a S=O or SO₂.

20. The compound of Claim 19 or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein the 1, 2, 3 or 4 R¹⁰ substituents are independently selected from -C₁₋₆alkyl or a 3- to 12-membered monocyclic heterocycloalkyl group, wherein the heterocycloalkyl group has 1, 2, 3 or 4 heteroatoms independently selected from O, N or S.

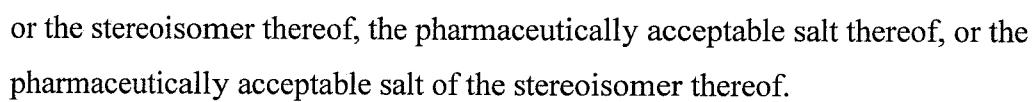
21. The compound of Claim 1, wherein R^{9A} is independently selected from -N=N=N,







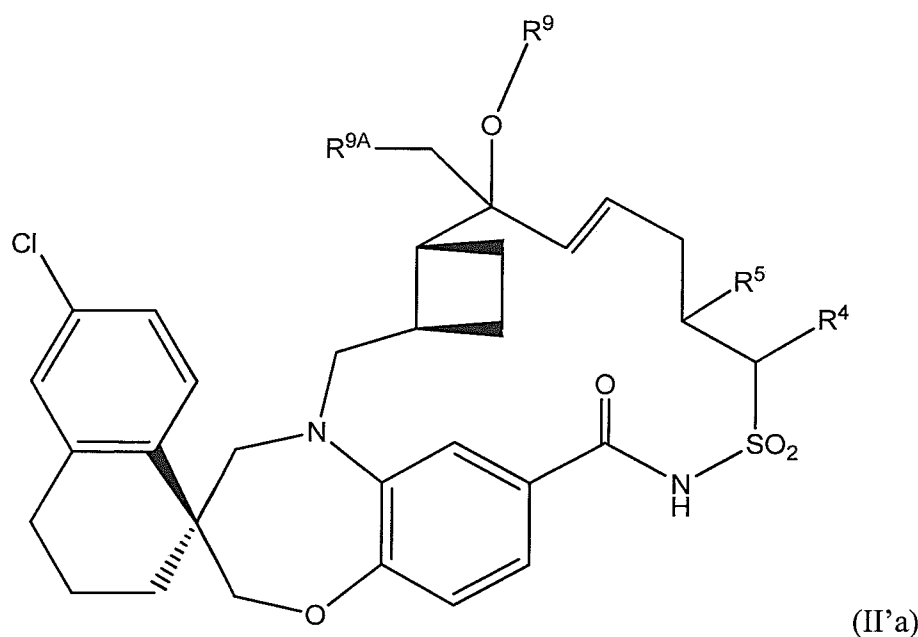




Chemical structure (II') is a complex molecule featuring a chlorophenyl group (a benzene ring with a chlorine atom, Cl) attached to a bicyclic system (a hexagon fused to a cyclohexane ring). This bicyclic system is connected via a nitrogen atom (N) to a cyclobutane ring. The cyclobutane ring is further substituted with an oxygen atom (O) and a side chain containing a double bond and a sulfonamide group (SO₂NH). The side chain also includes substituents R⁴ and R⁵. The oxygen atom is further substituted with R⁹ and R^{9A}.

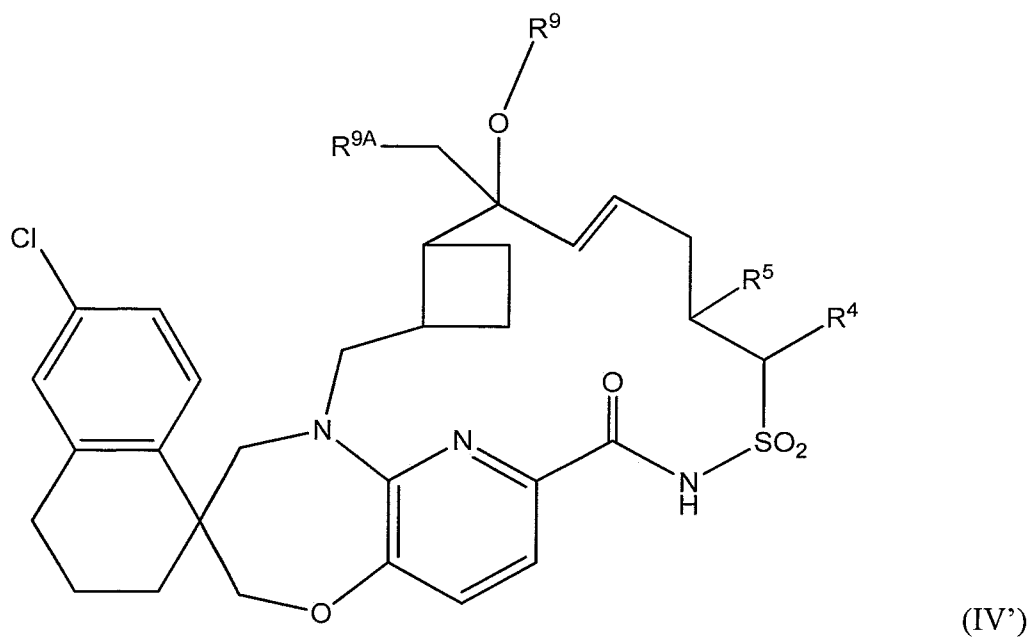
or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R⁴, R⁵, R⁹ and R^{9A} are as defined above.

23. The compound of Claim 1, wherein the compound of Formula I' has Formula II'a:



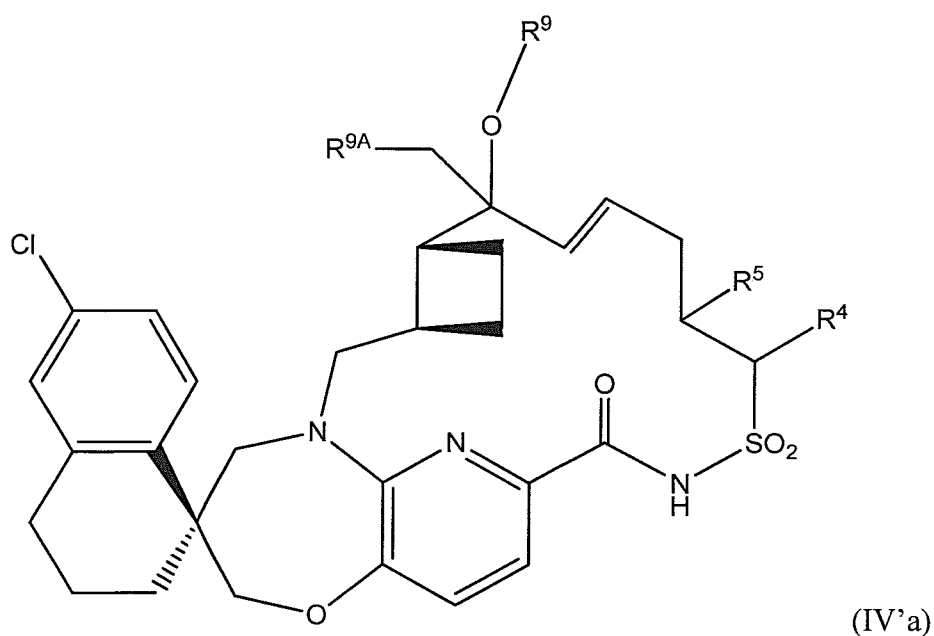
or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R⁴, R⁵, R⁹ and R^{9A} are as defined above.

24. The compound of Claim 1, wherein the compound of Formula I' has Formula IV':



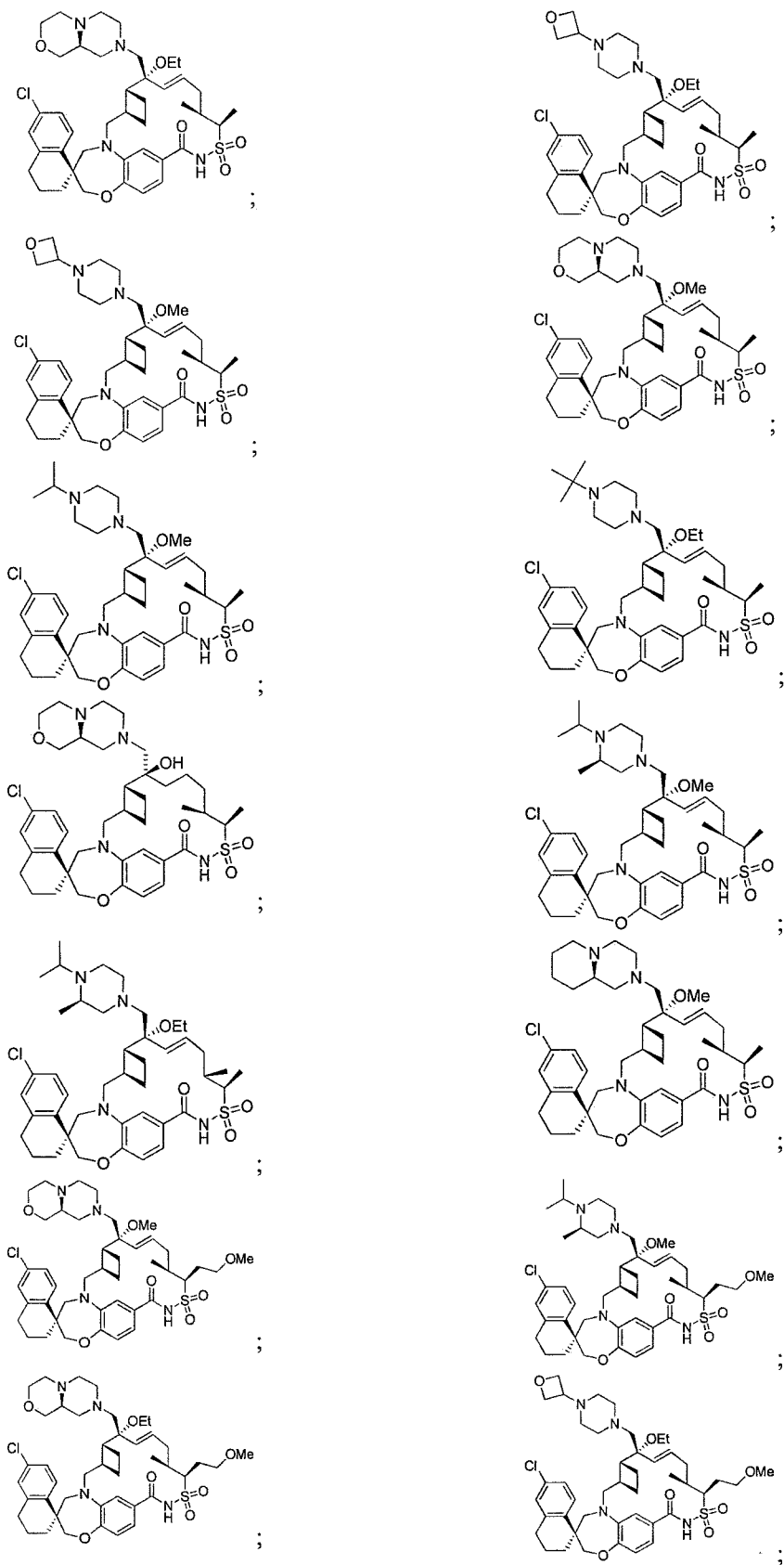
or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof wherein R⁴, R⁵, R⁹ and R^{9A} are as defined above.

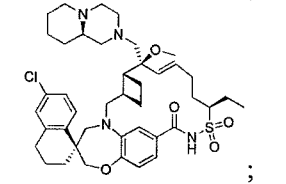
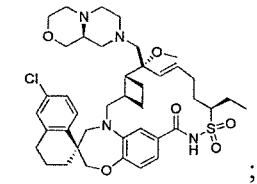
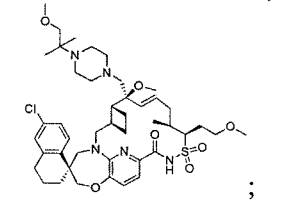
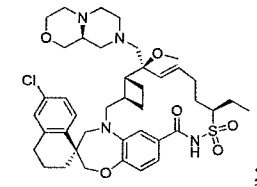
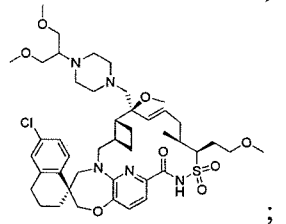
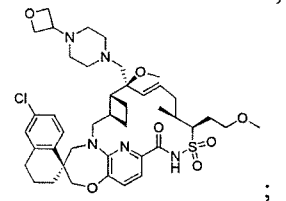
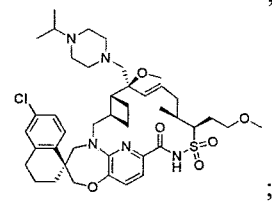
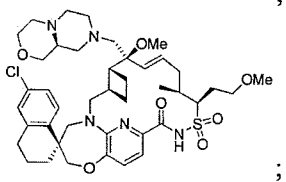
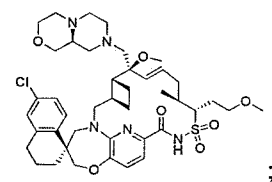
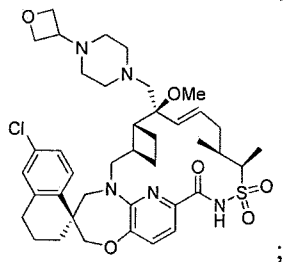
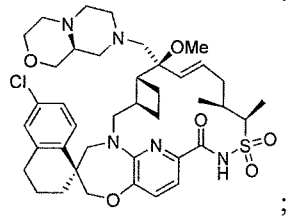
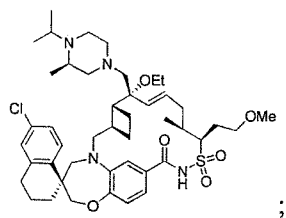
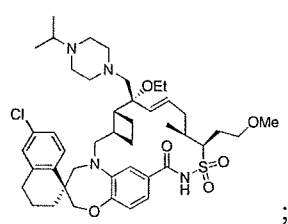
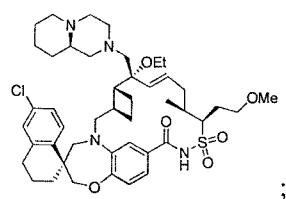
25. The compound of Claim 1, wherein the compound of Formula I' has Formula IV'a:

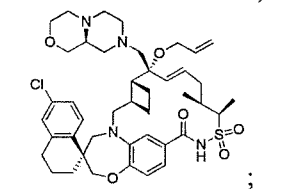
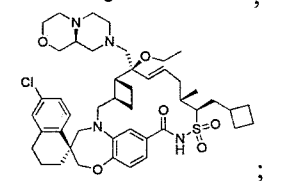
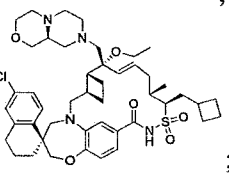
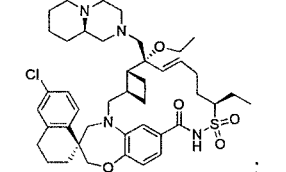
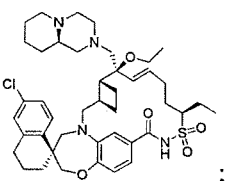
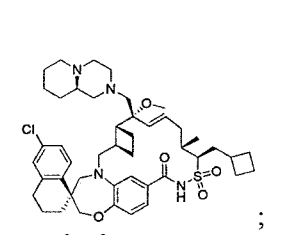
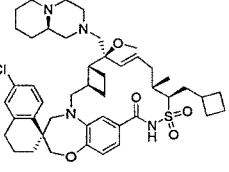
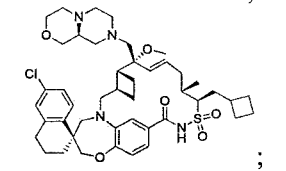
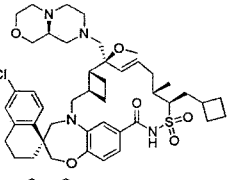
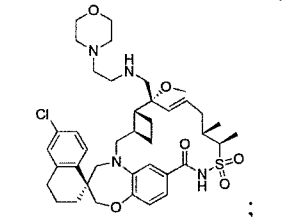
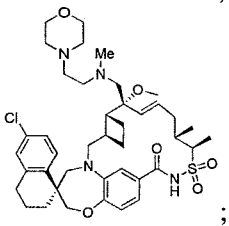
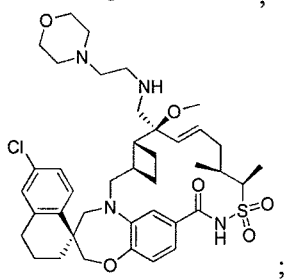
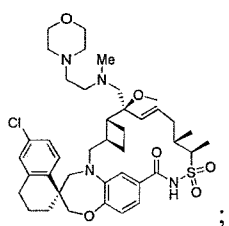
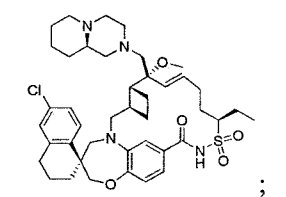
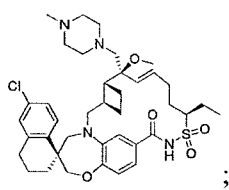


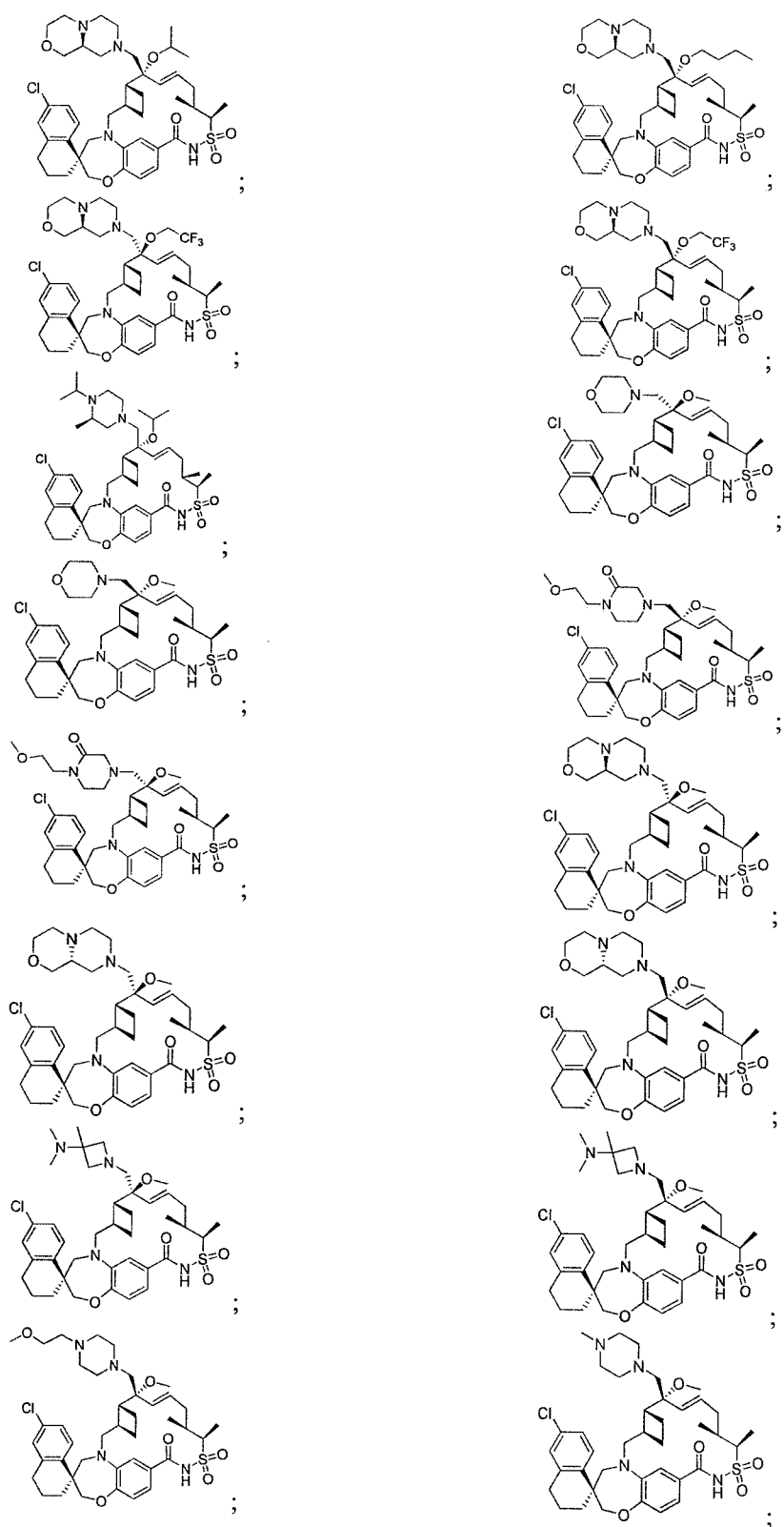
or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof, wherein R⁴, R⁵, R⁹ and R^{9A} are as defined above.

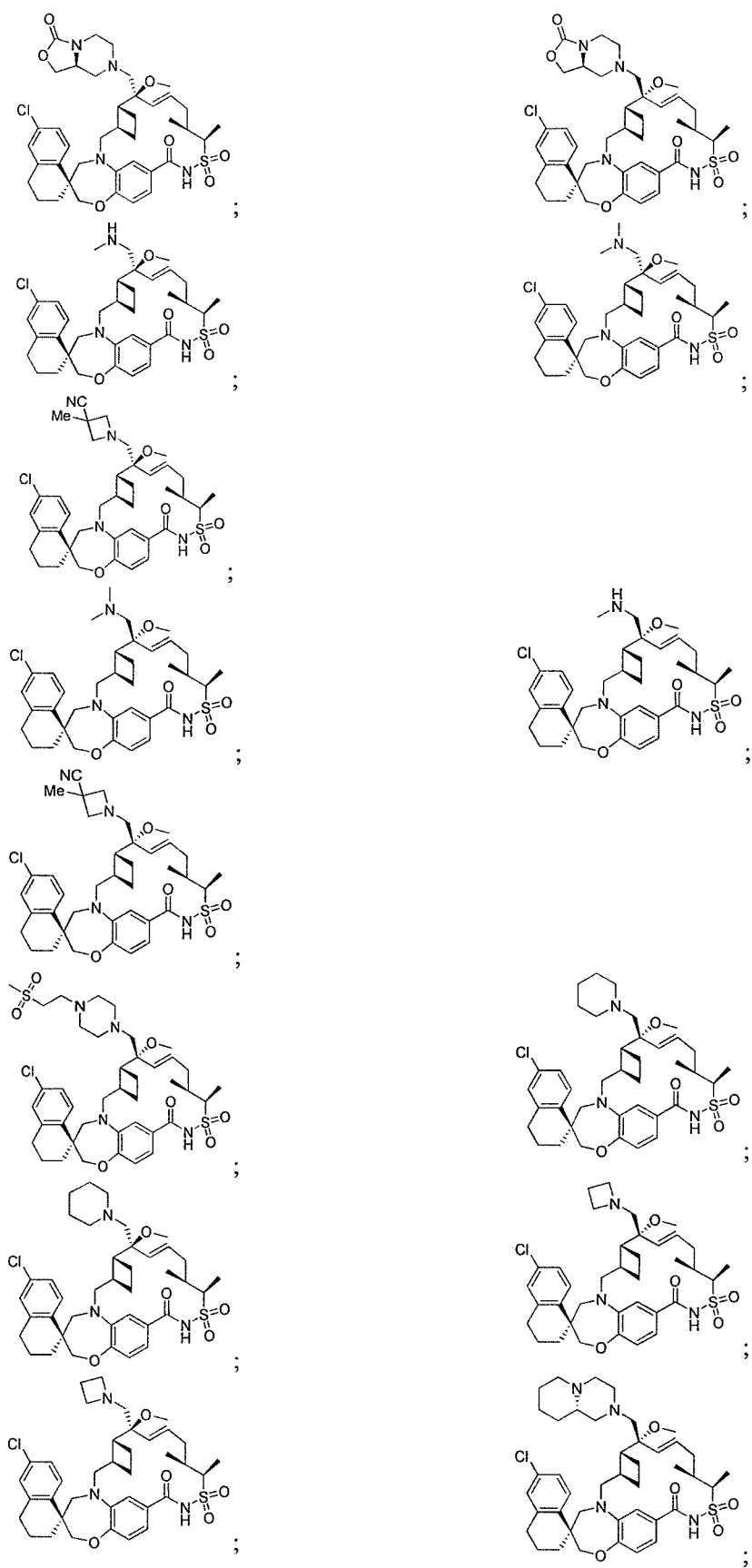
26. The compound of claim 1, wherein the compound has a structure selected from:

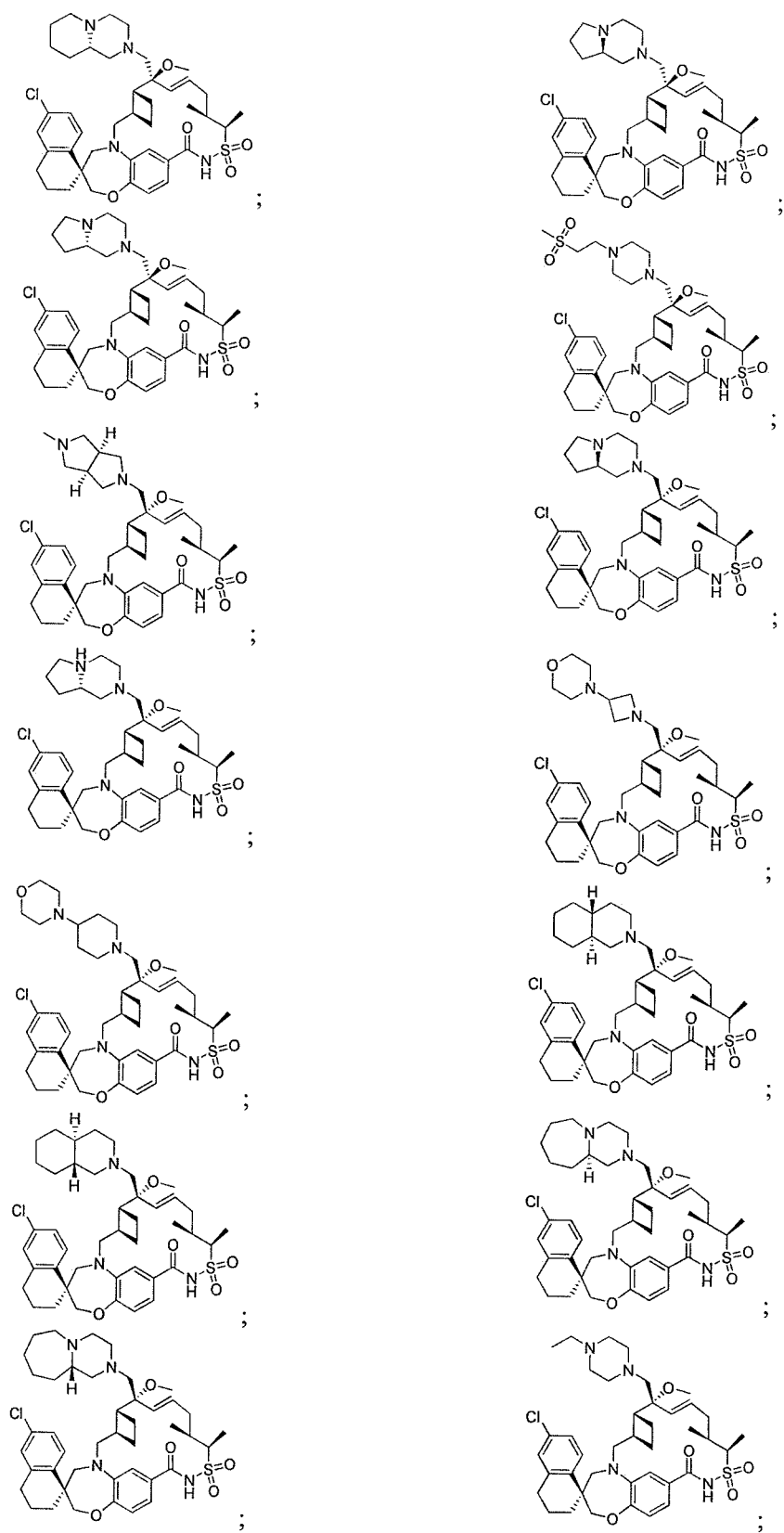


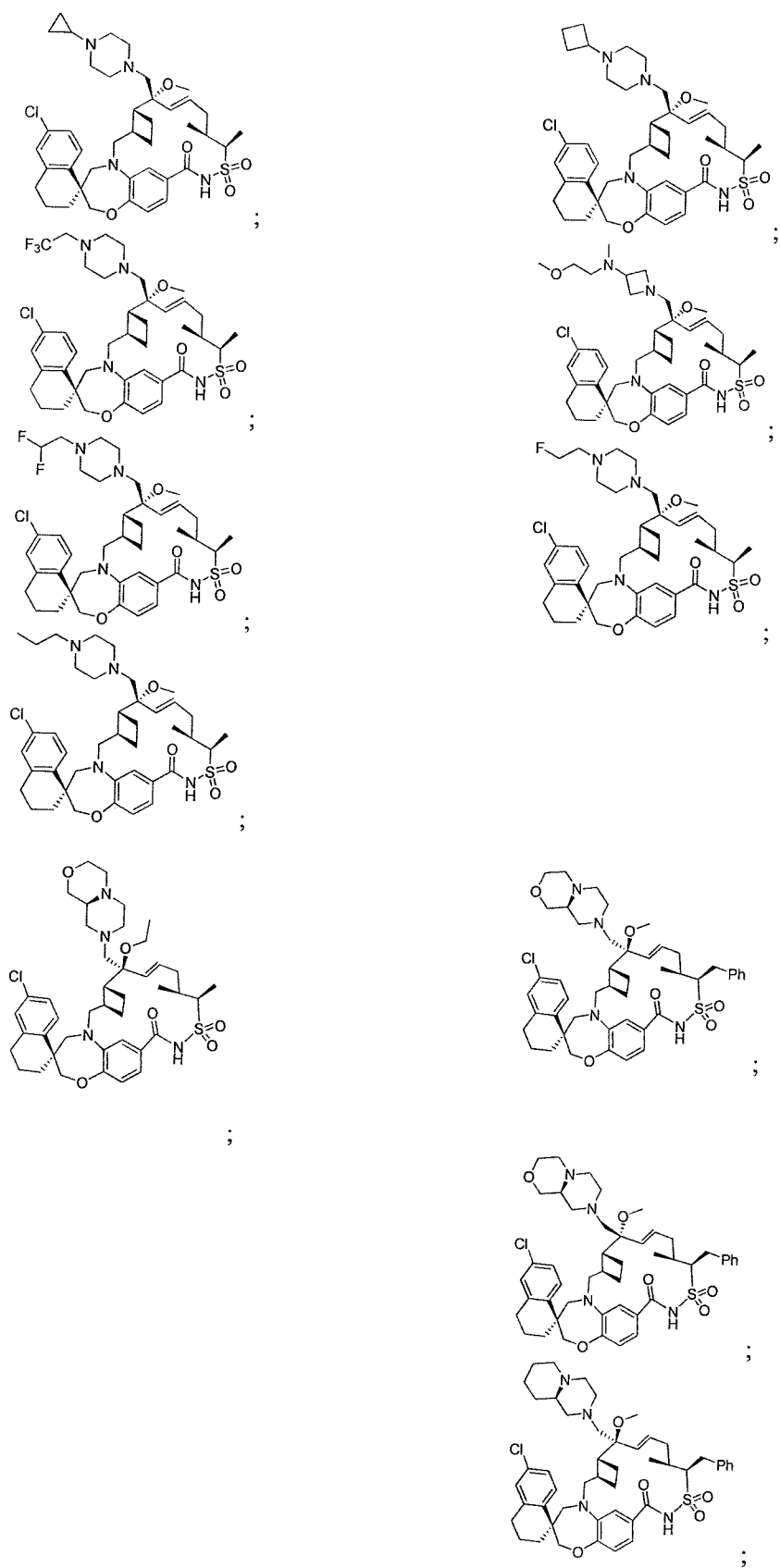


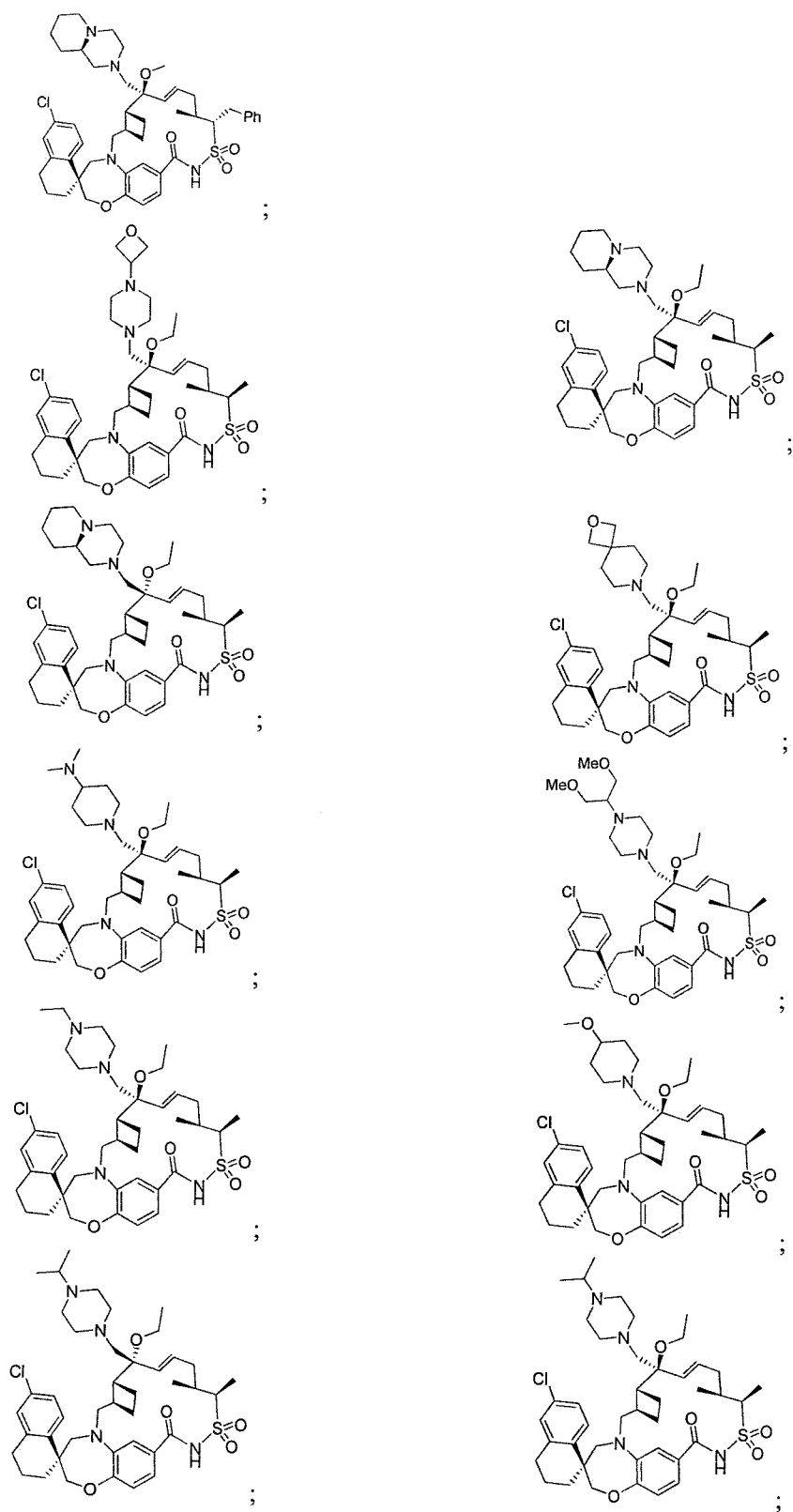


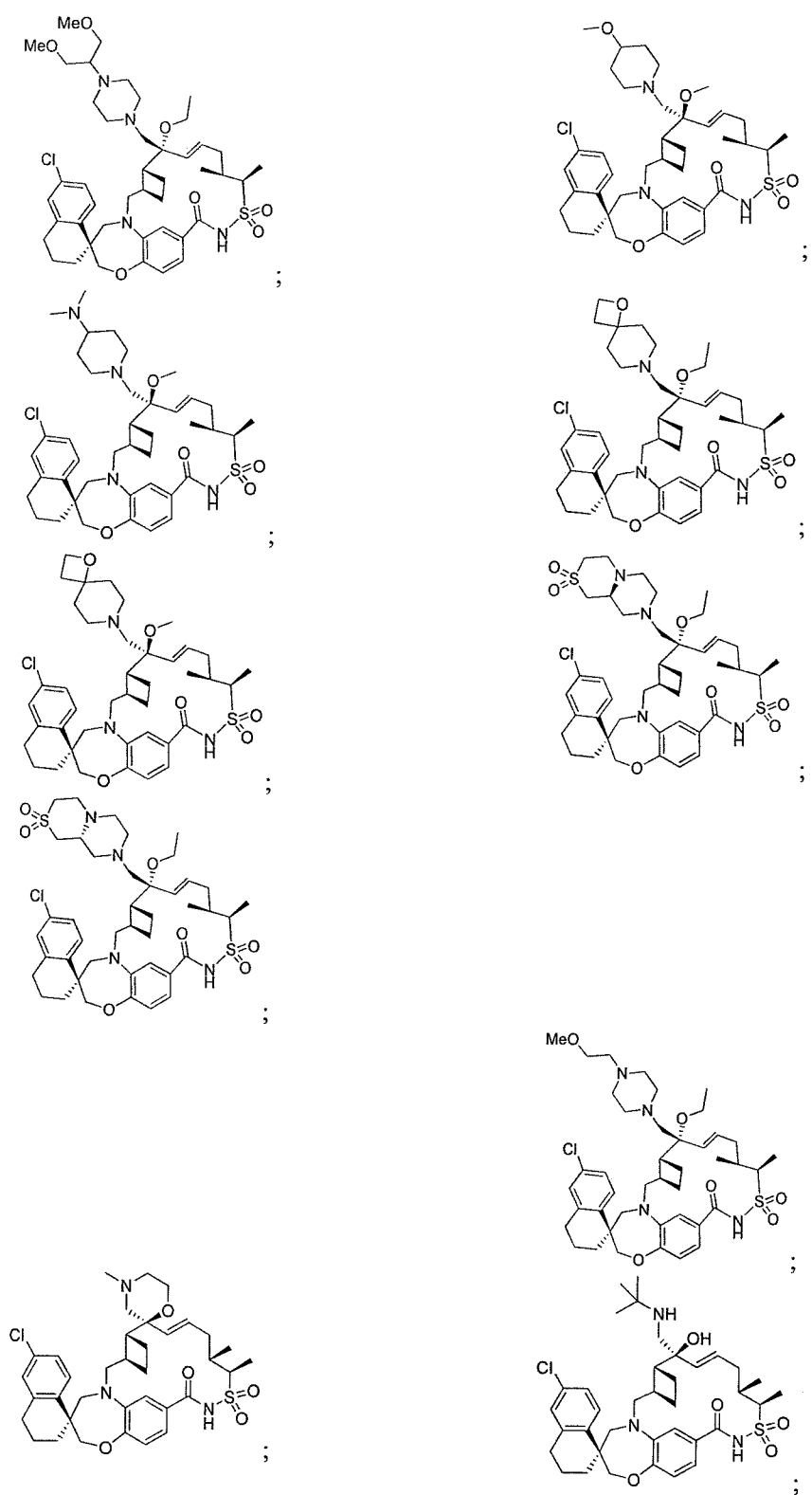


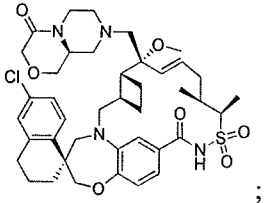
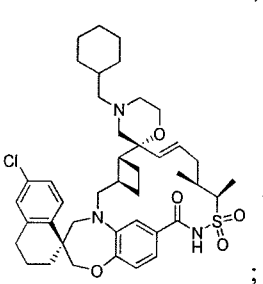
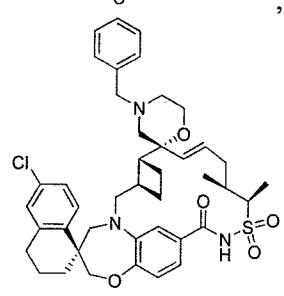
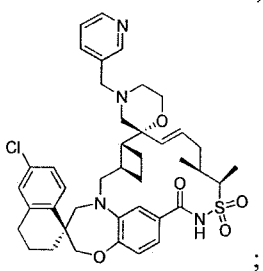
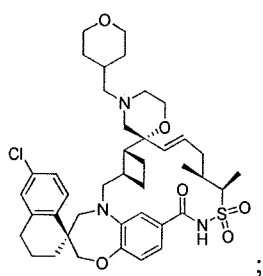
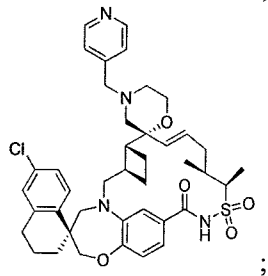
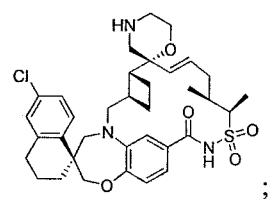
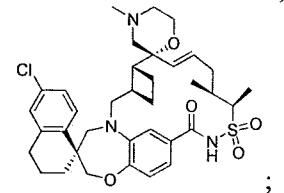
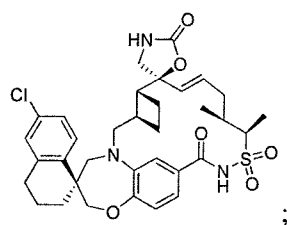
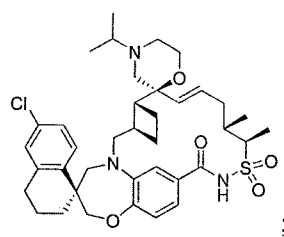
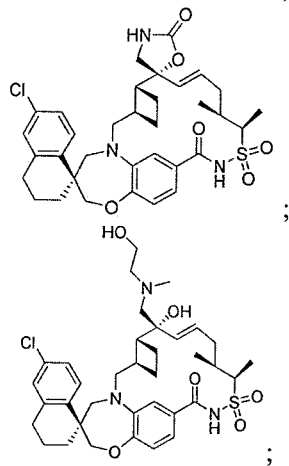
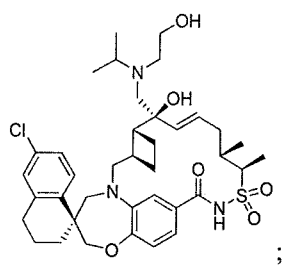


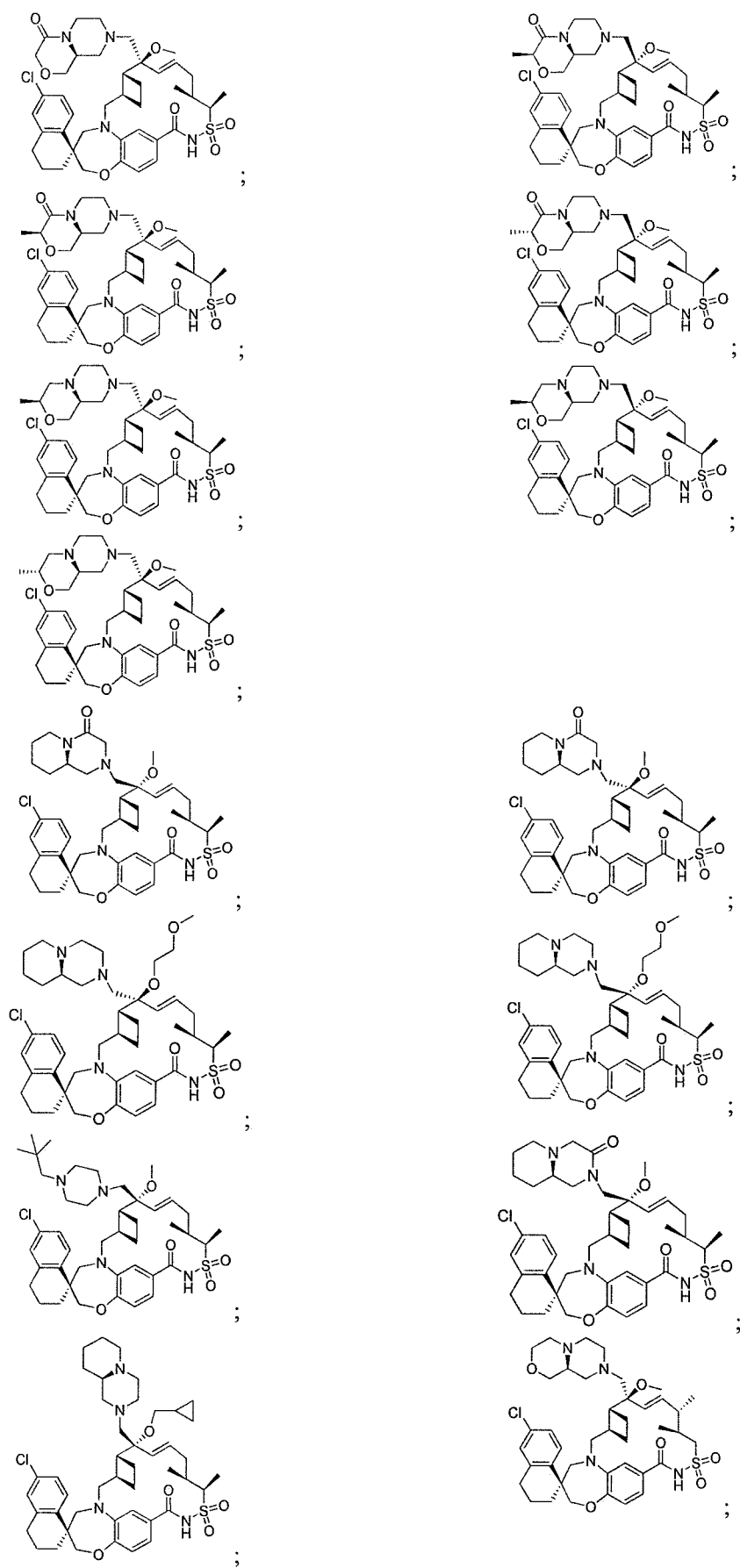


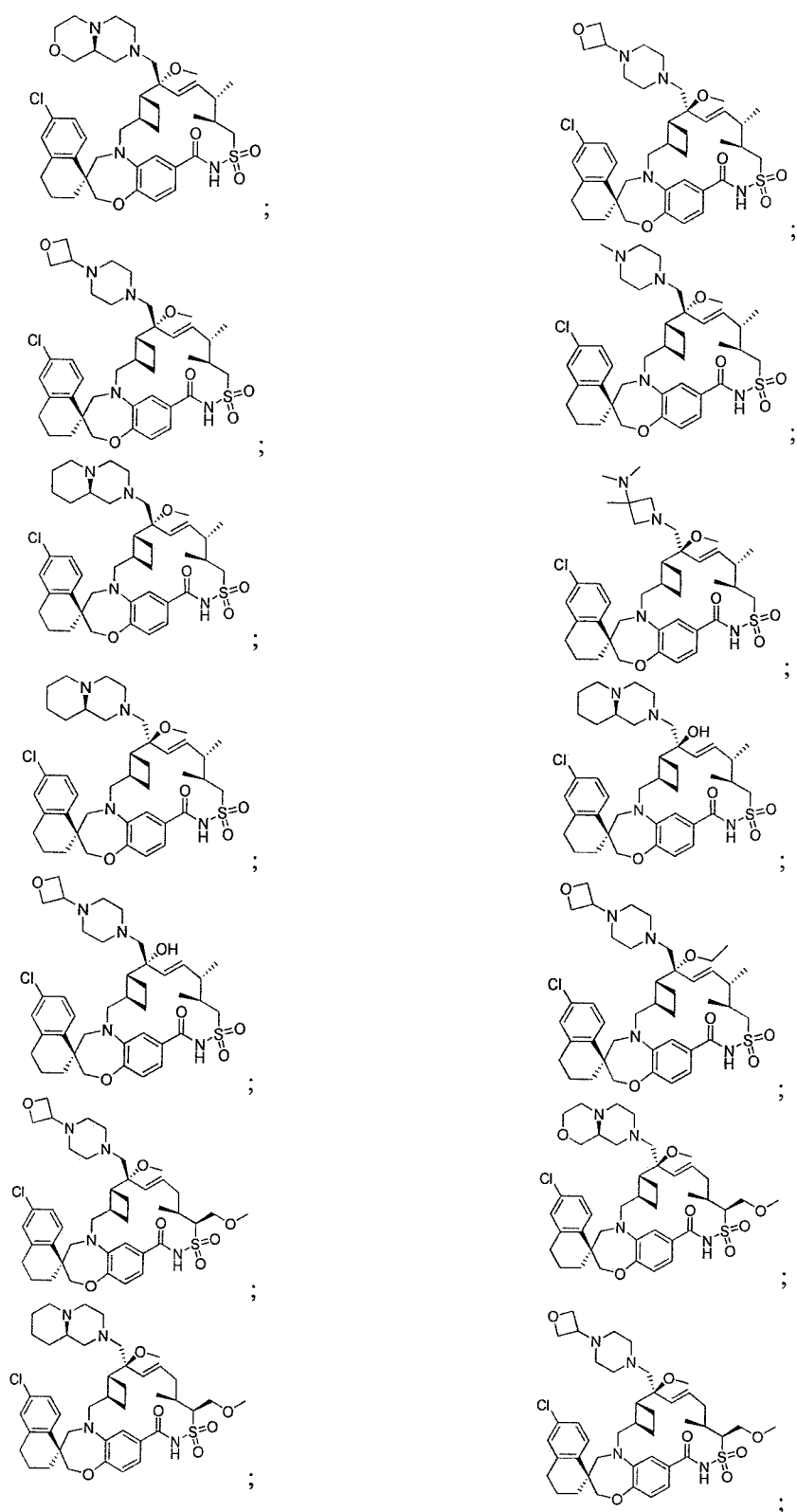


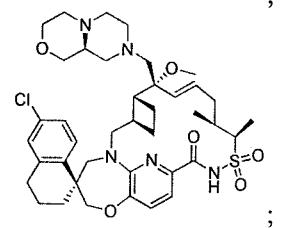
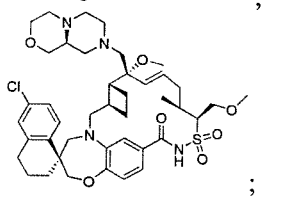
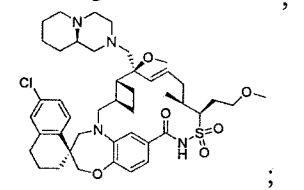
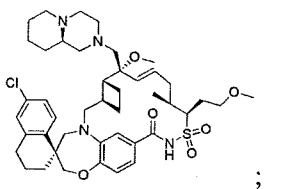
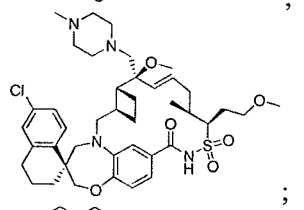
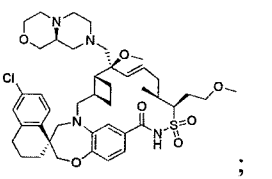
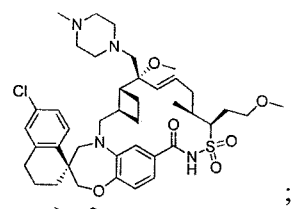
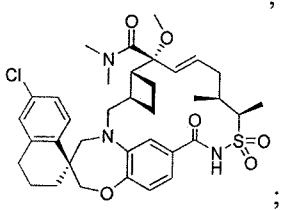
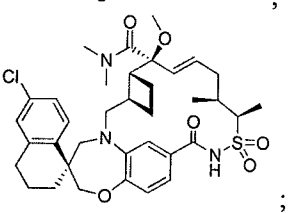
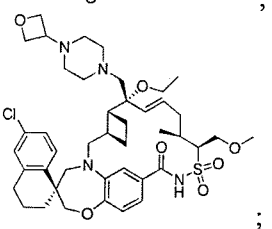
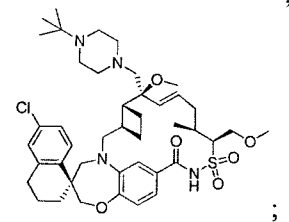
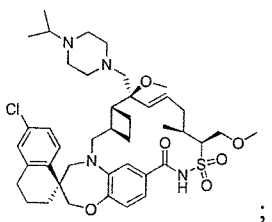
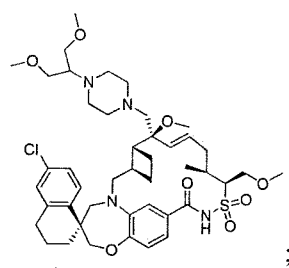
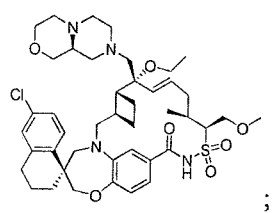


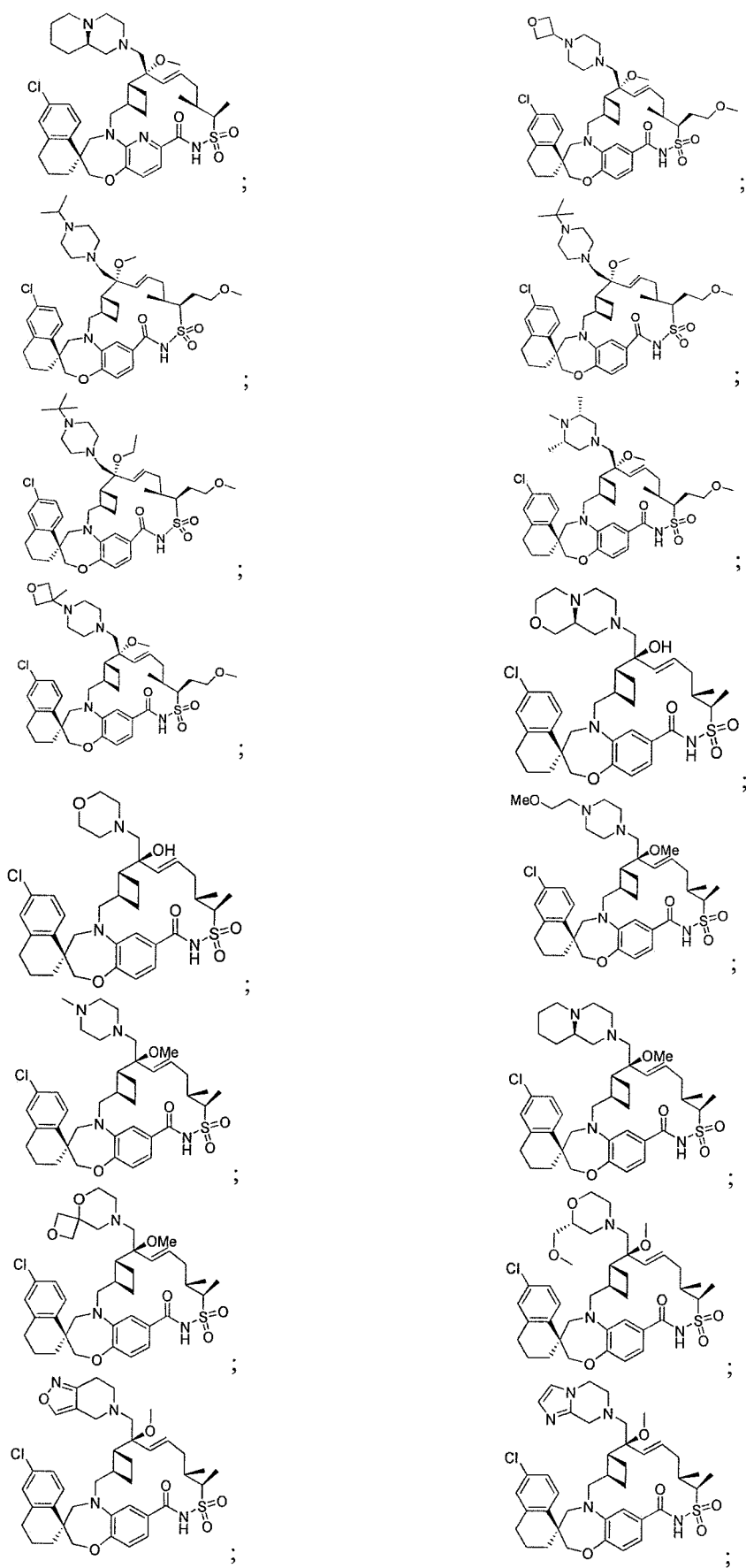


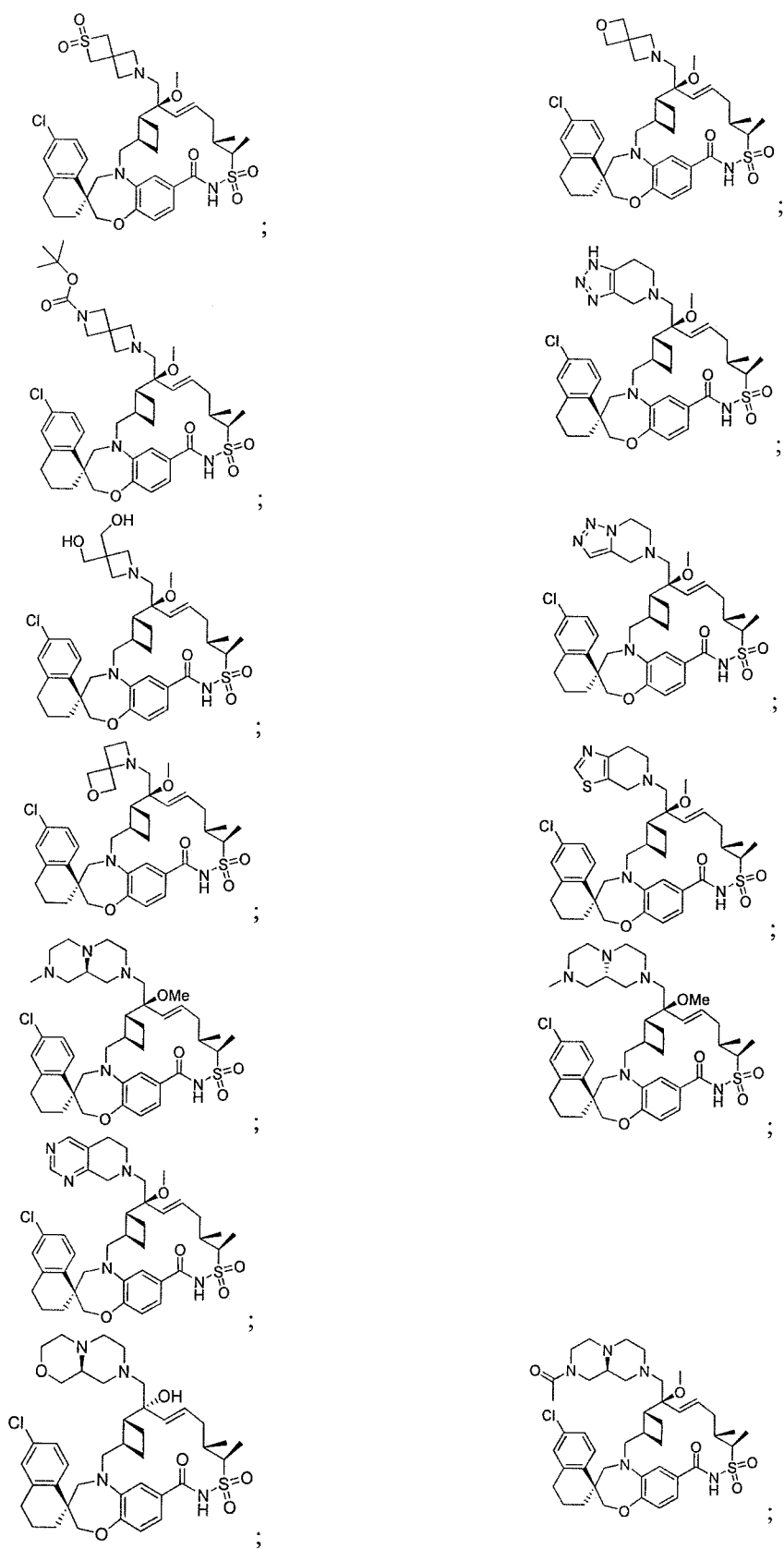


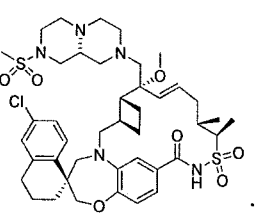
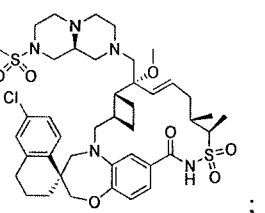
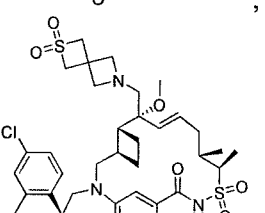
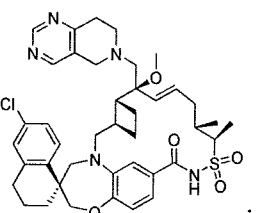
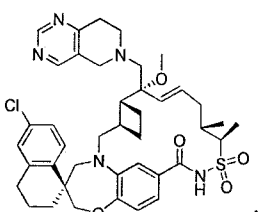
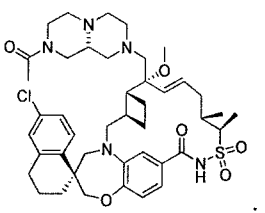
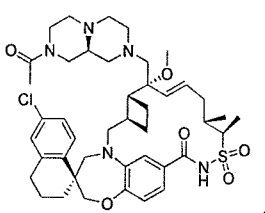
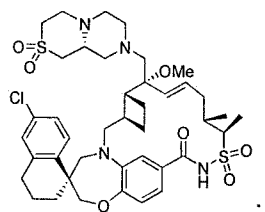
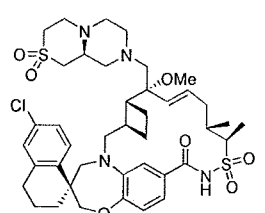
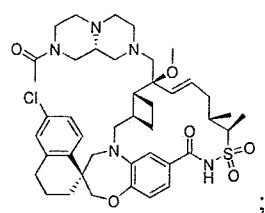


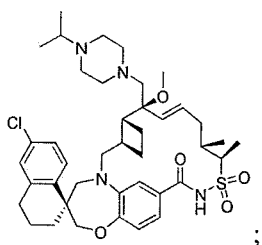
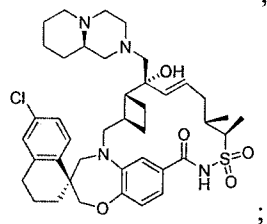
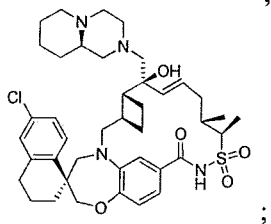
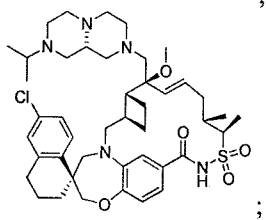
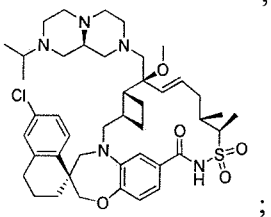
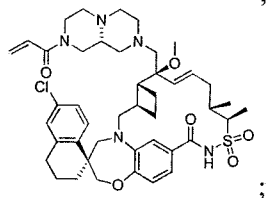
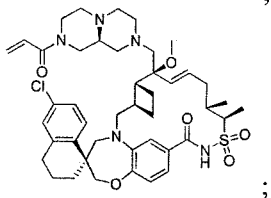
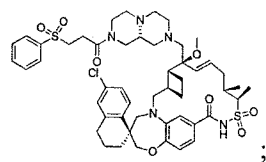
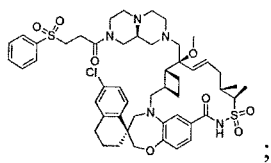
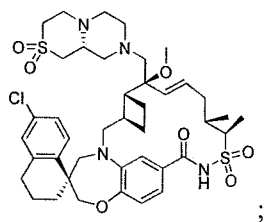
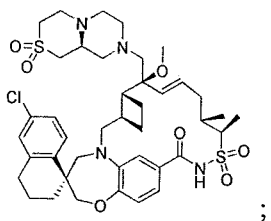
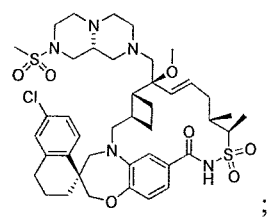
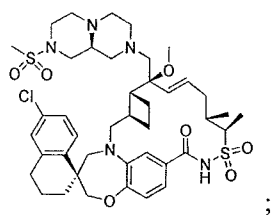


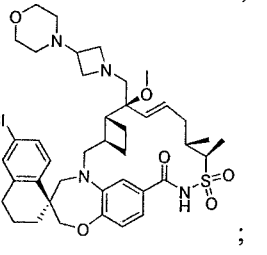
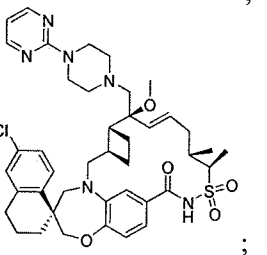
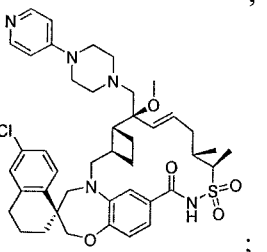
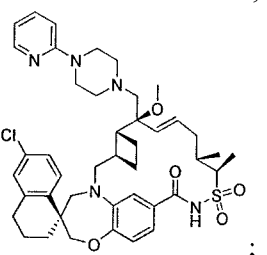
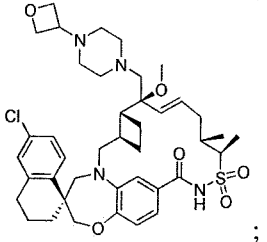
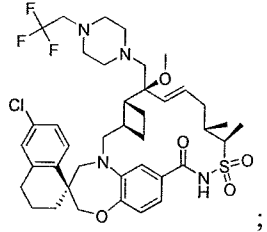
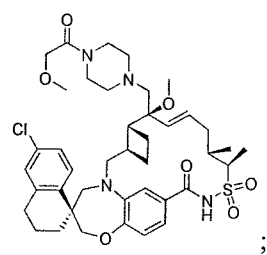
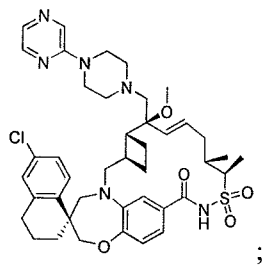
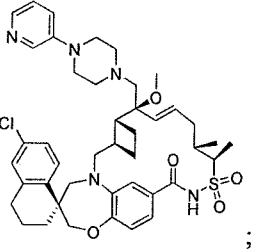
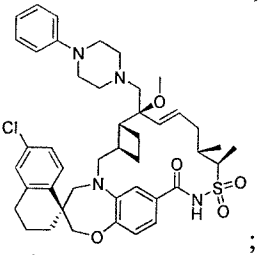
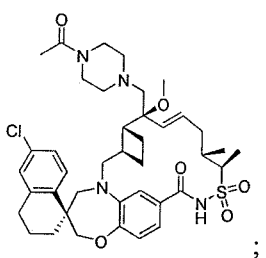
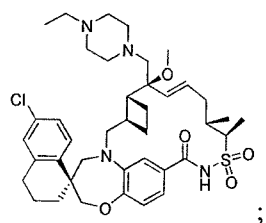


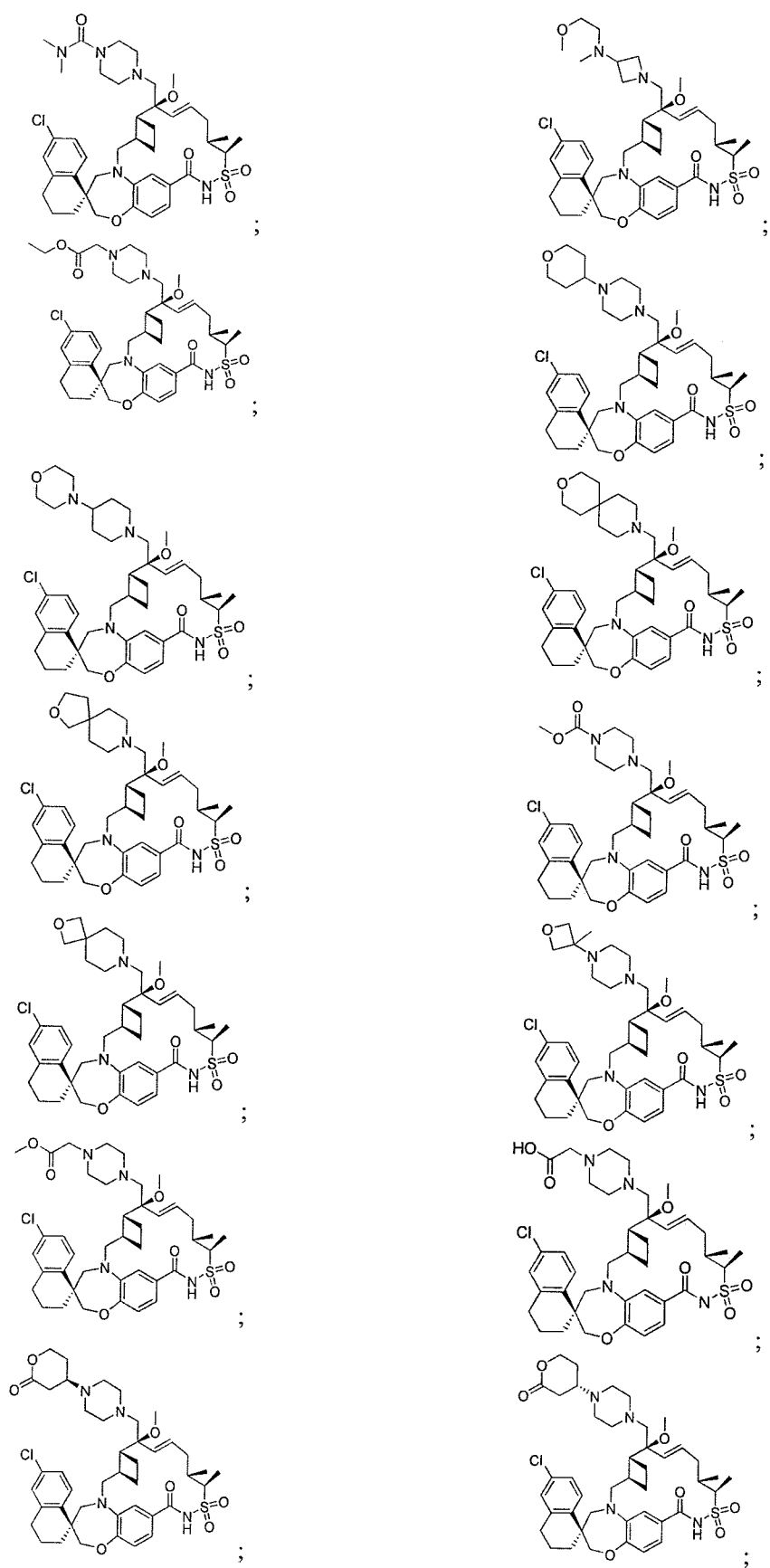


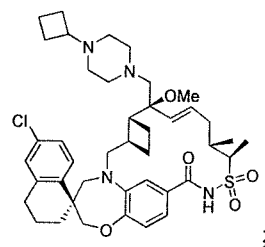
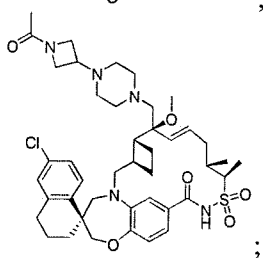
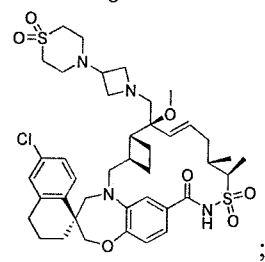
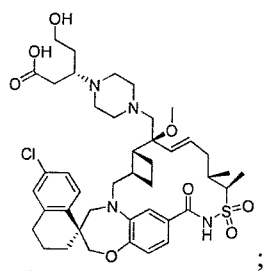
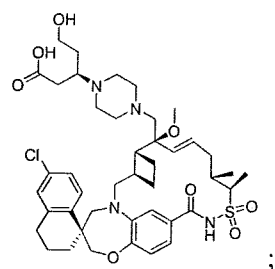
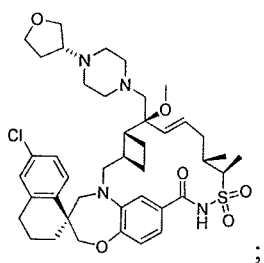
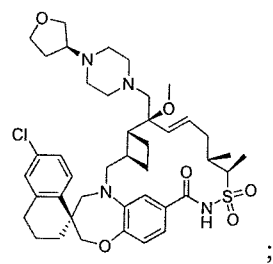
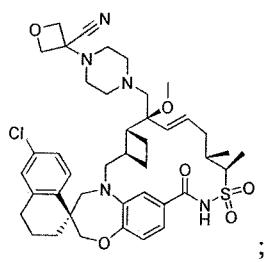


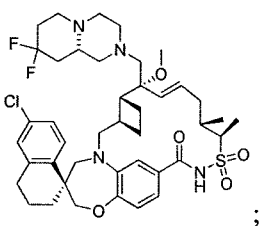
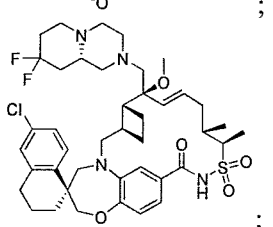
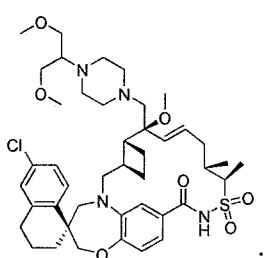
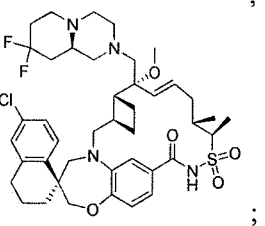
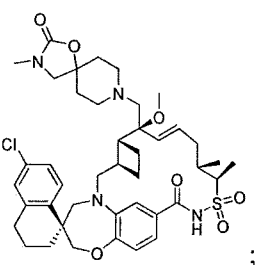
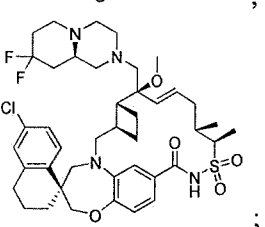
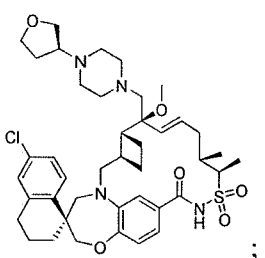
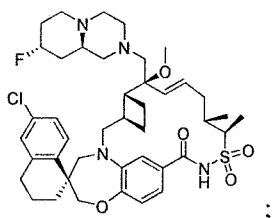
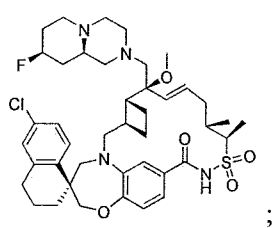
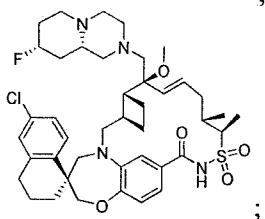
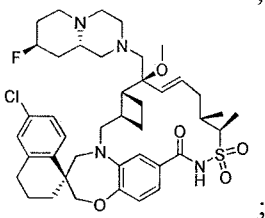
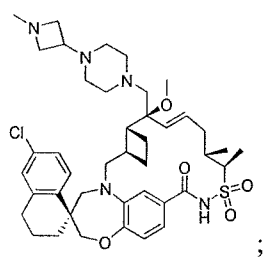


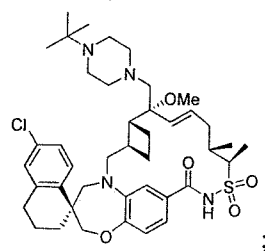
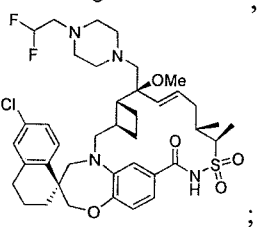
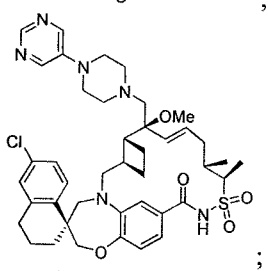
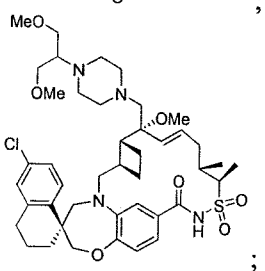
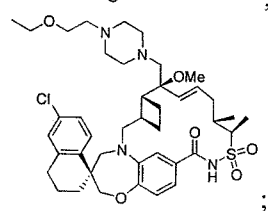
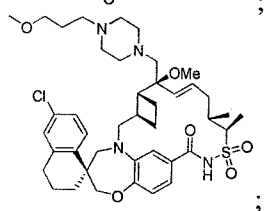
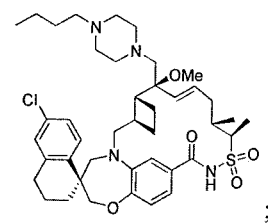
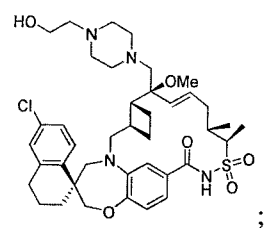
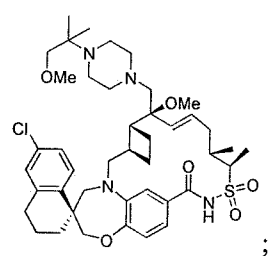
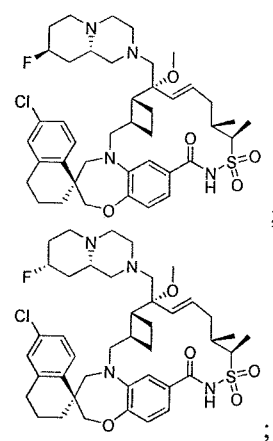
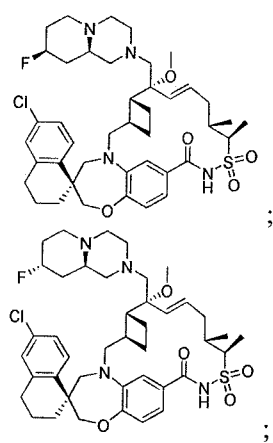


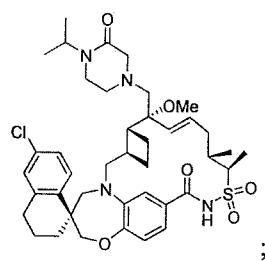
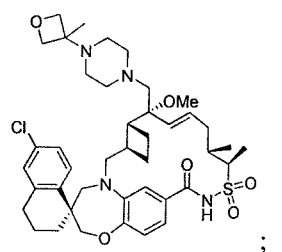
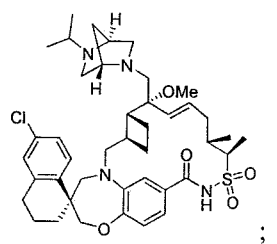
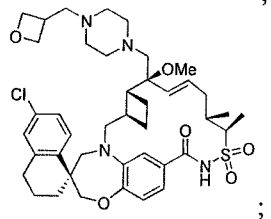
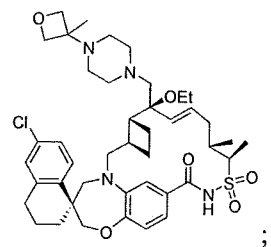
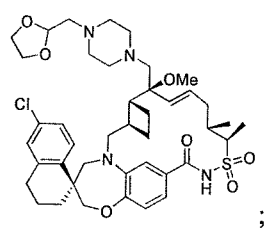
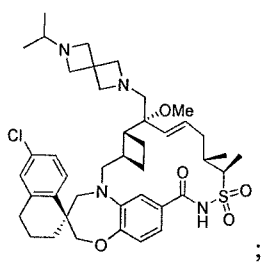
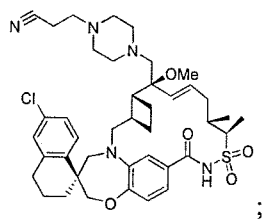
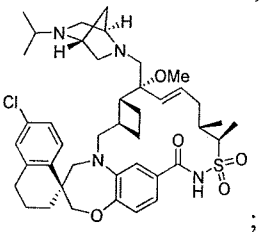
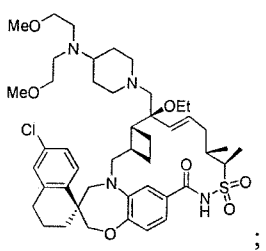
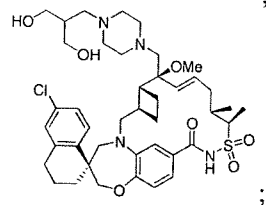
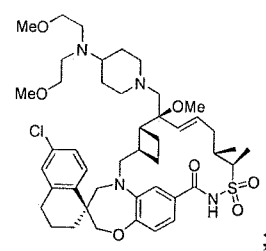


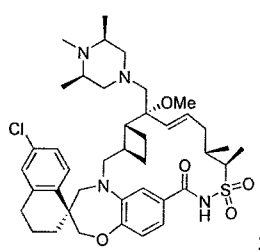
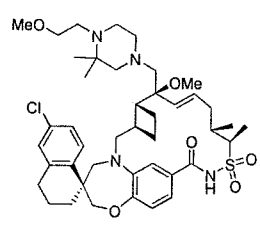
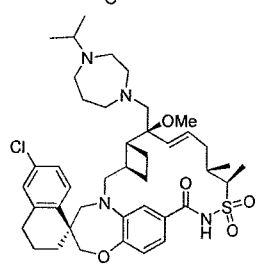
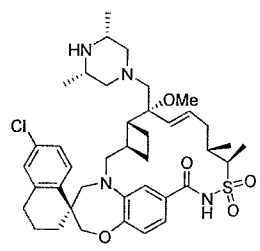
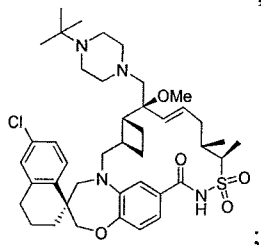
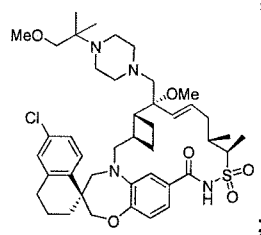
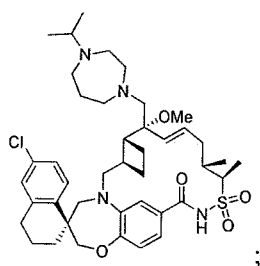
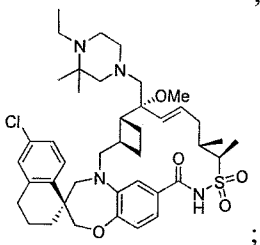
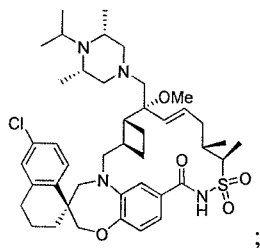
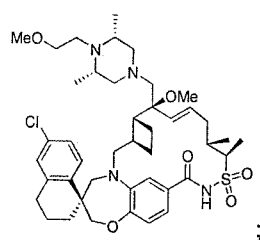


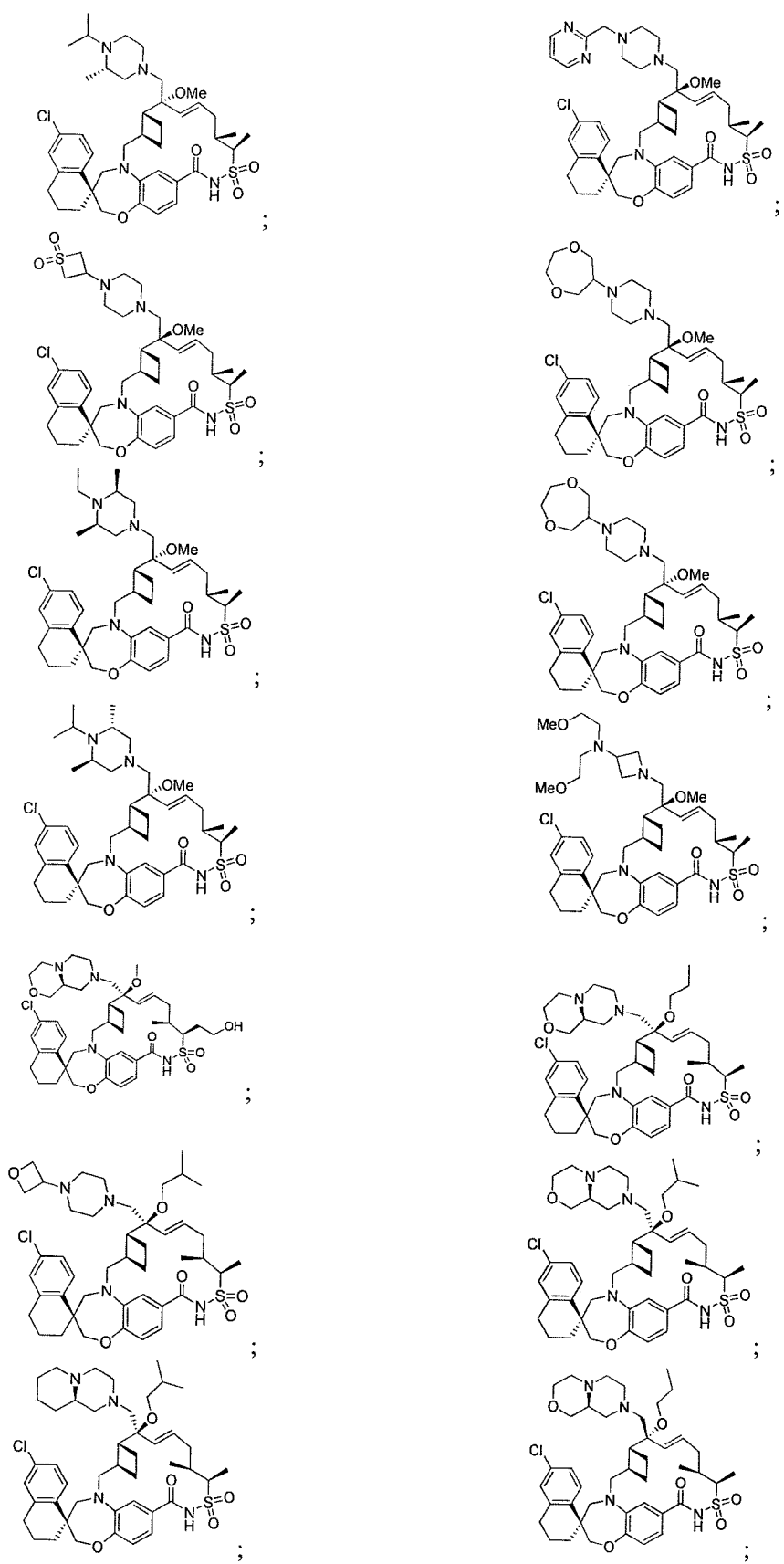


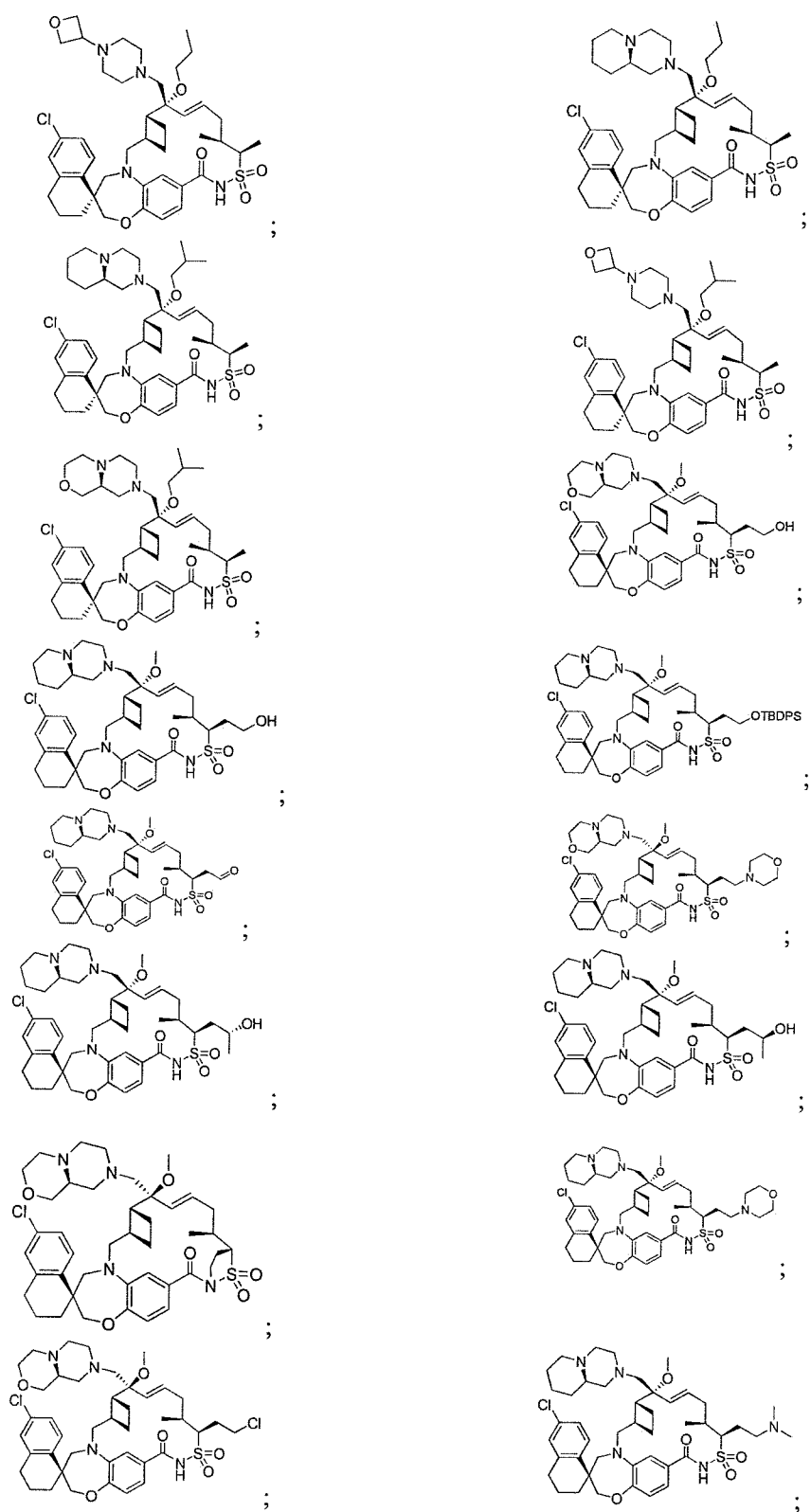


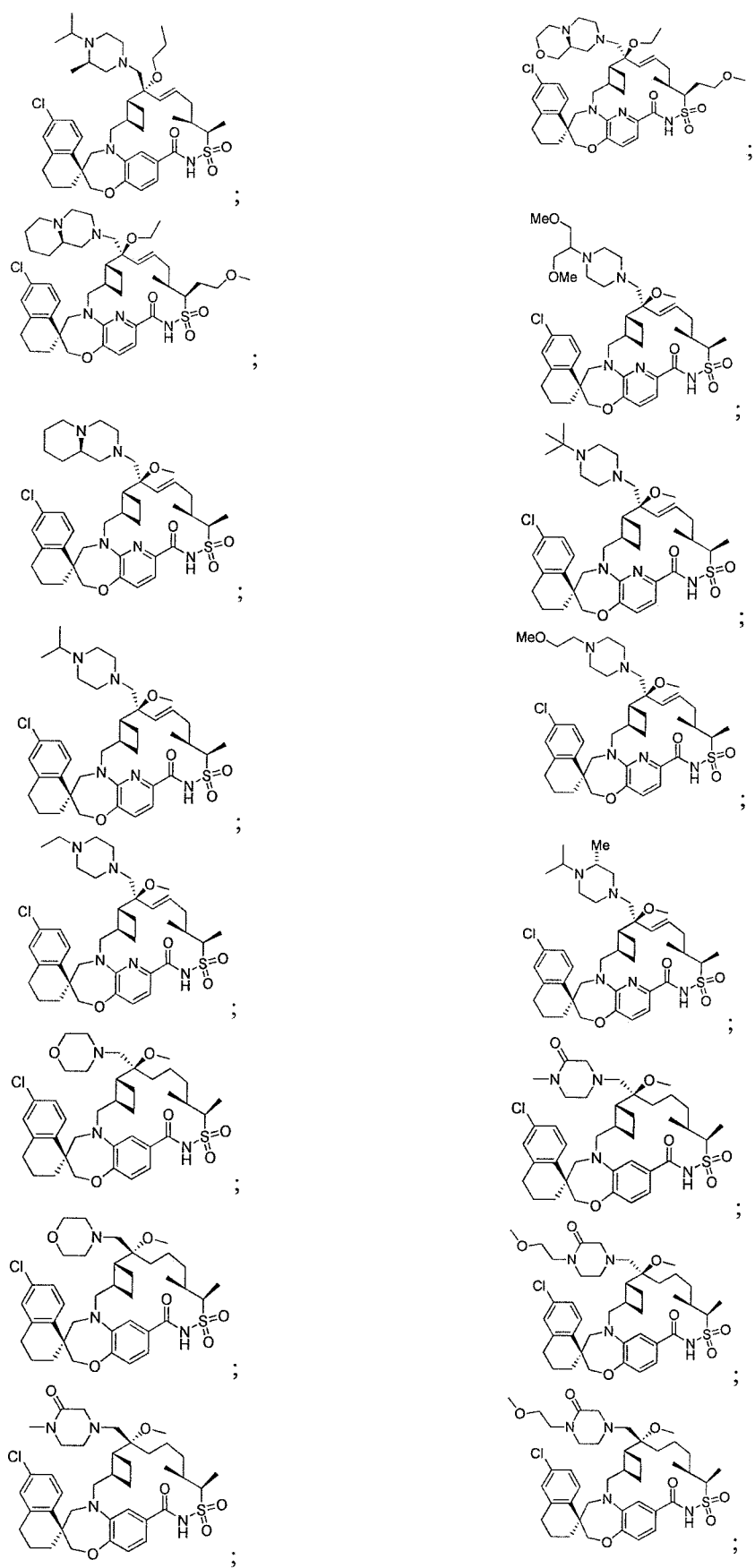


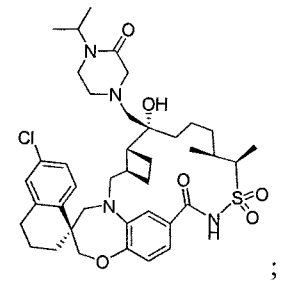
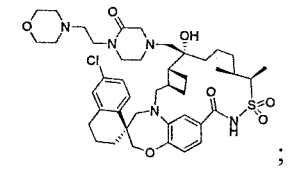
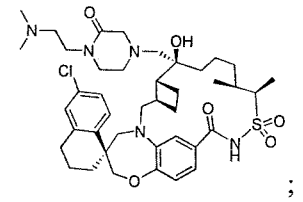
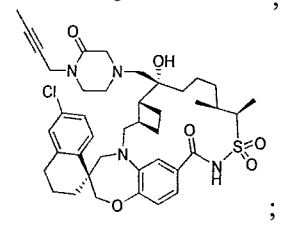
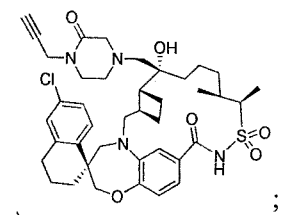
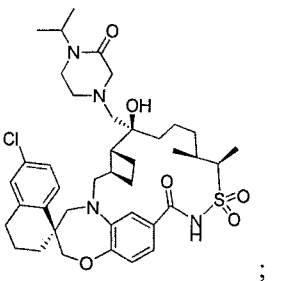
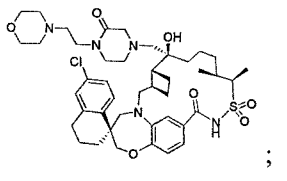
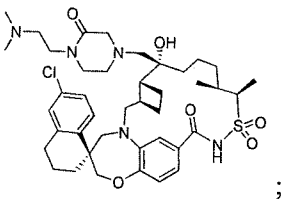
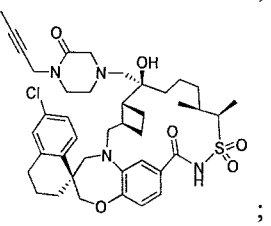
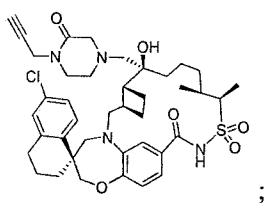
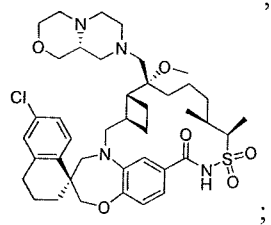
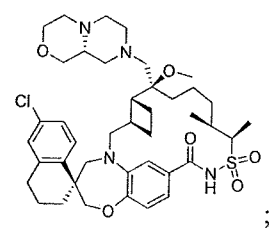


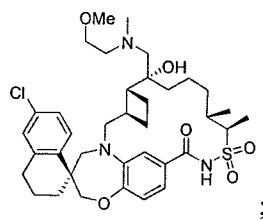
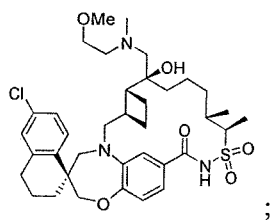
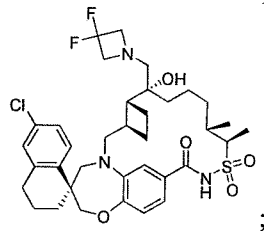
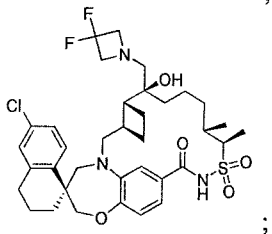
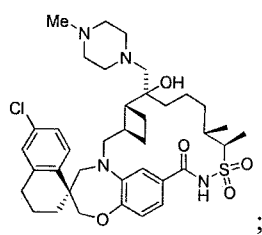
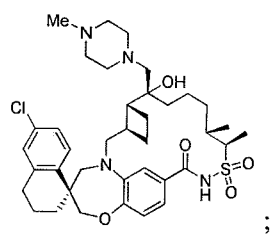
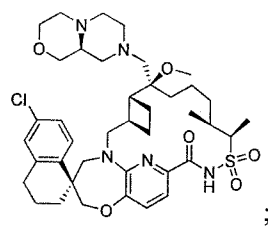
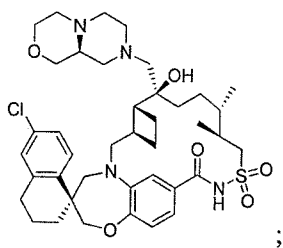
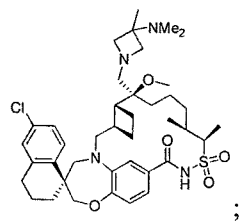
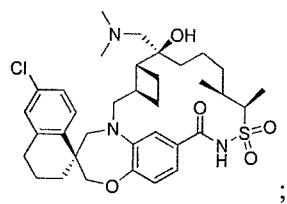
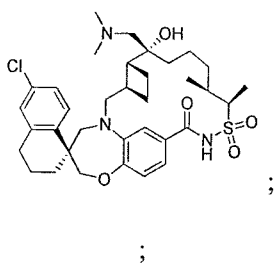


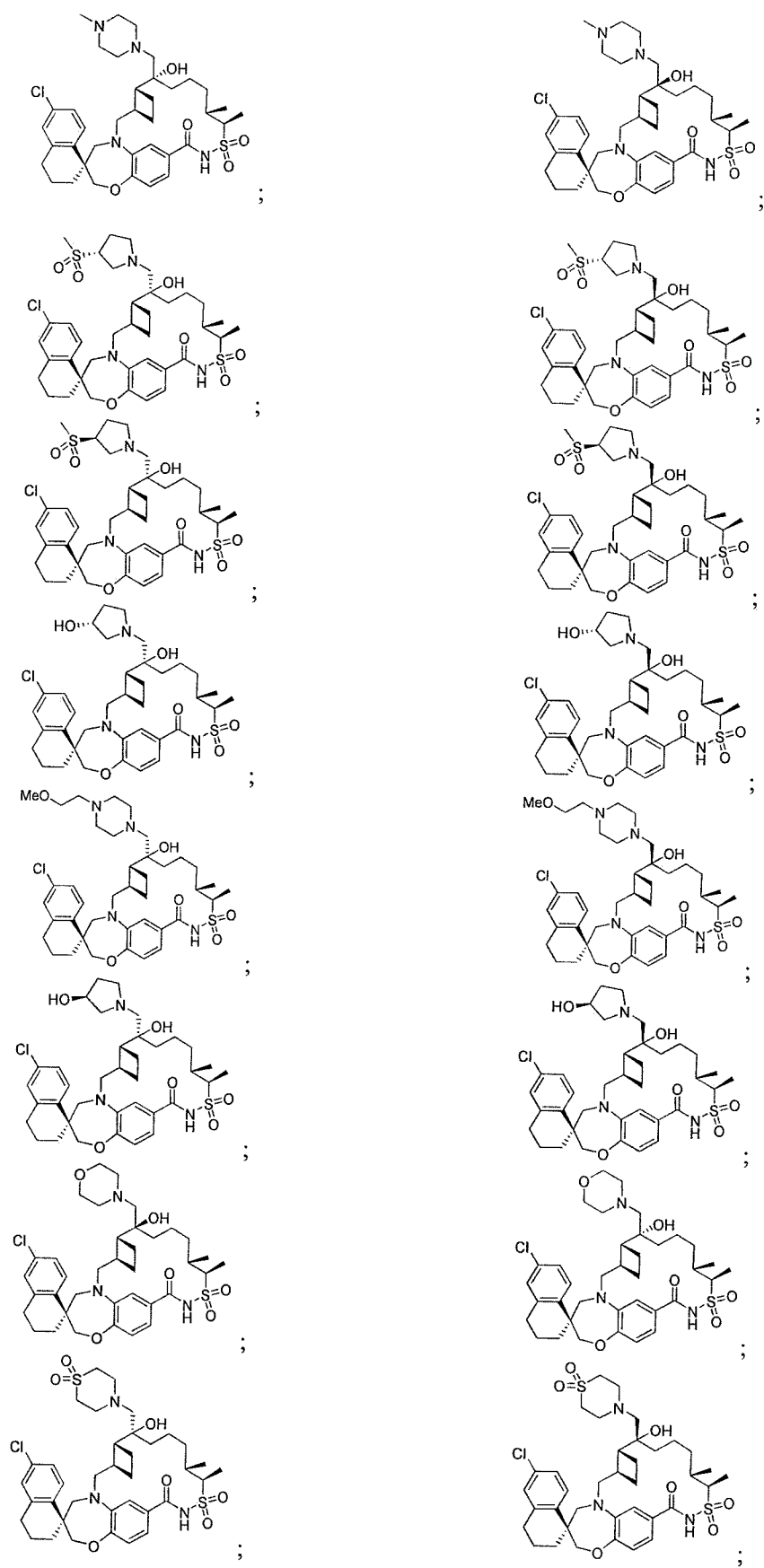


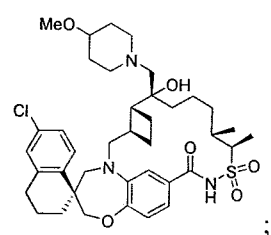
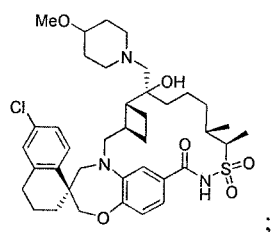
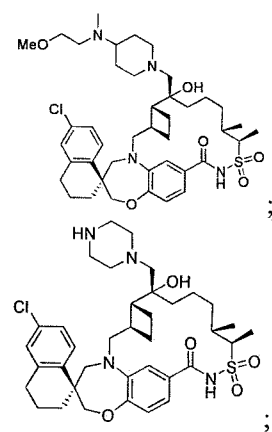
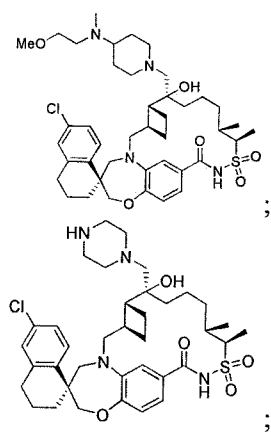
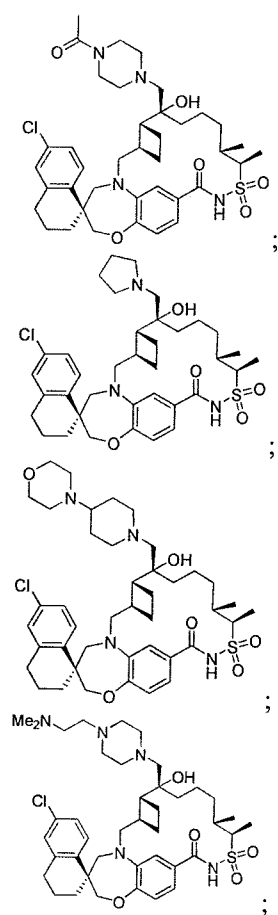
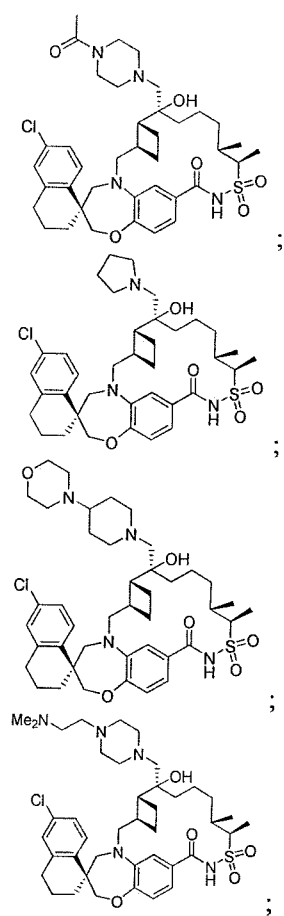


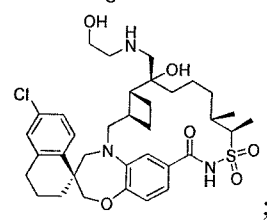
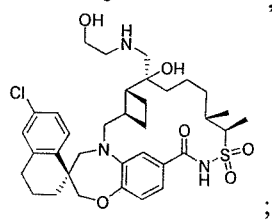
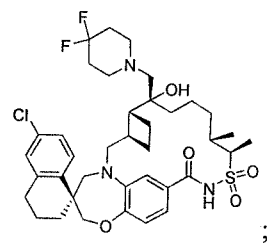
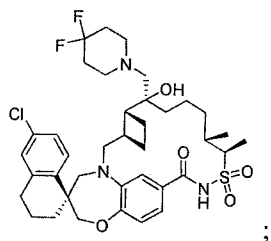
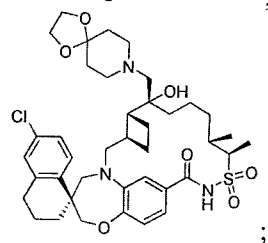
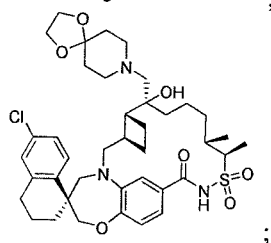
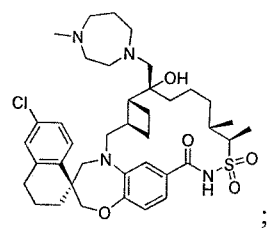
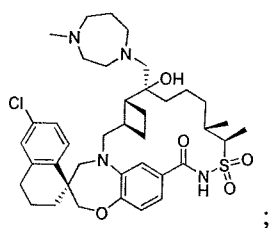
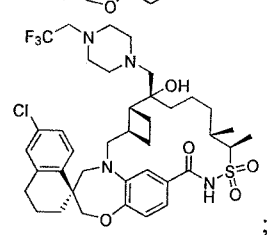
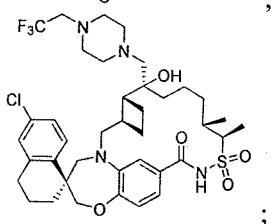
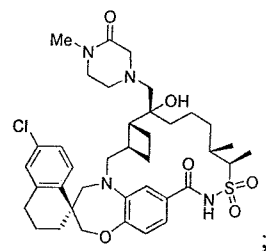
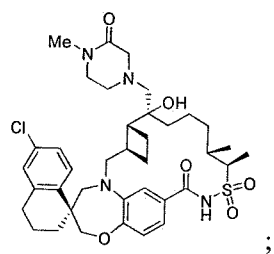
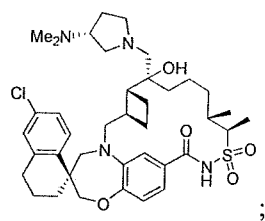
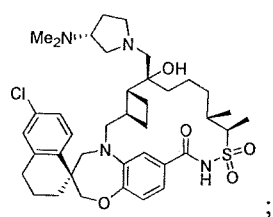


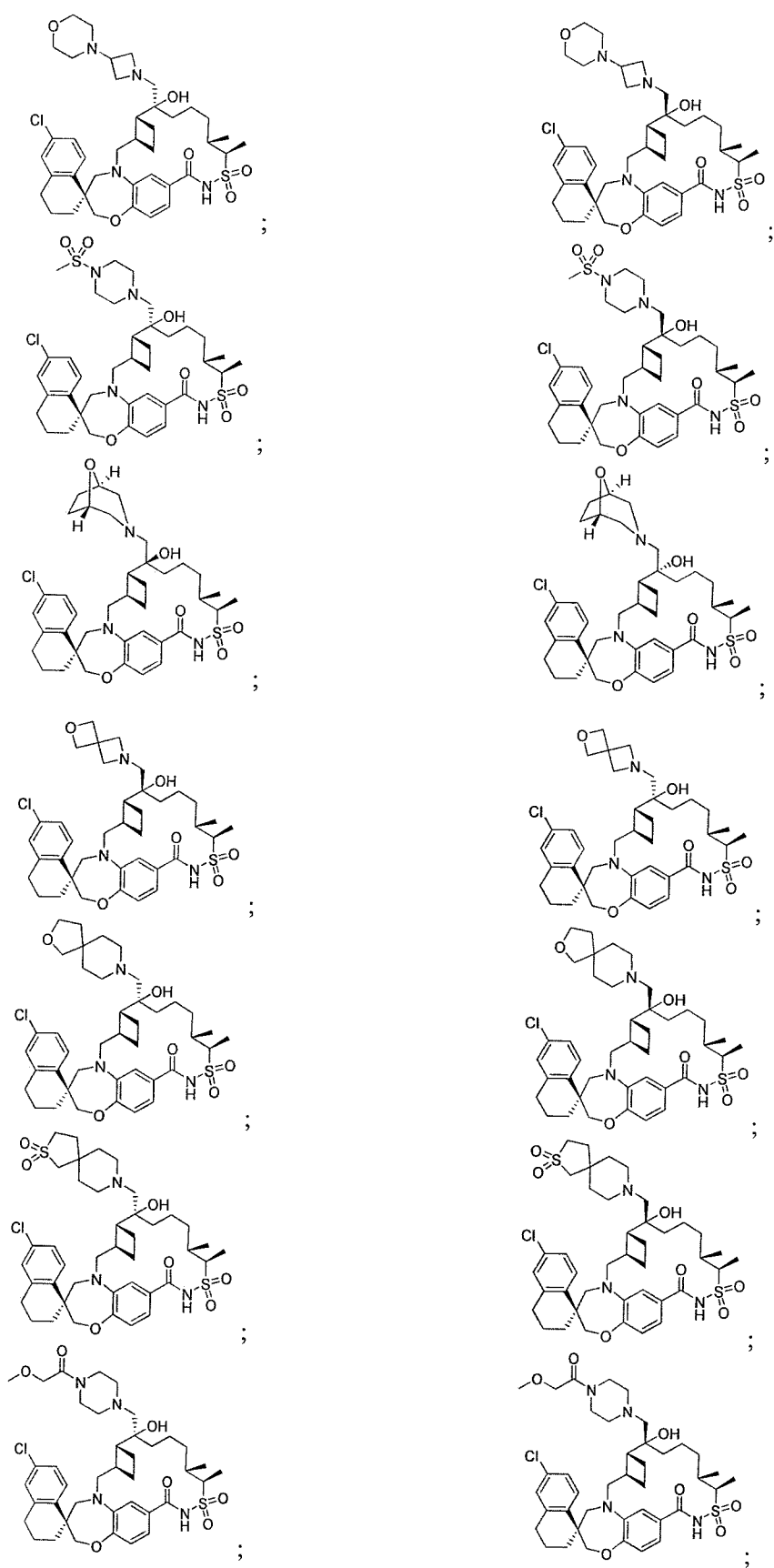


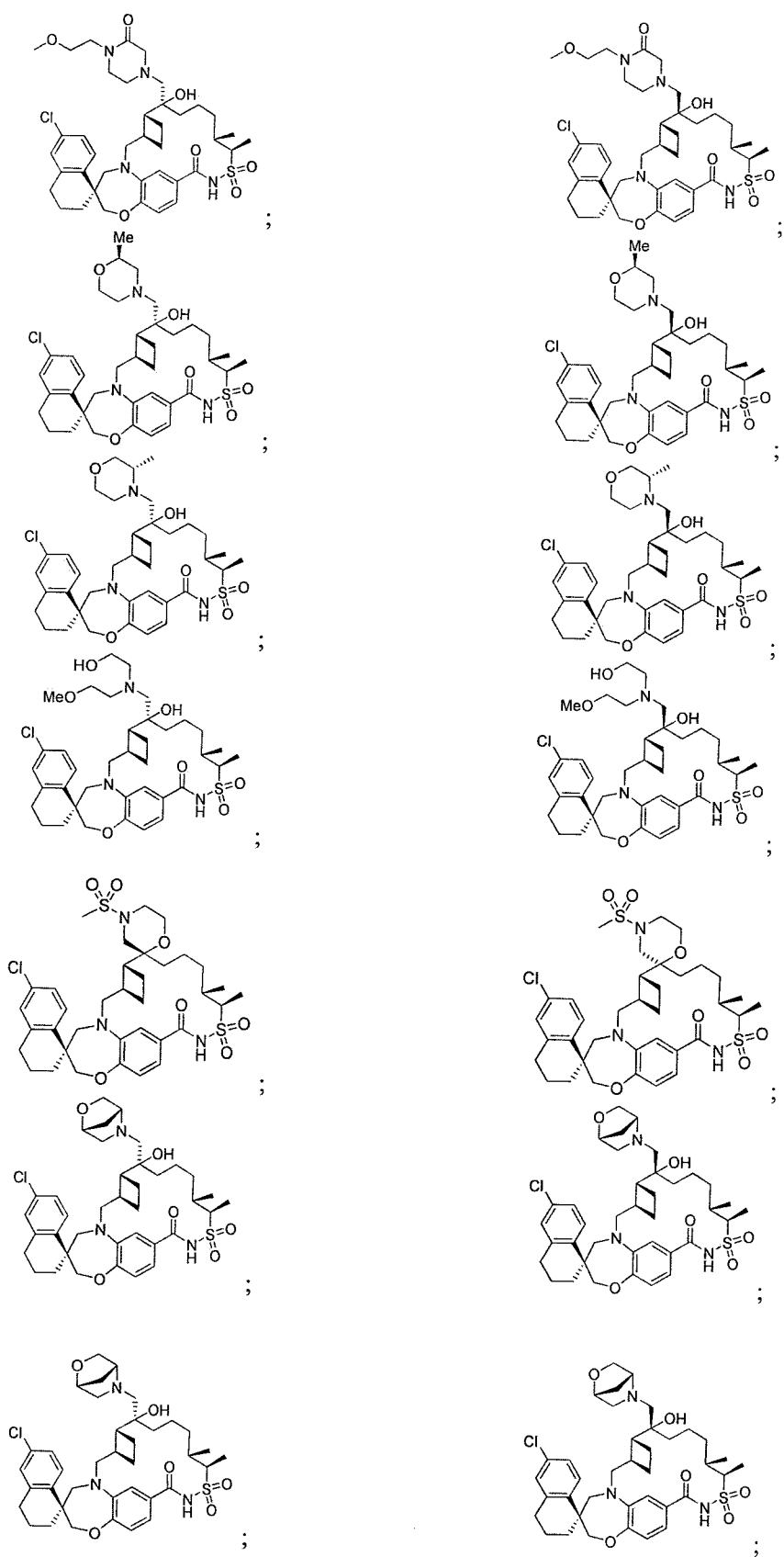


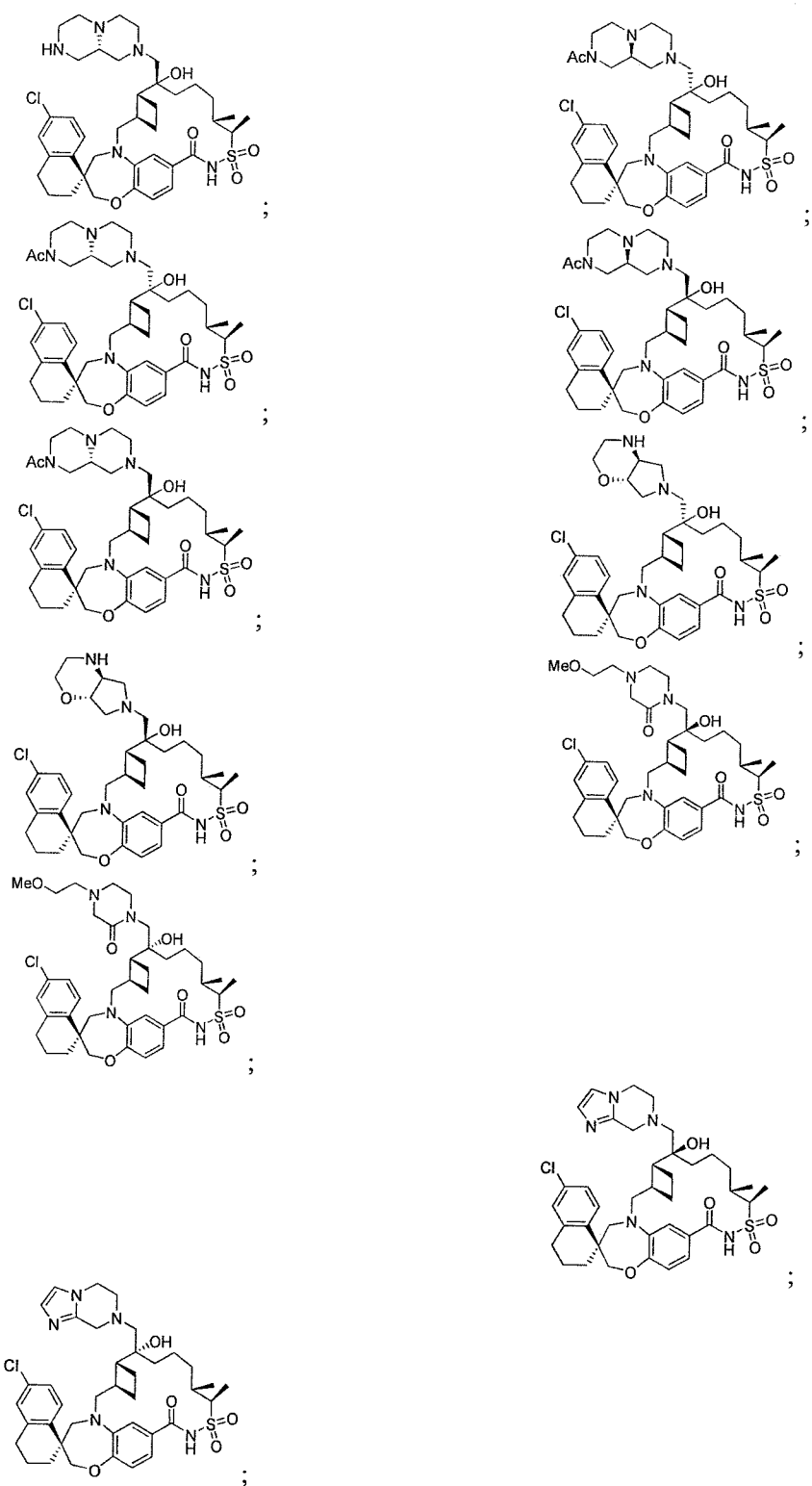


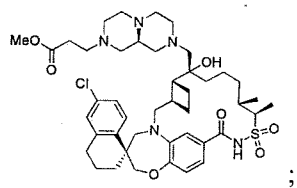
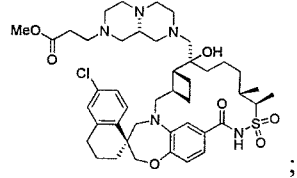
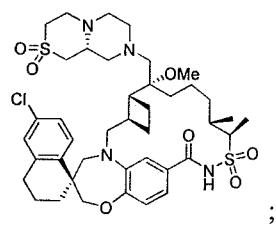
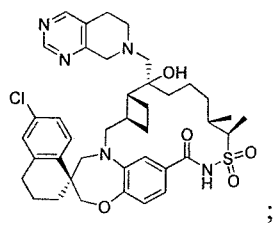
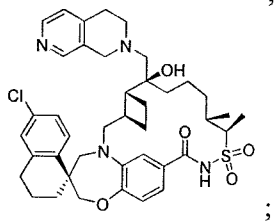
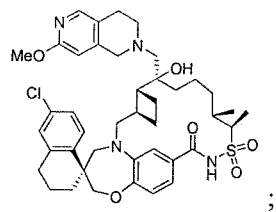
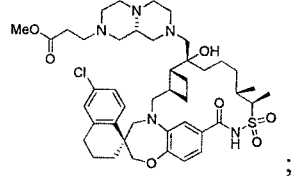
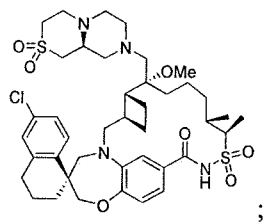
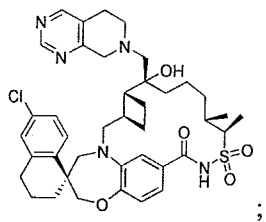
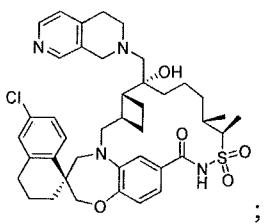
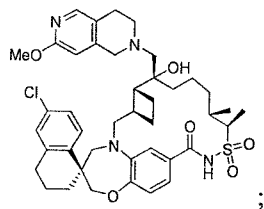


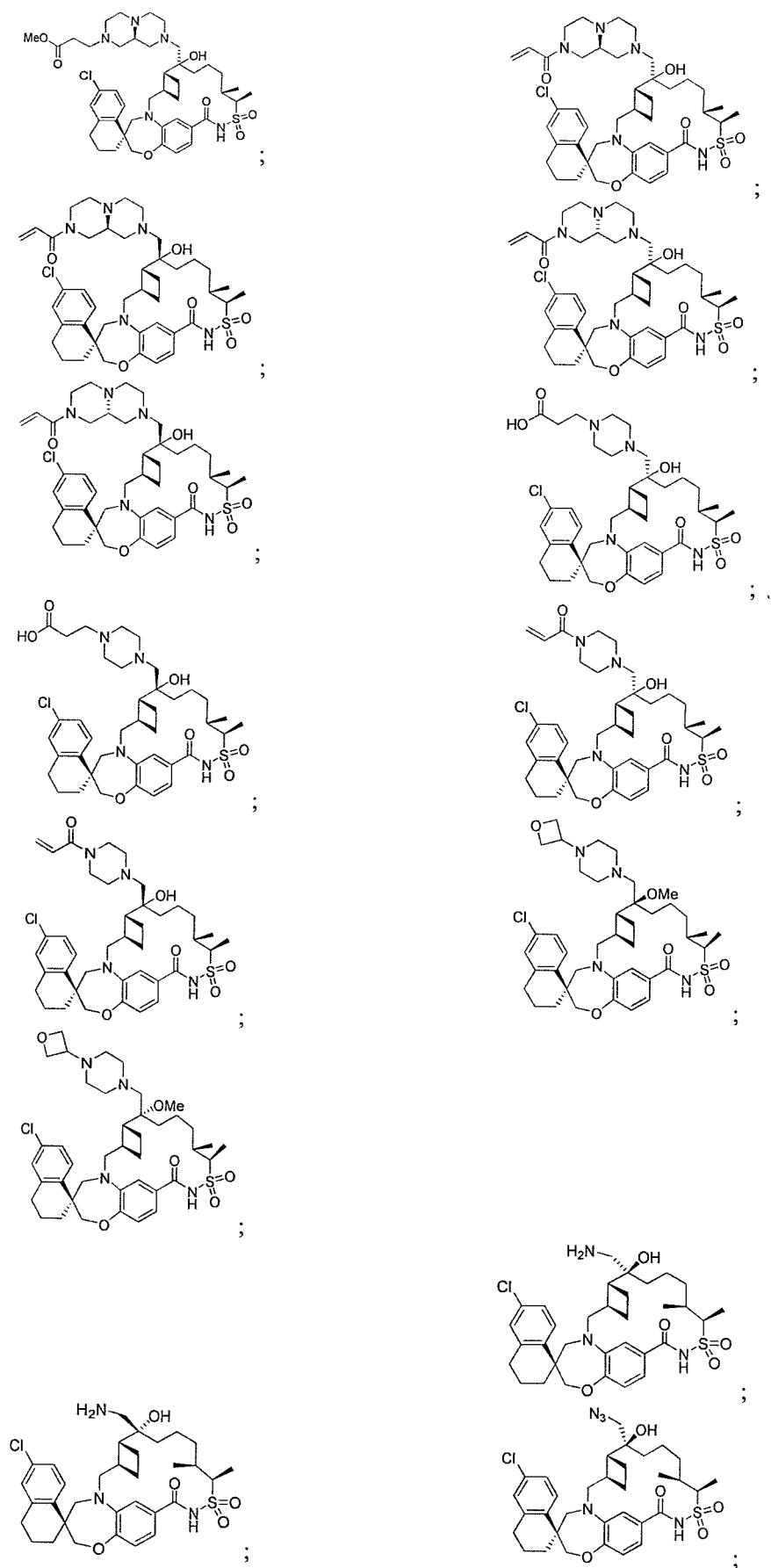


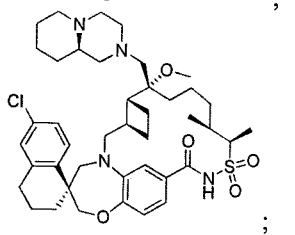
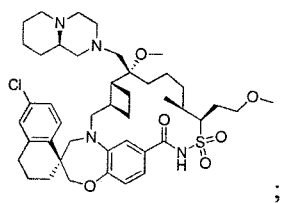
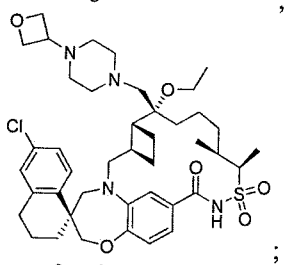
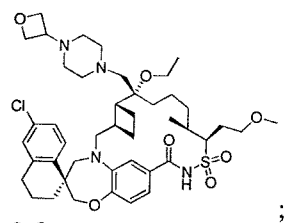
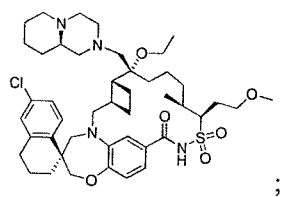
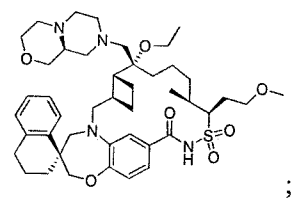
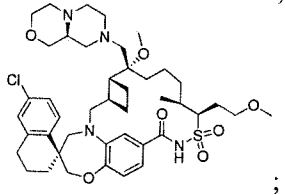
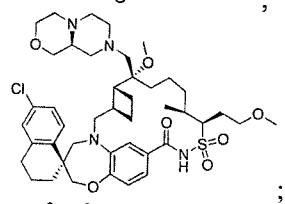
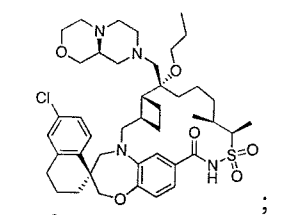
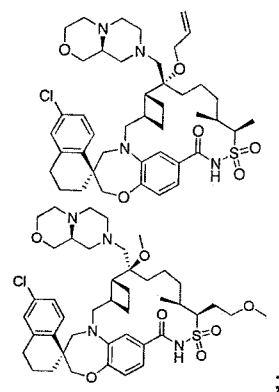
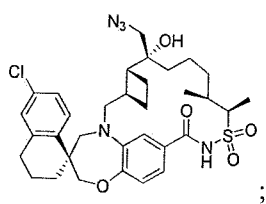


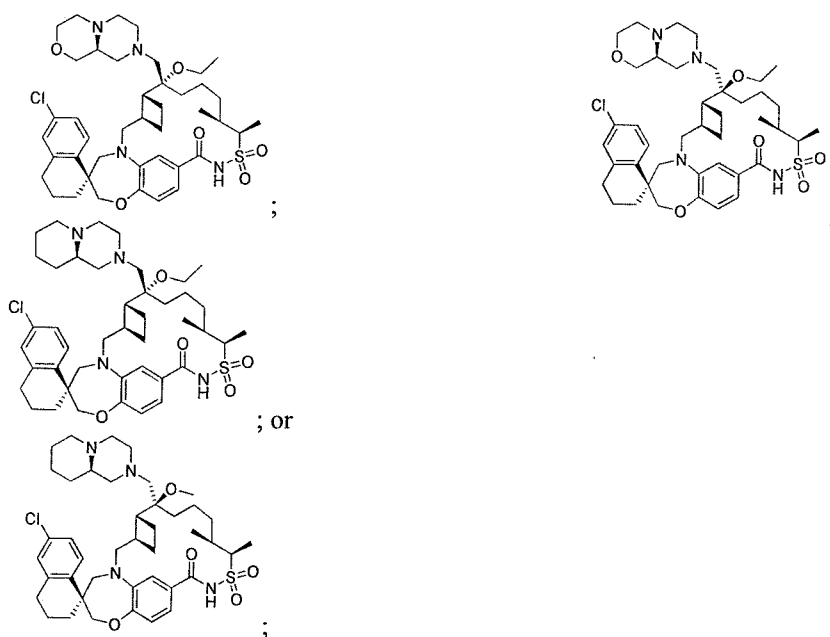








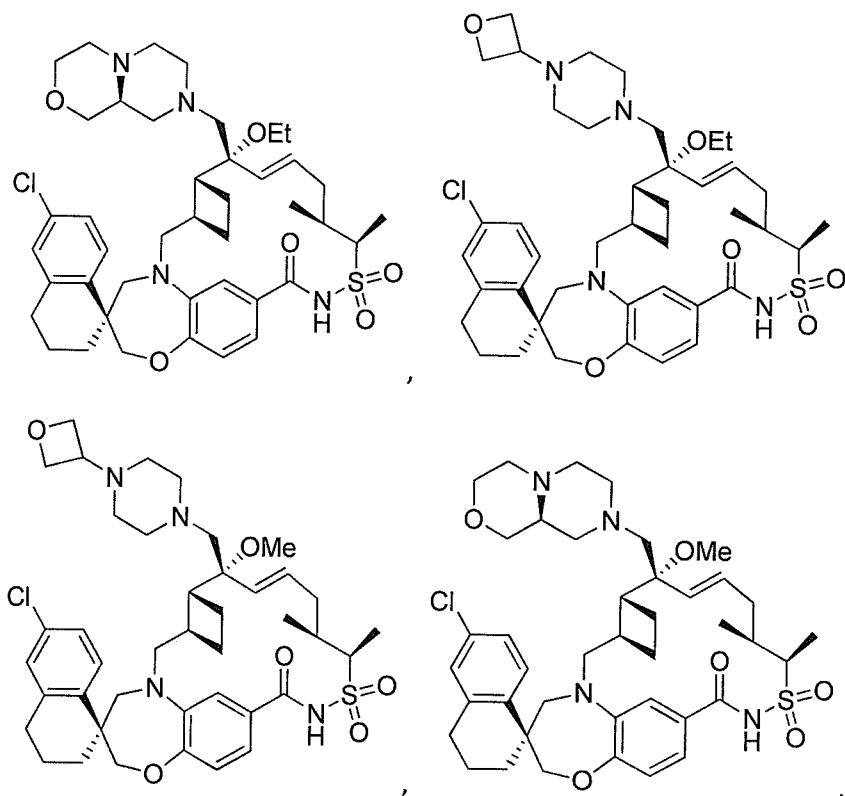


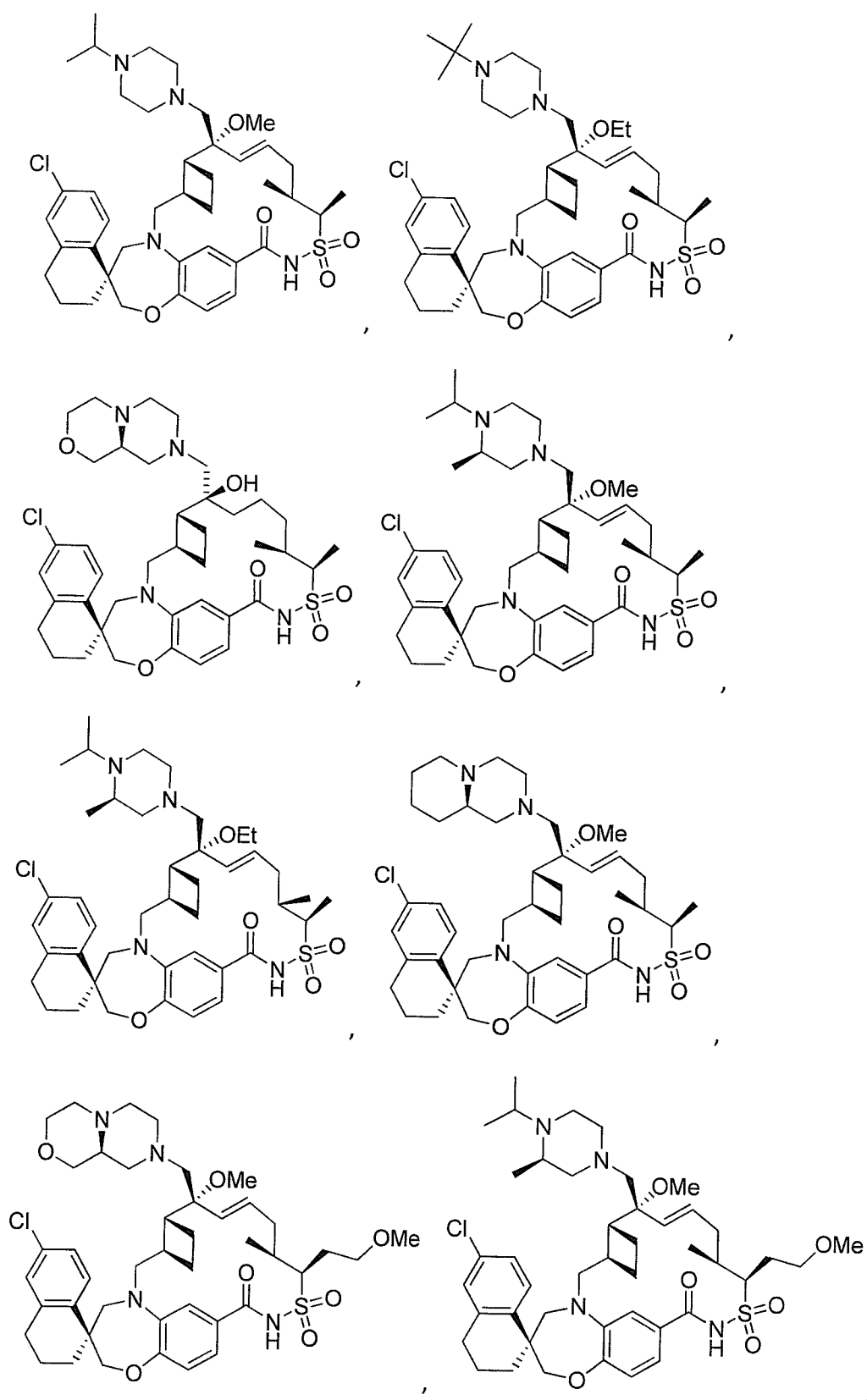


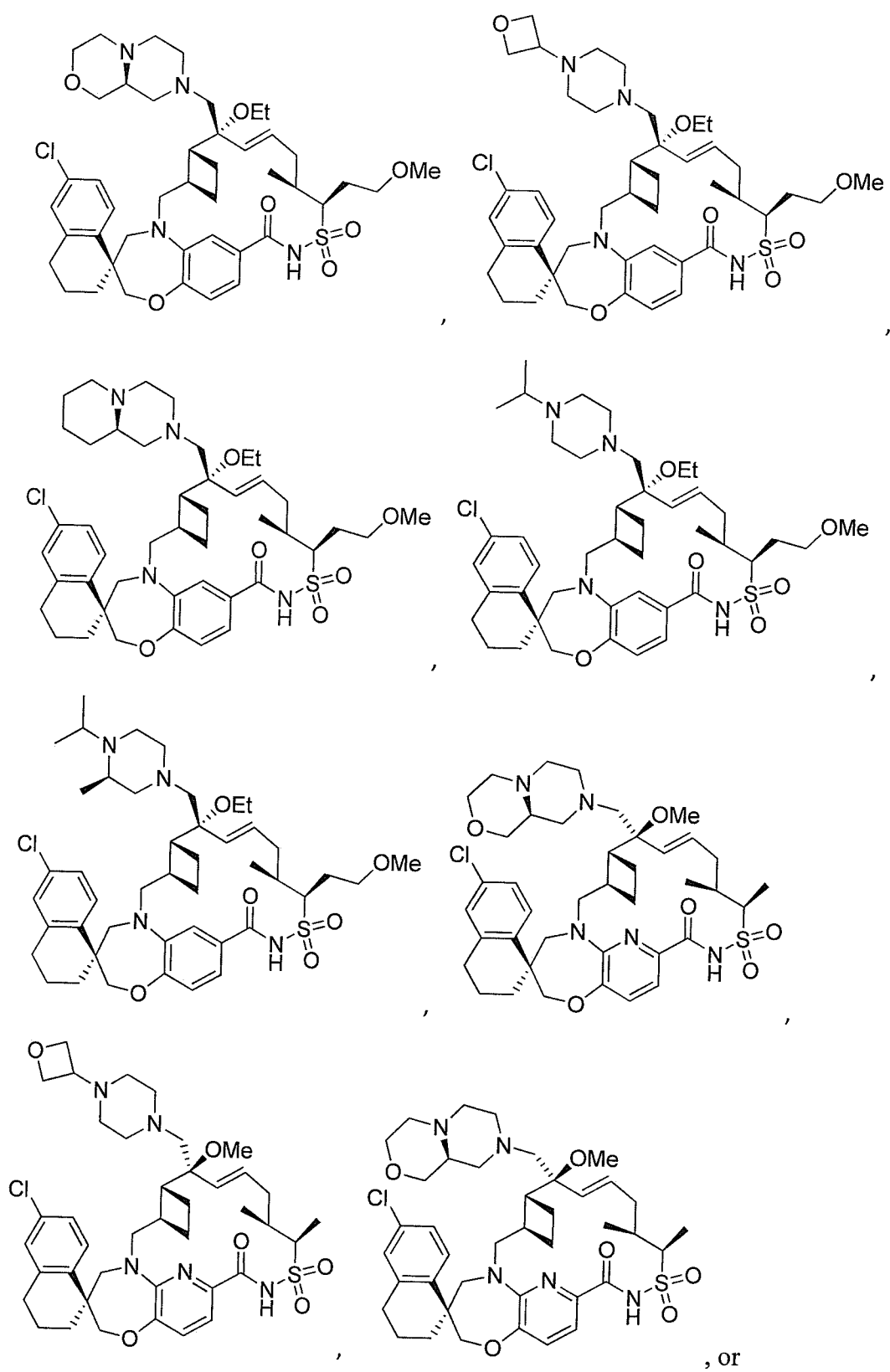
or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof.

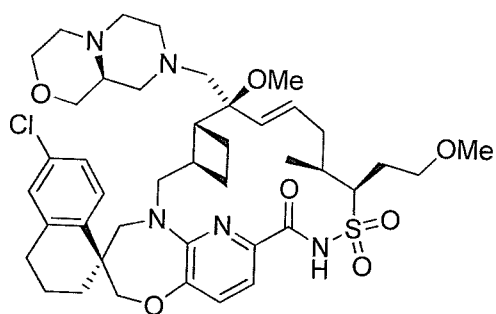
27. The compound of Claim 26 or the pharmaceutically acceptable salt thereof.

28. The compound of Claim 1, wherein the compound is selected from:







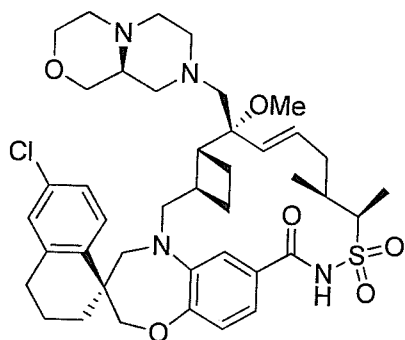


;

or the stereoisomer thereof, the pharmaceutically acceptable salt thereof, or the pharmaceutically acceptable salt of the stereoisomer thereof.

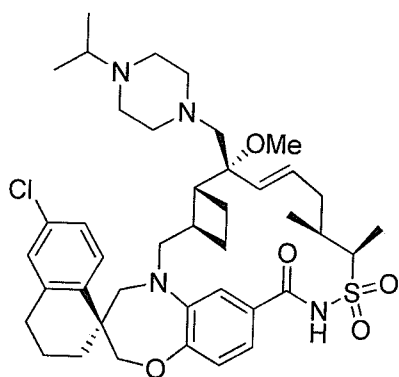
29. The compound of Claim 28 or the pharmaceutically acceptable salt thereof.

30. The compound of Claim 28, wherein the compound is



, or is the pharmaceutically acceptable salt thereof.

31. The compound of Claim 28, wherein the compound is



, or is the pharmaceutically acceptable salt thereof.

32. The compound of Claim 28, wherein the compound is

36. A pharmaceutical composition comprising the compound of any one of Claims 1-34 or the pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

37. A pharmaceutical composition comprising the compound of Claim 30 or the pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

38. A pharmaceutical composition comprising the compound of Claim 31 or the pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

39. A pharmaceutical composition comprising the compound of Claim 32 or the pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

40. A pharmaceutical composition comprising the compound of Claim 33 or the pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

41. Use of a compound according to any one of Claims 1-34 in the preparation of a medicament for treating cancer.

42. The use according to Claim 41, wherein the cancer is a hematologic malignancy.

43. The use according to Claim 41, wherein the cancer is selected from the group consisting of breast cancer, colorectal cancer, skin cancer, melanoma, ovarian cancer, kidney cancer, lung cancer, non-small cell lung cancer, lymphoma, non-Hodgkin's lymphoma, myeloma, multiple myeloma, leukemia, and acute myelogenous leukemia.

44. The use according to Claim 41, wherein the cancer is multiple myeloma, acute myelogenous leukemia, or non-Hodgkin's lymphoma.