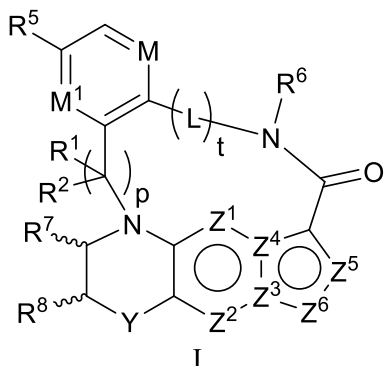


- [018] each of Z^1 , Z^2 , Z^3 , Z^4 , Z^5 , and Z^6 is independently N, NH, C or CH;
 [019] p is 1, 2, 3, or 4; and
 [020] t is 1, 2, 3, 4, or 5;
 [021] or a pharmaceutically acceptable salt thereof.
 [022] In another example, the disclosure relates to a compound of the formula I



- [023] wherein
 [024] L is independently -C(R¹)(R²)- or X;
 [025] X is O, S, S(O) or S(O)₂;
 [026] each R¹ and R² is independently H, deuterium, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl, -OR^a, -OC(O)R^a, -OC(O)R^a, -OC(O)NR^aR^b, -OS(O)R^a, -OS(O)₂R^a, -SR^a, -S(O)R^a, -S(O)₂R^a, -S(O)NR^aR^b, -S(O)₂NR^aR^b, -OS(O)NR^aR^b, -OS(O)₂NR^aR^b, -NR^aR^b, -NR^aC(O)R^b, -NR^aC(O)OR^b, -NR^aC(O)NR^aR^b, -NR^aS(O)R^b, -NR^aS(O)₂R^b, -NR^aS(O)NR^aR^b, -NR^aS(O)₂NR^aR^b, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^b, -PR^aR^b, -P(O)R^aR^b, -P(O)₂R^aR^b, -P(O)NR^aR^b, -P(O)₂NR^aR^b, -P(O)OR^a, -P(O)₂OR^a, -CN, or -NO₂, or R¹ and R² taken together with the carbon or carbons to which they are attached form a C₃-C₆ cycloalkyl or a 4- to 6-membered heterocycloalkyl, wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, mono- or bicyclic heteroaryl, 4- to 6-membered heterocycloalkyl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f, -OC(=N)NR^eR^f, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^eR^f, -OS(O)₂NR^eR^f, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^eR^f, -S(O)₂NR^eR^f, -NR^eR^f, -NR^eC(O)R^f, -NR^eC(O)OR^f, -NR^eC(O)NR^eR^f, -NR^eS(O)R^f, -NR^eS(O)₂R^f, -NR^eS(O)NR^eR^f, -NR^eS(O)₂NR^eR^f, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^f, -PR^eR^f, -P(O)R^eR^f, -P(O)₂R^eR^f, -P(O)NR^eR^f, -P(O)₂NR^eR^f, -P(O)OR^e, -P(O)₂OR^e, -CN, or -NO₂;
 [027] M is CR³ or N;
 [028] M¹ is CR⁴;

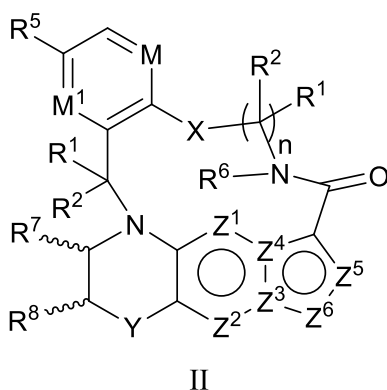
[0333] R⁹ and R¹⁰ are each independently H, deuterium, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl, wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is optionally substituted by a halogen, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f, -OC(=N)NR^eR^f, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^eR^f, -OS(O)₂NR^eR^f, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^eR^f, -S(O)₂NR^eR^f, -NR^eR^f, -NR^eC(O)R^f, -NR^eC(O)OR^f, -NR^eC(O)NR^eR^f, -NR^eS(O)R^f, -NR^eS(O)₂R^f, -NR^eS(O)NR^eR^f, -NR^eS(O)₂NR^eR^f, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^f, -PR^eR^f, -P(O)R^eR^f, -P(O)₂R^eR^f, -P(O)NR^eR^f, -P(O)₂NR^eR^f, -P(O)OR^e, or -P(O)₂OR^e;

[035] each of Z^1, Z^2, Z^3, Z^4, Z^5 , and Z^6 is independently N, NH, C or CH;

[037] t is 1, 2, 3, 4, or 5;

[038] or a pharmaceutically acceptable salt thereof.

[039] In another example, the disclosure relates to a compound or a pharmaceutically acceptable salt thereof, having the formula II



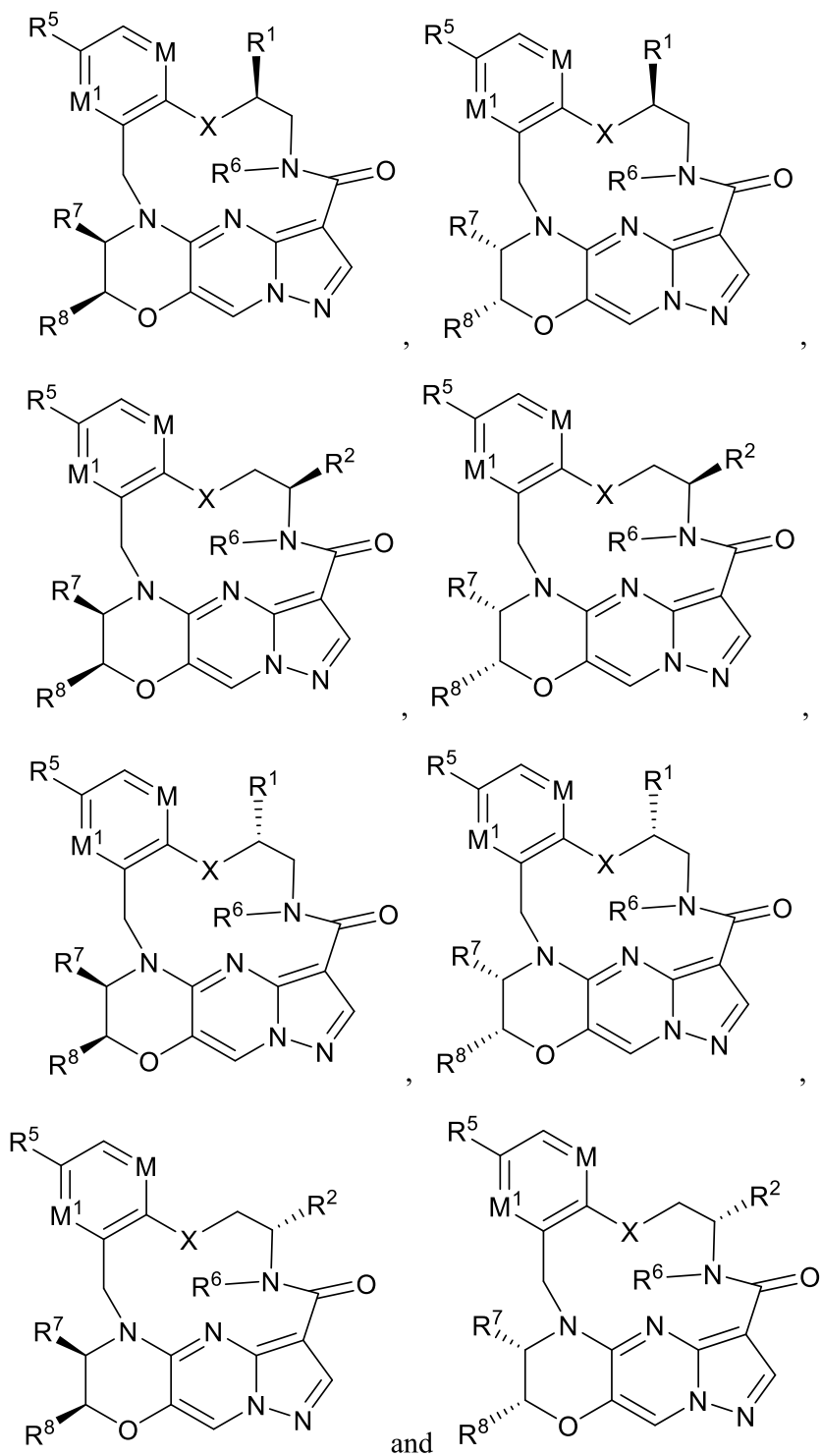
[041] M is CR^3 or N;

[043] X is O, S, S(O), or S(O)₂;

[0444] each R¹ and R² is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -OR^a, -SR^a, -NR^aR^b, -C(O)OR^a, -C(O)NR^aR^b; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl,

[051] n is 2 or 3.

[052] In another example, the disclosure relates to a compound selected from the group consisting of



[053] wherein

[054] M is CR³ or N;

[055] M¹ is CR⁴;

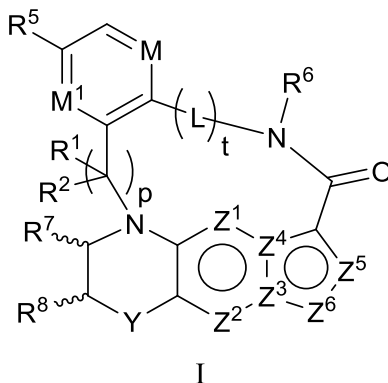
alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)₂NH₂, -C(O)C₁-C₆ alkyl, -C(O)OC₁-C₆ alkyl, -C(O)N(C₁-C₆ alkyl)₂, -C(O)NH(C₁-C₆ alkyl), -C(O)NH₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, -P(O)₂(C₁-C₆ alkyl)₂, -P(O)N(C₁-C₆ alkyl)₂, -P(O)₂N(C₁-C₆ alkyl)₂, -P(O)OC₁-C₆ alkyl, or -P(O)₂OC₁-C₆ alkyl.

[0062a] In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above, or a pharmaceutically acceptable salt thereof, and optionally at least one diluent, carrier or excipient.

[0062b] In another aspect, there is provided the use of a compound as defined above or a pharmaceutical composition as defined above, in the manufacture of a medicament for the treatment of cancer.

[0063] Additional embodiments, features, and advantages of the disclosure will be apparent from the following detailed description and through practice of the disclosure. The compounds of the present disclosure can be described as embodiments in any of the following enumerated clauses. It will be understood that any of the embodiments described herein can be used in connection with any other embodiments described herein to the extent that the embodiments do not contradict one another.

[0064] 1. A compound of the formula I



[0065] wherein

[0066] L is independently -C(R¹)(R²)- or X;

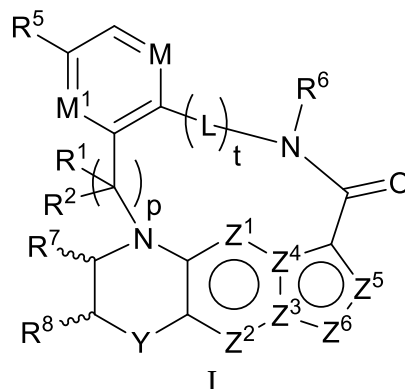
[0067] X is -O-, -S-, -S(O)- or -S(O)₂-;

[0068] each R¹ and R² is independently H, deuterium, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl, -OR^a, -OC(O)R^a, -OC(O)R^a, -OC(O)NR^aR^b, -OS(O)R^a, -OS(O)₂R^a, -SR^a, -S(O)R^a, -S(O)₂R^a, -S(O)NR^aR^b, -S(O)₂NR^aR^b, -OS(O)NR^aR^b, -OS(O)₂NR^aR^b, -NR^aR^b, -NR^aC(O)R^b, -NR^aC(O)OR^b, -NR^aC(O)NR^aR^b, -NR^aS(O)R^b, -NR^aS(O)₂R^b, -NR^aS(O)NR^aR^b, -NR^aS(O)₂NR^aR^b, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^b, -PR^aR^b, -P(O)R^aR^b, -P(O)₂R^aR^b,

-P(O)NR^aR^b, -P(O)₂NR^aR^b, -P(O)OR^a, -P(O)₂OR^a, -CN, or -NO₂, or R¹ and R² taken together with the carbon or carbons to which they are attached form a C₃-C₆ cycloalkyl or a 4- to 6-membered heterocycloalkyl, wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, mono- or bicyclic heteroaryl, 4- to 6-membered heterocycloalkyl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f,

WHAT IS CLAIMED IS:

1. A compound of the formula I



wherein

each L is independently -C(R¹)(R²)- or X; with the proviso that, when t is 1, then L is -C(R¹)(R²)-;

X is O, S, S(O) or S(O)₂;

each R¹ and R² is independently H, deuterium, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl, -OR^a, -OC(O)R^a, -OC(O)R^a, -OC(O)NR^aR^b, -OS(O)R^a, -OS(O)₂R^a, -SR^a, -S(O)R^a, -S(O)₂R^a, -S(O)NR^aR^b, -S(O)₂NR^aR^b, -OS(O)NR^aR^b, -OS(O)₂NR^aR^b, -NR^aR^b, -NR^aC(O)R^b, -NR^aC(O)OR^b, -NR^aC(O)NR^aR^b, -NR^aS(O)R^b, -NR^aS(O)₂R^b, -NR^aS(O)NR^aR^b, -NR^aS(O)₂NR^aR^b, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^b, -PR^aR^b, -P(O)R^aR^b, -P(O)₂R^aR^b, -P(O)NR^aR^b, -P(O)₂NR^aR^b, -P(O)OR^a, -P(O)₂OR^a, -CN, or -NO₂, or R¹ and R² taken together with the carbon or carbons to which they are attached form a C₃-C₆ cycloalkyl or a 4- to 6-membered heterocycloalkyl, wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, mono- or bicyclic heteroaryl, 4- to 6-membered heterocycloalkyl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f, -OC(=N)NR^eR^f, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^eR^f, -OS(O)₂NR^eR^f, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^eR^f, -S(O)₂NR^eR^f, -NR^eR^f, -NR^eC(O)R^f, -NR^eC(O)OR^f, -NR^eC(O)NR^eR^f, -NR^eS(O)R^f, -NR^eS(O)₂R^f, -NR^eS(O)NR^eR^f, -NR^eS(O)₂NR^eR^f, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^f, -PR^eR^f, -P(O)R^eR^f, -P(O)₂R^eR^f, -P(O)NR^eR^f, -P(O)₂NR^eR^f, -P(O)OR^e, -P(O)₂OR^e, -CN, or -NO₂;

M is CR³ or N;

M¹ is CR⁴;

each R³, R⁴, and R⁵ is independently hydrogen, deuterium, halogen, -OR^c, -OC(O)R^c, -OC(O)NR^cR^d, -OC(=N)NR^cR^d, -OS(O)R^c, -OS(O)₂R^c, -OS(O)NR^cR^d, -OS(O)₂NR^cR^d, -SR^c, -S(O)R^c, -S(O)₂R^c, -S(O)NR^cR^d, -S(O)₂NR^cR^d, -NR^cR^d, -NR^cC(O)R^d, -NR^cC(O)OR^d, -NR^cC(O)NR^cR^d, -NR^cC(=N)NR^cR^d, -NR^cS(O)R^d, -NR^cS(O)₂R^d, -NR^cS(O)NR^cR^d, -NR^cS(O)₂NR^cR^d, -C(O)R^c, -C(O)OR^c, -C(O)NR^cR^d, -C(=N)NR^cR^d, -PR^cR^d, -P(O)R^cR^d, -P(O)₂R^cR^d, -P(O)NR^cR^d, -P(O)₂NR^cR^d, -P(O)OR^c, -P(O)₂OR^c, -CN, -NO₂, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl, or R⁴ and R⁵ taken together with the ring to which they are attached form a C₅-C₈ cycloalkyl, or a 5- to 8-membered heterocycloalkyl, wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, mono- or bicyclic heteroaryl, C₅-C₈ cycloalkyl, or 5- to 8-membered heterocycloalkyl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f, -OC(=N)NR^eR^f, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^eR^f, -OS(O)₂NR^eR^f, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^eR^f, -S(O)₂NR^eR^f, -NR^eR^f, -NR^eC(O)R^f, -NR^eC(O)OR^f, -NR^eC(O)NR^eR^f, -NR^eS(O)R^f, -NR^eS(O)₂R^f, -NR^eS(O)NR^eR^f, -NR^eS(O)₂NR^eR^f, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^f, -PR^eR^f, -P(O)R^eR^f, -P(O)₂R^eR^f, -P(O)NR^eR^f, -P(O)₂NR^eR^f, -P(O)OR^e, -P(O)₂OR^e, -CN, or -NO₂;

R⁶ is H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl, wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₃-C₆ cycloalkyl, or 5- to 7-membered heterocycloalkyl, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f, -OC(=N)NR^eR^f, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^eR^f, -OS(O)₂NR^eR^f, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^eR^f, -S(O)₂NR^eR^f, -NR^eR^f, -NR^eC(O)R^f, -NR^eC(O)OR^f, -NR^eC(O)NR^eR^f, -NR^eS(O)R^f, -NR^eS(O)₂R^f, -NR^eS(O)NR^eR^f, -NR^eS(O)₂NR^eR^f, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^f, -PR^eR^f, -P(O)R^eR^f, -P(O)₂R^eR^f, -P(O)NR^eR^f, -P(O)₂NR^eR^f, -P(O)OR^e, -P(O)₂OR^e, -CN, or -NO₂;

R⁷ and R⁸ combine to form a C₃-C₇ cycloalkyl, a 5- to 8-membered heterocycloalkyl, C₆-C₁₀ aryl, or 5- to 7-membered heteroaryl; wherein each hydrogen atom in C₃-C₇ cycloalkyl, a 5- to 8-membered heterocycloalkyl, C₆-C₁₀ aryl, or 5- to 7-membered heteroaryl is independently optionally substituted by deuterium, halogen, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f, -OC(=N)NR^eR^f, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^eR^f, -OS(O)₂NR^eR^f, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^eR^f, -S(O)₂NR^eR^f, -NR^eR^f, -NR^eC(O)R^f, -NR^eC(O)OR^f, -NR^eC(O)NR^eR^f, -NR^eS(O)R^f, -NR^eS(O)₂R^f, -NR^eS(O)NR^eR^f, -NR^eS(O)₂NR^eR^f, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^f, -PR^eR^f, -P(O)R^eR^f, -P(O)₂R^eR^f, -P(O)NR^eR^f, -P(O)₂NR^eR^f, -P(O)OR^e, -P(O)₂OR^e, -CN, or -NO₂;

Y is O, S, NR⁹, or CR⁹R¹⁰;

R⁹ and R¹⁰ are each independently H, deuterium, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl, wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is optionally substituted by a halogen, -OR^e, -OC(O)R^e, -OC(O)NR^eR^f, -OC(=N)NR^eR^f, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^eR^f, -OS(O)₂NR^eR^f, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^eR^f, -S(O)₂NR^eR^f, -NR^eR^f, -NR^eC(O)R^f, -NR^eC(O)OR^f, -NR^eC(O)NR^eR^f, -NR^eS(O)R^f, -NR^eS(O)₂R^f, -NR^eS(O)NR^eR^f, -NR^eS(O)₂NR^eR^f, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^f, -PR^eR^f, -P(O)R^eR^f, -P(O)₂R^eR^f, -P(O)NR^eR^f, -P(O)₂NR^eR^f, -P(O)OR^e, or -P(O)₂OR^e; each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from the group consisting of H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, 5- to 7- membered heteroaryl;

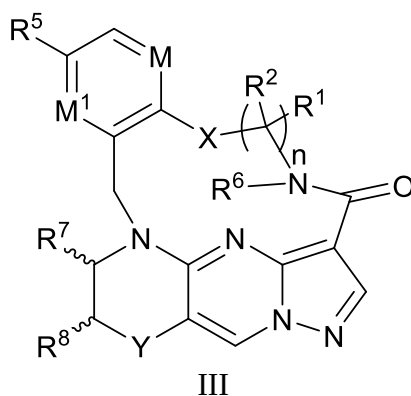
each of Z¹, Z², Z³, Z⁴, Z⁵, and Z⁶ is independently N, NH, C or CH;

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

t is 1, 2, 3, 4, or 5;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, having formula III, IV, or V





3. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Y is O.

4. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein M is CR³.

5. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R³ is H, deuterium, C₁-C₆ alkyl or halogen; or, wherein R³ is H or F; or wherein M is N.

6. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R⁴ is H, deuterium, C₁-C₆ alkyl or halogen; or
wherein R⁴ is H or Cl; or
wherein R⁵ is F.

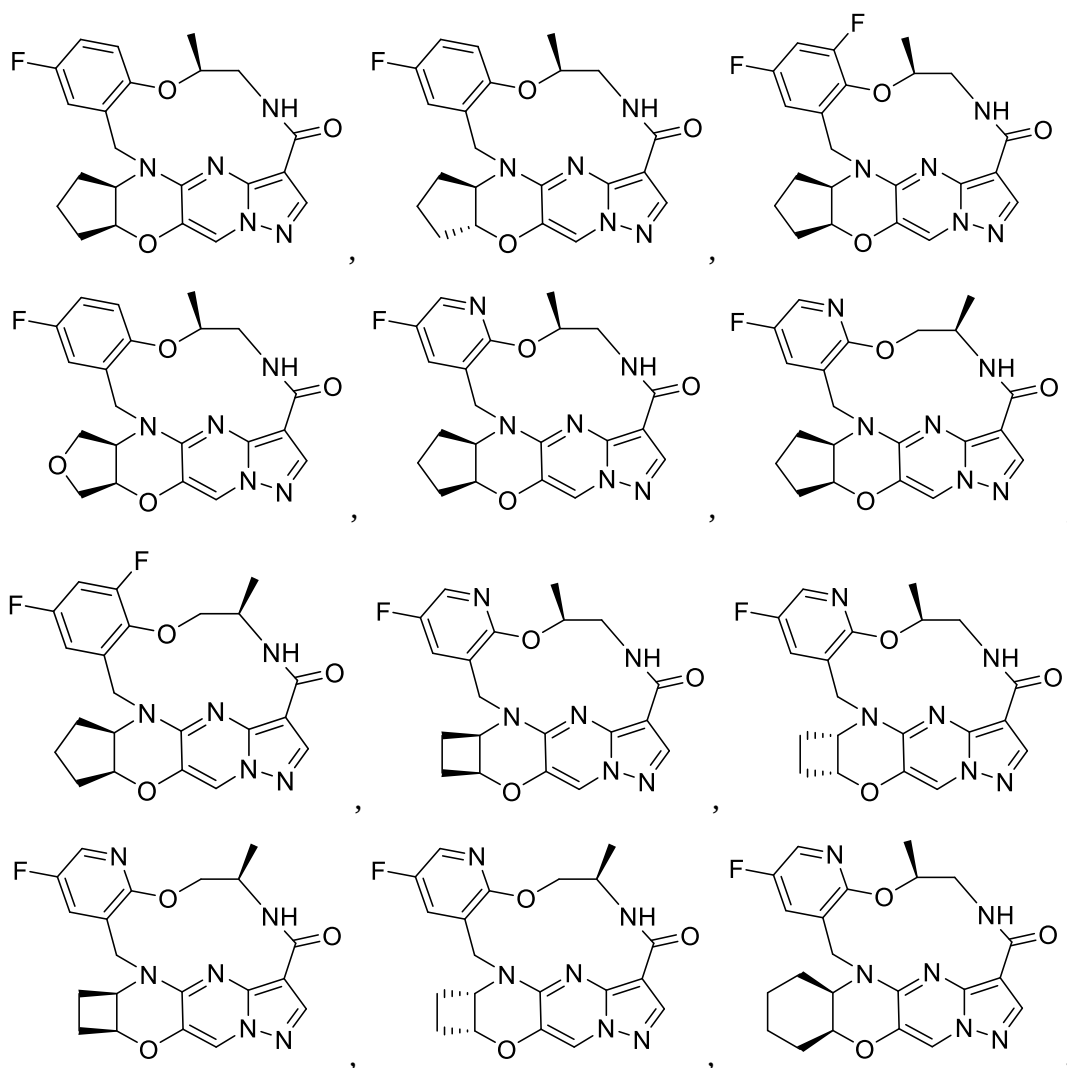
7. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R² is H; or
wherein R¹ is H; or
wherein R¹ is C₁-C₆ alkyl.

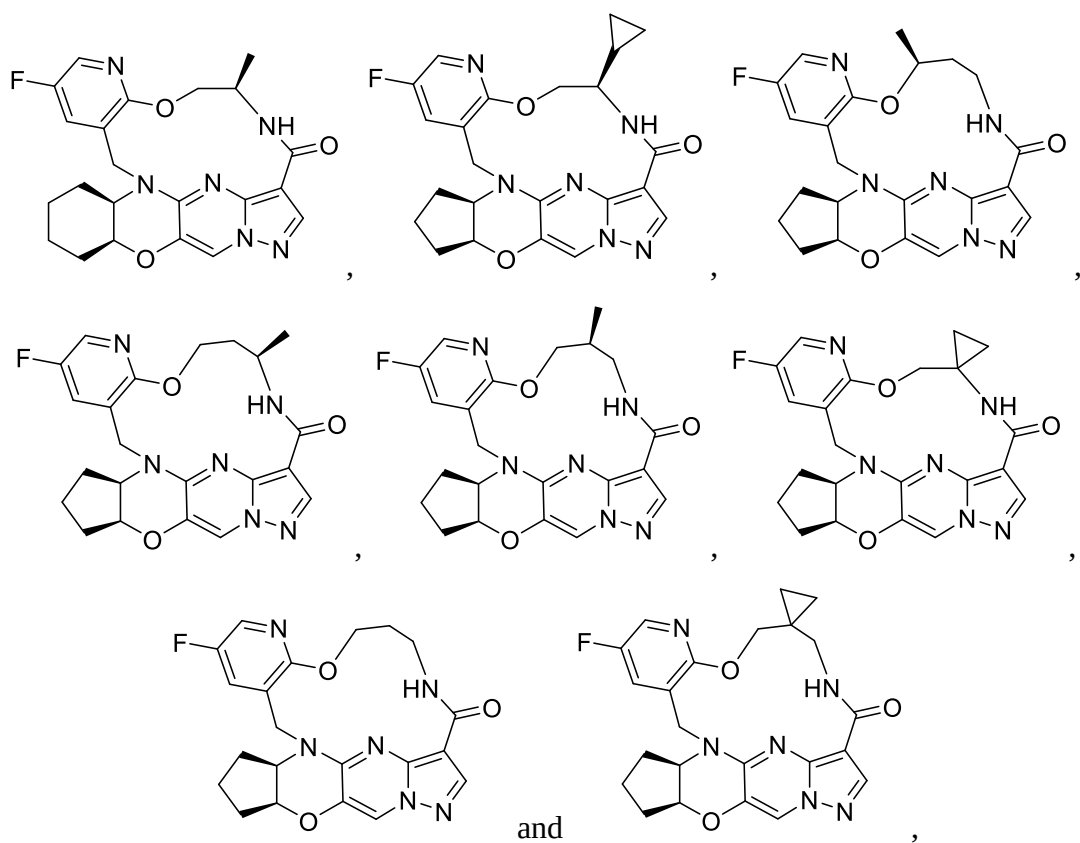
8. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^1 is H, and R^2 is C_1 - C_6 alkyl; or R^1 is C_1 - C_6 alkyl, and R^2 is H; or R^1 is H or C_1 - C_6 alkyl, and R^2 is H; or R^1 is H, and R^2 is C_3 - C_7 cycloalkyl; or R^1 is C_3 - C_7 cycloalkyl, and R^2 is H.

9. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^7 and R^8 combine to form a tetrahydrofuran ring; or wherein R^7 and R^8 combine to form a cyclobutane ring, cyclopentane ring, or cyclohexane ring.

10. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X is O.

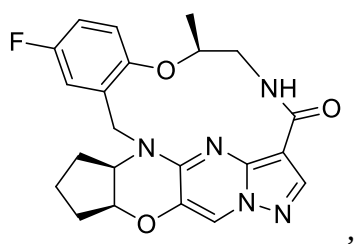
11. The compound of claim 1, selected from the group consisting of





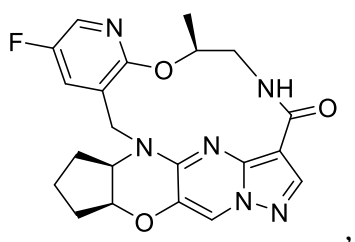
or a pharmaceutically acceptable salt thereof.

12. The compound of claim 1 having formula



or a pharmaceutically acceptable salt thereof.

13. The compound of claim 1 having formula



or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising a compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, and optionally at least one diluent, carrier or excipient.

15. Use of a compound of any one of claims 1 to 13, or a pharmaceutical composition of claim 14, in the manufacture of a medicament for the treatment of cancer.