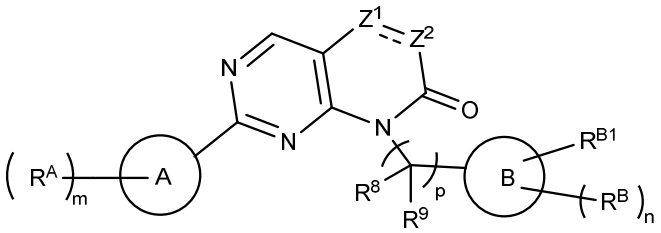
CLAIMS

WHAT IS CLAIMED IS:

1. A compound having the structure of Formula (IIIa), or a pharmaceutically acceptable salt thereof,



Formula (IIIa)

wherein,

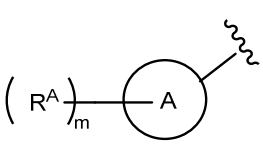
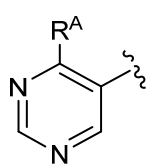
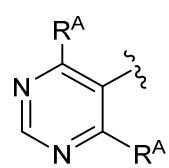
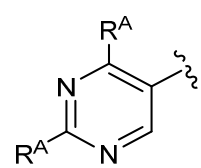
Z^1 is N, NR^1, O, S, CR^1, or $C(R^1)_2$;

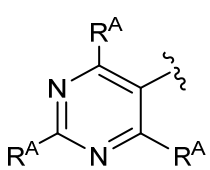
Z^2 is N, NR^2, O, CR^2, $C(R^2)_2$, $S(=O)_2$, C(=O), or C(=S);

$\overline{---}$ is a single bond or a double bond;

each of R^1 and R^2 is independently selected from hydrogen, halo, -CN, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl;

each of R^8 and R^9 is independently selected from hydrogen, halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl; or R^8 and R^9 taken together form an oxo; or R^8 and R^9 taken together with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or heterocycloalkyl;

 is  ,  ,  , or

 ;

each of R^A is independently selected from halogen, $-NO_2$, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-}

$_6$ alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})_2S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, and $-S(O)_2N(R^{12})(R^{11})$;

R^{11} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, optionally substituted $-C_{1-4}$ alkylene-C_{3-8} cycloalkyl, optionally substituted $-C_{1-4}$ alkylene-C_{2-7} heterocycloalkyl, optionally substituted $-C_{1-4}$ alkylene-phenyl, or optionally substituted $-C_{1-4}$ alkylene-heteroaryl;

each of R^{12} is independently selected from hydrogen, $-NO_2$, -CN, C_{1-6} alkyl, C_{1-6} aminoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, C_{1-6} heteroalkyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, -OH, oxo, amino, $-NO_2$, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} haloalkyl;

B is 6 membered heteroaryl, phenyl or a phenyl isostere;

R^{B1} is halo, -CN, $-NO_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, $-S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl;

each R^B is independently halo, -CN, $-NO_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, $-S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-}

$_{9}$ heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl; or

R^{B1} and one of R^{B} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted phenyl, optionally substituted naphthyl, optionally substituted monocyclic heteroaryl, optionally substituted bicyclic heteroaryl, optionally substituted C_{3-8} cycloalkyl, or optionally substituted C_{2-9} heterocycloalkyl; or

R^{B1} and one of R^{B} on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl; or

two of R^{B} on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl;

n is 0, 1, 2, 3 or 4; and

p is 1.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein,

Z^1 is N, NR^1, O, S, CR^1, or $C(R^1)_2$;

Z^2 is N, NR^2, O, CR^2, $C(R^2)_2$, $S(=O)_2$, C(=O), or C(=S);

$\overline{---}$ is a single bond or a double bond;

each of R^1 and R^2 is independently selected from hydrogen, halo, -CN, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl,

wherein the alkyl, heteroalkyl, alkenyl, or alkynyl is optionally substituted with one or more substituents independently selected from: halogen, amino, oxo, -OH, $-NO_2$, -CN, and C_{1-3} alkoxy;

each of R^8 and R^9 is independently selected from hydrogen, halo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or R^8 and R^9 taken together form an oxo; or R^8 and R^9 taken together with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or heterocycloalkyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, amino, -OH, -NO_2, oxo, -CN, C_{1-3} alkoxy, C_{1-3} alkyl and C_{1-3} haloalkyl;

each of R^A is independently selected from halogen, -NO_2, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})_2S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, and -$S(O)_2N(R^{12})(R^{11})$,

wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, -OH, -NO_2, oxo, amino, -CN, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, -OH, amino, -NO_2, oxo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} haloalkyl;

R^{11} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, optionally substituted -C_{1-4} alkylene-C_{3-8} cycloalkyl, optionally substituted -C_{1-4} alkylene-C_{2-7} heterocycloalkyl, optionally substituted -C_{1-4} alkylene-phenyl, or optionally substituted -C_{1-4} alkylene-heteroaryl,

wherein the alkyl, alkenyl, alkynyl, heteroalkyl, alkylene, cycloalkyl, heterocycloalkyl, phenyl, or heteroaryl is optionally substituted with one or more substituents independently selected from: halogen, -OH, amino, -NO_2, oxo, C_{1-6} alkoxy, -CN, C_{1-6} alkyl, and C_{1-6} haloalkyl;

each of R^{12} is independently selected from hydrogen, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} aminoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, C_{1-6} heteroalkyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, -OH, oxo, amino, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} haloalkyl;

B is 6 membered heteroaryl, phenyl or a phenyl isostere;

R^{B1} is halo, -CN, -NO_2, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, -$S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl,

wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, naphthyl, phenyl or heteroaryl is optionally substituted with one or more substituents independently selected from: halogen, -NO_2, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, and -$S(O)_2N(R^{12})(R^{11})$, wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, -OH, -NO_2, amino, -$NH(C_{1-6}$ alkyl), -$N(C_{1-6}$ alkyl)$_2$, oxo, -CN, C_{1-3} alkoxy, C_{1-3} alkyl and C_{1-3} haloalkyl;

each R^B is independently halo, -CN, -NO_2, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, -$S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl,

wherein the the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, naphthyl, phenyl or heteroaryl is optionally substituted with one

or more substituents independently selected from: halogen, -OH, -NO_2, amino, oxo, -CN, C_{1-3} alkoxy, C_{1-3} alkyl and C_{1-3} haloalkyl; or

R^{B1} and one of R^B on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted phenyl, optionally substituted naphthyl, optionally substituted monocyclic heteroaryl, optionally substituted bicyclic heteroaryl, optionally substituted C_{3-8} cycloalkyl, or optionally substituted C_{2-9} heterocycloalkyl,

wherein the phenyl, naphthyl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, -OH, amino, -NO_2, oxo, C_{1-6} alkoxy, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl; or

R^{B1} and one of R^B on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl,

wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, -OH, amino, -NO_2, oxo, C_{1-6} alkoxy, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl; or

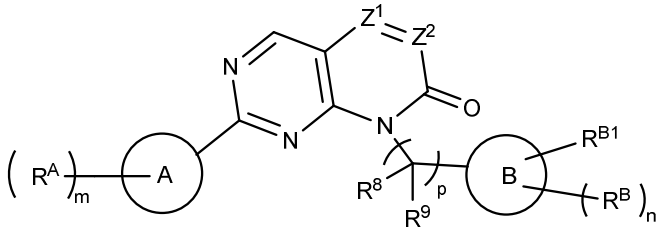
two of R^B on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl,

wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, -OH, amino, -NO_2, oxo, C_{1-6} alkoxy, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl;

n is 0, 1, 2, 3 or 4; and

p is 1.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein the compound has a structure of Formula (IIIa-1),



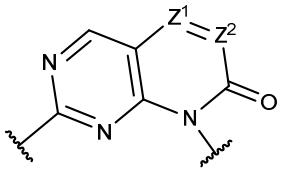
Formula (IIIa-1),

wherein

Z^1 is N or CR^1; and

Z^2 is N or CR^2.

4. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein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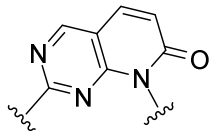
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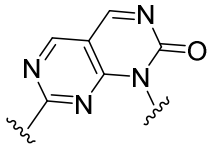
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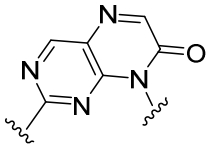
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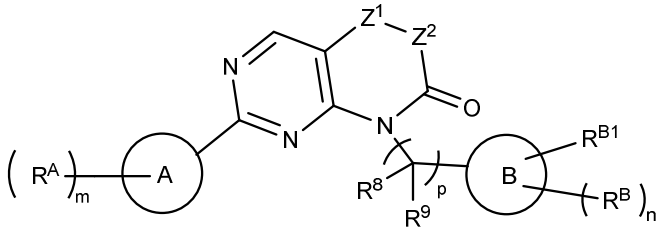
5. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein the compound has a structure of Formula (IIIa-2),



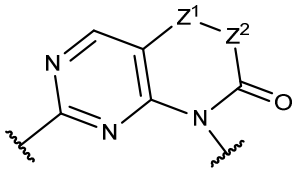
Formula (IIIa-2),

wherein

Z^1 is NR^1, O, S, or $C(R^1)_2$;

Z^2 is NR^2, O, or $C(R^2)_2$.

6. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein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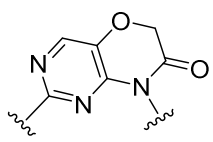
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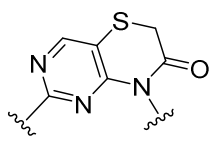
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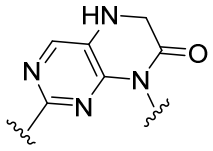
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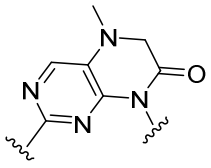
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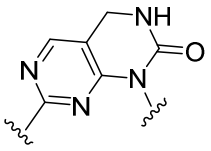
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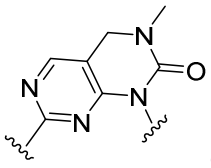
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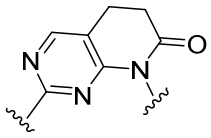
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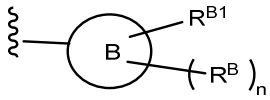
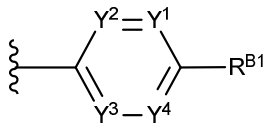
7. The compound of any of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein

 is  ,

Y^1 is N or CR^{Y1};

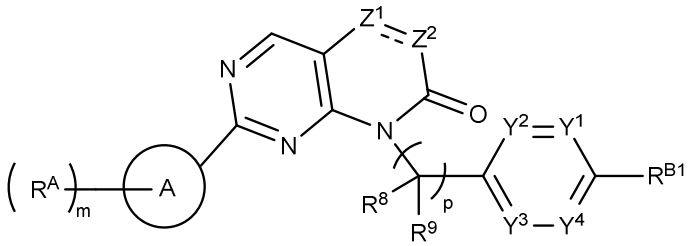
Y^2 is N or CR^{Y2};

Y^3 is N or CR^{Y3};

Y^4 is N or CR^{Y4}; and

each of R^{Y1}, R^{Y2}, R^{Y3} and R^{Y4} is independently selected from hydrogen, halo, -CN, -OR^{11}, -SR^{11}, -$N(R^{12})_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl.

8. The compound of claim 1 or 2, or a salt or solvate thereof, wherein the compound has a structure of Formula (IIIc'),



Formula (IIIc')

wherein,

Y^1 is N or CR^{Y1};

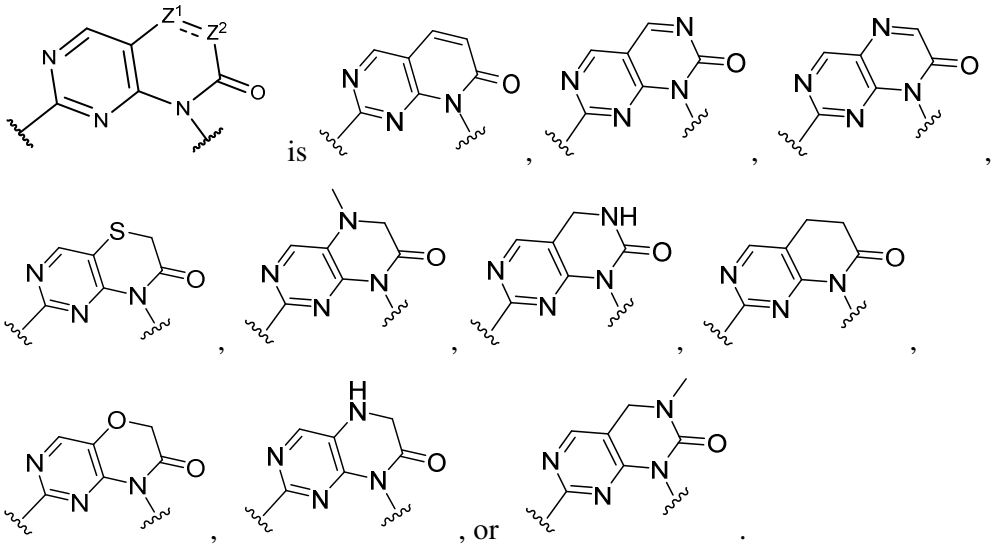
Y^2 is N or CR^{Y2};

Y^3 is N or CR^{Y3};

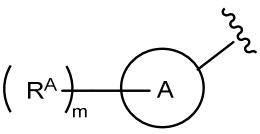
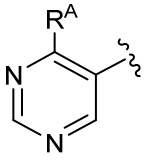
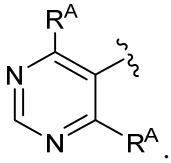
Y^4 is N or CR^{Y4};

each of R^{Y1}, R^{Y2}, R^{Y3} and R^{Y4} is independently selected from hydrogen, halo, -CN, -OR^{11}, -SR^{11}, -$N(R^{12})_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl.

9. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein

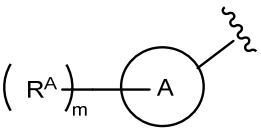
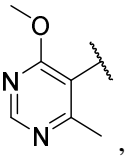
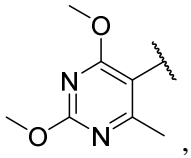
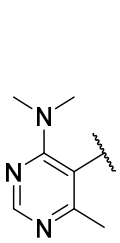
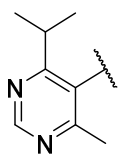
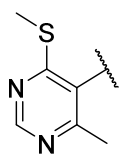
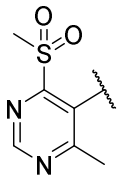
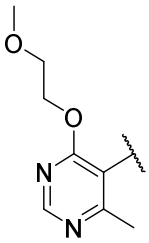
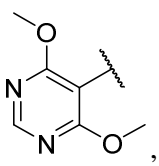
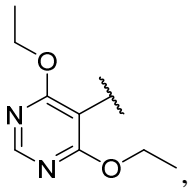
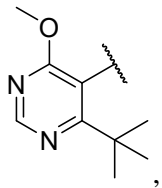
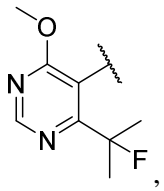
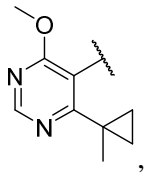
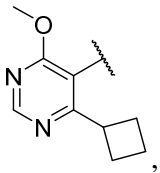
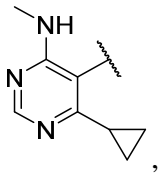
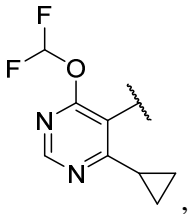
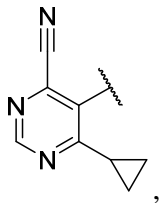
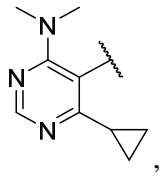
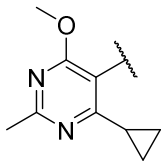
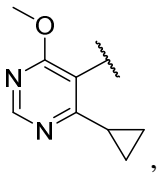
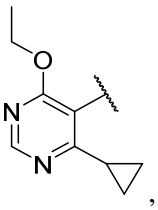
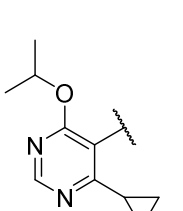
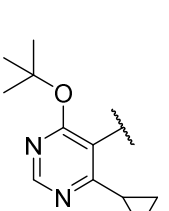
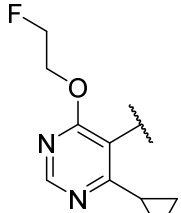
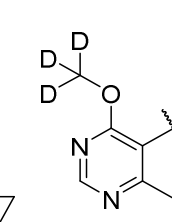
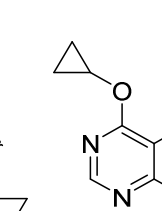
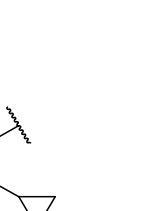
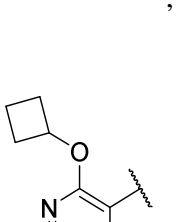
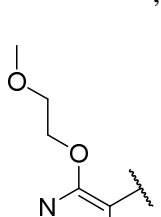
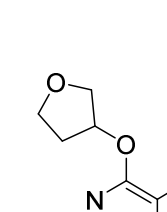
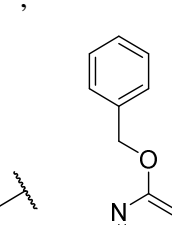
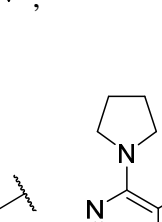
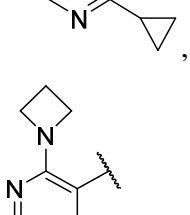
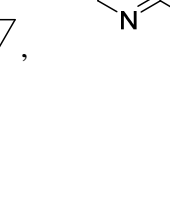
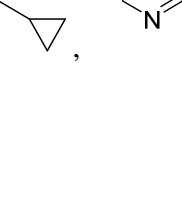
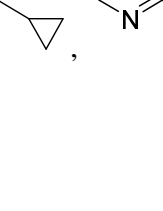
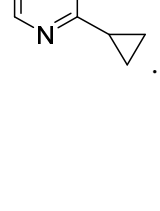


10. The compound of any of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein ring B is a phenyl isostere, wherein the phenyl isostere is cubane or ethynyl.

11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein  is  or  .

12. The compound of any one of claims 1 to 11, wherein each of R^A is independently selected from halogen, $-NO_2$, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})_2S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, and $-S(O)_2N(R^{12})(R^{11})$.

13. The compound of claim 12, wherein each R^A is independently substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, oxo, C_{1-6} alkoxy, C_{3-6} cycloalkyl, and amino.

14. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein  is selected from:  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  .

15. The compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein each of R^8 and R^9 is hydrogen.

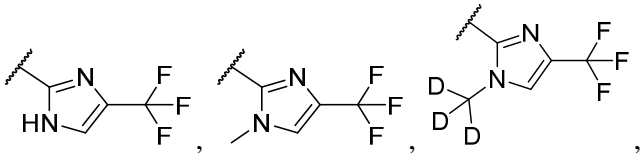
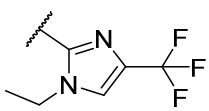
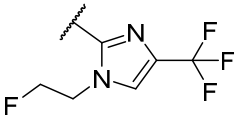
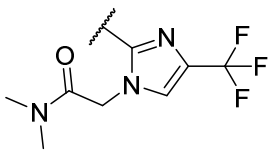
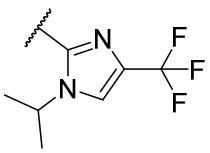
16. The compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein R^8 and R^9 taken together form an oxo.

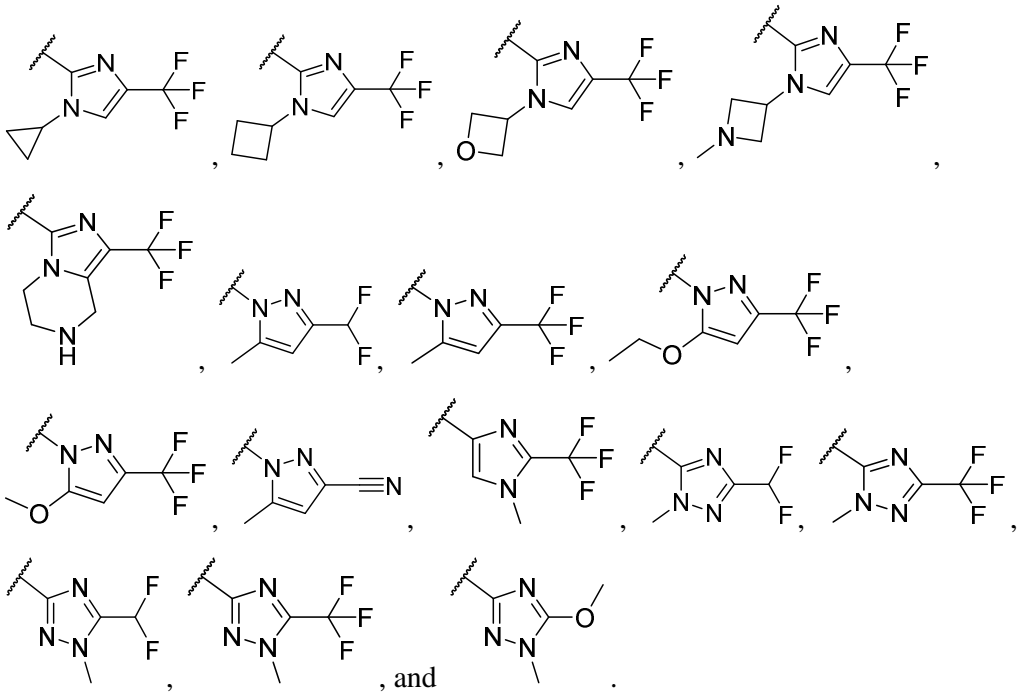
17. The compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein R^8 and R^9 taken together with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or heterocycloalkyl.

18. The compound of any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein B is phenyl or 6 membered heteroaryl.

19. The compound of any one of claims 1 to 18 , or a pharmaceutically acceptable salt thereof, wherein R^{B1} is optionally substituted monocyclic 5-6 membered heterocycloalkyl or heteroaryl.

20. The compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-NO_2$, oxo, -CN, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} aminoalkyl, optionally substituted C_{1-6} hydroxyalkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, and optionally substituted C_{2-7} heterocycloalkyl.

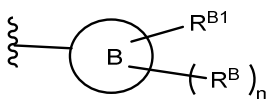
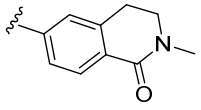
21. The compound of claim 1, 18 or 19, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is selected from:  , , ,  ,  ,  ,  ,



22. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^{B1} and one of R^B on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl.

23. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^{B1} and one of R^B on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted phenyl, optionally substituted naphthyl, optionally substituted monocyclic heteroaryl, optionally substituted bicyclic heteroaryl, optionally substituted C_{3-8} cycloalkyl, or optionally substituted C_{2-9} heterocycloalkyl.

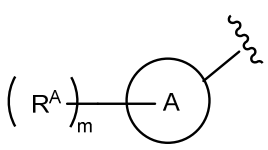
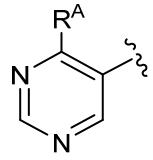
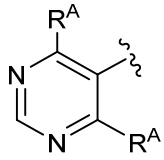
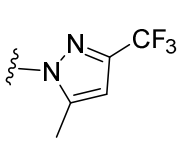
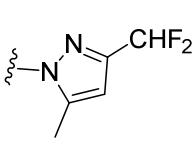
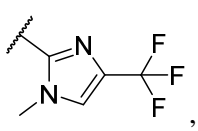
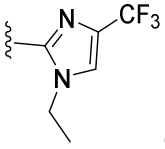
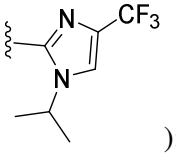
24. The compound of claim 23, or a pharmaceutically acceptable salt thereof, wherein R^{B1} and one of R^B on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted 5 or 6 membered monocyclic heterocycloalkyl.

25. The compound of claim 24, or a pharmaceutically acceptable salt thereof, wherein  is  .

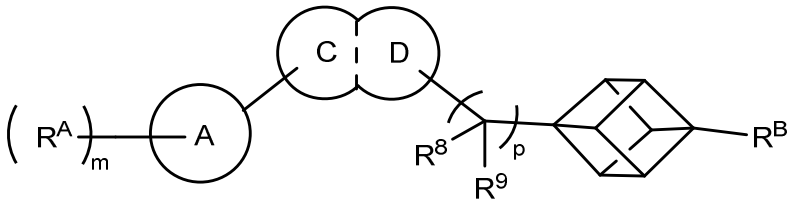
26. The compound of any one of claims 1 to 6 or 11 to 24, or a pharmaceutically acceptable salt thereof, wherein R^B is halo, -CN, -NO_2, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl.

27. The compound of any one of claims 1 to 6 or 11 to 24, or a pharmaceutically acceptable salt thereof, wherein two of R^B on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-6} cycloalkyl or optionally substituted C_{2-5} heterocycloalkyl.

28. The compound of any one of claims 1 to 21, or a pharmaceutically acceptable salt thereof, wherein n is 0.

29. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein Z_1 is CR^1; Z_2 is CR^2; each of R^1 and R^2 is hydrogen; each R^8 and R^9 is hydrogen;  is  or  ; and each R^A is independently selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_{3-6} cycloalkyl (e.g., cyclopropyl); B is cubane; R^{B1} is 5 membered heteroaryl optionally substituted with one or more substituents selected from C_{1-3} haloalkyl and C_{1-3} alkyl (e.g.,  ,  ,  ,  or ); and n is 0.

30. A compound having the structure of Formula (VI), or a pharmaceutically acceptable salt thereof,



Formula (VI)

wherein,

ring C is phenyl or a 6 membered heteroaryl, wherein each of the phenyl or heteroaryl is optionally substituted;

ring D is an aromatic, saturated or partially saturated 6 membered carbocycle or heterocycle, wherein each of the carbocycle or heterocycle is optionally substituted;

each of R^8 and R^9 is independently selected from hydrogen, halo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl; or R^8 and R^9 taken together form an oxo; or R^8 and R^9 taken together with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or heterocycloalkyl;

ring A is phenyl, naphthyl, monocyclic heteroaryl, or bicyclic heteroaryl;

each of R^A is independently selected from halogen, $-NO_2$, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})_2S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, and $-S(O)_2N(R^{12})(R^{11})$;

R^{11} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, optionally substituted $-C_{1-4}$ alkylene-C_{3-8} cycloalkyl, optionally substituted $-C_{1-4}$ alkylene-C_{2-7}

heterocycloalkyl, optionally substituted -C_{1-4} alkylene-phenyl, or optionally substituted -C_{1-4} alkylene-heteroaryl;

each of R^{12} is independently selected from hydrogen, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} aminoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, and C_{3-6} carbocycle, 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, -OH, oxo, amino, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} haloalkyl;

R^B is hydrogen, halo, -CN, -NO_2, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, -$S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl; or

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

p is 0 or 1.

31. The compound of claim 30, or a pharmaceutically acceptable salt thereof, wherein

ring C is phenyl or a 6 membered heteroaryl, wherein each of the phenyl or heteroaryl is optionally substituted with 1, 2, 3 or 4 R^{1C}, and

each R^{1C} is independently halogen, -CN, -NO_2, -OH, -OR^a, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -NR^cR^d, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$NR^bS(=O)_2R^a$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^cR^d$, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}aminoalkyl, C_{1-6}heteroalkyl, C_{2-6}alkenyl, C_2-C_6alkynyl, C_{3-8} cycloalkyl, C_{2-7} heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is optionally and independently substituted with one or more R^{1Ca};

ring D is an aromatic, saturated or partially saturated 6 membered carbocycle or heterocycle, wherein each of the carbocycle or heterocycle is optionally substituted with 1, 2, 3, 4 or 5, or 6 R^{1D}, and

each R^{1D} is independently halogen, -CN, -NO_2, -OH, -OR^a, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -NR^cR^d, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$NR^bS(=O)_2R^a$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^cR^d$, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}aminoalkyl, C_{1-6}heteroalkyl, C_{2-6}alkenyl, C_2-C_6alkynyl, C_{3-8} cycloalkyl, C_{2-7} heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is optionally and independently substituted with one or more R^{1Da};

each of R^8 and R^9 is independently selected from hydrogen, halo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl; or R^8 and R^9 taken together form an oxo; or R^8 and R^9 taken together with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or heterocycloalkyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, amino, -OH, -NO_2, oxo, -CN, C_{1-3} alkoxy, C_{1-3} alkyl and C_{1-3} haloalkyl;

ring A is phenyl, naphthyl, monocyclic heteroaryl, or bicyclic heteroaryl;

each of R^A is independently selected from halogen, -NO_2, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})_2S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, and -$S(O)_2N(R^{12})(R^{11})$,

wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, -OH, -NO_2, oxo, amino, -CN, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, -OH, amino, -NO_2, oxo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} haloalkyl;

R^{11} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl,

optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, optionally substituted -C_{1-4} alkylene-C_{3-8} cycloalkyl, optionally substituted -C_{1-4} alkylene-C_{2-7} heterocycloalkyl, optionally substituted -C_{1-4} alkylene-phenyl, or optionally substituted -C_{1-4} alkylene-heteroaryl,

wherein the alkyl, alkenyl, alkynyl, heteroalkyl, alkylene, cycloalkyl, heterocycloalkyl, phenyl, or heteroaryl is optionally substituted with one or more substituents independently selected from: halogen, -OH, amino, -NO_2, oxo, C_{1-6} alkoxy, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl;

each of R^{12} is independently selected from hydrogen, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} aminoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, and C_{3-6} carbocycle, 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, -OH, oxo, amino, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} haloalkyl;

R^B is hydrogen, halo, -CN, -NO_2, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, -$S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl,

wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, naphthyl, phenyl or heteroaryl is optionally substituted with one or more substituents independently selected from: halogen, -NO_2, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, and -$S(O)_2N(R^{12})(R^{11})$, wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, or heterocycloalkyl is optionally

substituted with one or more substituents independently selected from: halogen, -OH, $-NO_2$, amino, $-NH(C_{1-6}$ alkyl), $-N(C_{1-6}$ alkyl$)_2$, oxo, -CN, C_{1-3} alkoxy, C_{1-3} alkyl and C_{1-3} haloalkyl;

each R^a is independently C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_1-C_6heteroalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkylene-cycloalkyl, -C_1-C_6alkylene-heterocycloalkyl, -C_1-C_6alkylene-aryl, or -C_1-C_6alkylene-heteroaryl; wherein each alkyl, alkylene, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, halogen, -CN, -OH, -OC_1-C_6alkyl, -S(=O)C_1-C_6alkyl, -S(=O)$_2C_1$-C_6alkyl, -S(=O)$_2NH_2$, -S(=O)$_2$NHC_1-C_6alkyl, -S(=O)$_2$N(C_1-C_6alkyl)$_2$, $-NH_2$, -NHC_1-C_6alkyl, -N(C_1-C_6alkyl)$_2$, -NHC(=O)OC_1-C_6alkyl, -C(=O)C_1-C_6alkyl, -C(=O)OH, -C(=O)OC_1-C_6alkyl, -C(=O)NH_2, -C(=O)N(C_1-C_6alkyl)$_2$, -C(=O)NHC_1-C_6alkyl, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, or C_1-C_6heteroalkyl;

each R^b is independently hydrogen, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_1-C_6heteroalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkylene-cycloalkyl, -C_1-C_6alkylene-heterocycloalkyl, -C_1-C_6alkylene-aryl, or -C_1-C_6alkylene-heteroaryl; wherein each alkyl, alkylene, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, halogen, -CN, -OH, -OC_1-C_6alkyl, -S(=O)C_1-C_6alkyl, -S(=O)$_2C_1$-C_6alkyl, -S(=O)$_2NH_2$, -S(=O)$_2$NH C_1-C_6alkyl, -S(=O)$_2$N(C_1-C_6alkyl)$_2$, $-NH_2$, -NHC_1-C_6alkyl, -N(C_1-C_6alkyl)$_2$, -NHC(=O)OC_1-C_6alkyl, -C(=O)C_1-C_6alkyl, -C(=O)OH, -C(=O)OC_1-C_6alkyl, -C(=O)NH_2, -C(=O)N(C_1-C_6alkyl)$_2$, -C(=O)NHC_1-C_6alkyl, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, or C_1-C_6heteroalkyl;

each R^c and R^d are independently hydrogen, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_1-C_6heteroalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkylene-cycloalkyl, -C_1-C_6alkylene-heterocycloalkyl, -C_1-C_6alkylene-aryl, or -C_1-C_6alkylene-heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, halogen, -CN, -OH, -OC_1-C_6alkyl, -S(=O)C_1-C_6alkyl, -

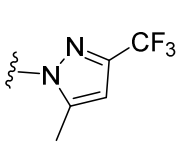
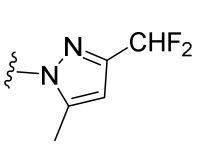
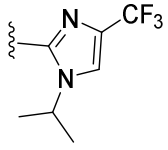
$S(=O)_2C_1$-C_6alkyl, -$S(=O)_2NH_2$, -$S(=O)_2NHC_1$-C_6alkyl, -$S(=O)_2N(C_1$-C_6alkyl$)_2$, -NH_2, -NHC_1-C_6alkyl, -$N(C_1$-C_6alkyl$)_2$, -$NHC(=O)OC_1$-C_6alkyl, -C(=O) C_1-C_6alkyl, -C(=O)OH, -$C(=O)OC_1$-C_6alkyl, -$C(=O)NH_2$, -$C(=O)N(C_1$-C_6alkyl$)_2$, -$C(=O)NHC_1$-C_6alkyl, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, or C_1-C_6heteroalkyl;

or R^c and R^d are taken together with the atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, halogen, -CN, -OH, -OC_1-C_6alkyl, -$S(=O)C_1$-C_6alkyl, -$S(=O)_2C_1$-C_6alkyl, -$S(=O)_2NH_2$, -$S(=O)_2NHC_1$-C_6alkyl, -$S(=O)_2N(C_1$-C_6alkyl$)_2$, -NH_2, -NHC_1-C_6alkyl, -$N(C_1$-C_6alkyl$)_2$, -$NHC(=O)OC_1$-C_6alkyl, -C(=O) C_1-C_6alkyl, -C(=O)OH, -$C(=O)OC_1$-C_6alkyl, -$C(=O)NH_2$, -$C(=O)N(C_1$-C_6alkyl$)_2$, -$C(=O)NHC_1$-C_6alkyl, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, or C_1-C_6heteroalkyl;

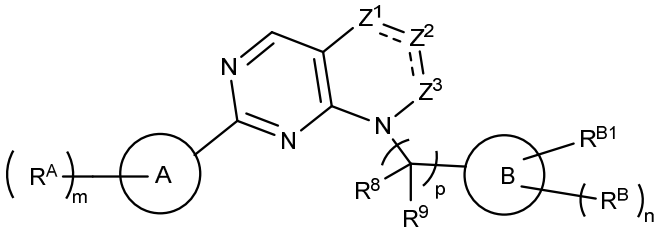
each R^{1Ca} and R^{1Da} is independently halogen, -CN, -NO_2, -OH, -OR^a, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -NR^cR^d, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$NR^bS(=O)_2R^a$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^cR^d$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_1-C_6heteroalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

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

p is 0 or 1.

32. The compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein R^B is  ,  , or  .

33. A compound having the structure of Formula (III), or a pharmaceutically acceptable salt thereof,



Formula (III)

wherein,

Z^1 is N, NR^1, O, S, CR^1, or $C(R^1)_2$;

Z^2 is N, NR^2, O, CR^2, $C(R^2)_2$, $S(=O)_2$, C(=O), or C(=S);

Z^3 is N, NR^3, CR^3, $C(R^3)_2$, $S(=O)_2$, C(=O), or C(=S);

$\overline{---}$ is a single bond or a double bond;

each of R^1, R^2, and R^3 is independently selected from hydrogen, halo, -CN, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl;

each of R^8 and R^9 is independently selected from hydrogen, halo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl; or R^8 and R^9 taken together form an oxo; or R^8 and R^9 taken together with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or heterocycloalkyl;

ring A is phenyl, naphthyl, monocyclic heteroaryl, or bicyclic heteroaryl;

each of R^A is independently selected from halogen, $-NO_2$, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})_2S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, and $-S(O)_2N(R^{12})(R^{11})$;

R^{11} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-7} heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, optionally substituted $-C_{1-4}$ alkylene-C_{3-8} cycloalkyl, optionally substituted $-C_{1-4}$ alkylene-C_{2-7}

heterocycloalkyl, optionally substituted -C_{1-4} alkylene-phenyl, or optionally substituted -C_{1-4} alkylene-heteroaryl;

each of R^{12} is independently selected from hydrogen, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} aminoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, C_{1-6} heteroalkyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, -OH, oxo, amino, -NO_2, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} haloalkyl;

B is 6 membered heteroaryl, phenyl or a phenyl isostere;

R^{B1} is halo, -CN, -NO_2, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, -$S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl;

each R^B is independently halo, -CN, -NO_2, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, -OR^{11}, -SR^{11}, -$N(R^{12})(R^{11})$, -$C(O)R^{12}$, -$C(O)OR^{12}$, -$OC(O)R^{12}$, -$OC(O)N(R^{12})(R^{11})$, -$C(O)N(R^{12})(R^{11})$, -$N(R^{12})C(O)R^{12}$, -$N(R^{12})C(O)OR^{12}$, -$N(R^{12})C(O)N(R^{12})(R^{11})$, -$N(R^{12})S(O)_2(R^{12})$, -$S(O)R^{12}$, -$S(O)_2R^{12}$, -$S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl; or

R^{B1} and one of R^B on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted phenyl, optionally substituted naphthyl, optionally substituted monocyclic heteroaryl, optionally substituted bicyclic heteroaryl, optionally substituted C_{3-8} cycloalkyl, or optionally substituted C_{2-9} heterocycloalkyl; or

R^{B1} and one of R^B on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl; or

two of R^B on the same atom are taken together with the atom to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl;

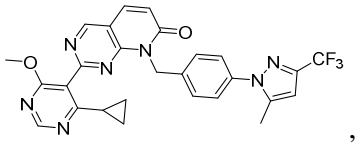
m is 1, 2, 3, or 4;

n is 0, 1, 2, 3 or 4; and

p is 0 or 1.

34. The compound of any one of claims 1, 30 or 33, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from compounds of Table 1.

35. A compound, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of: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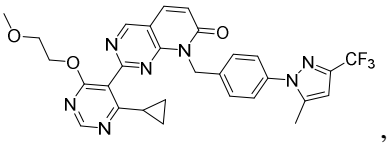
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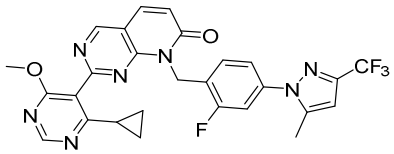
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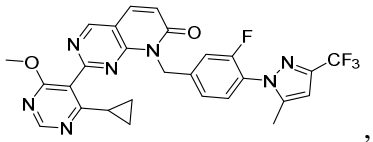
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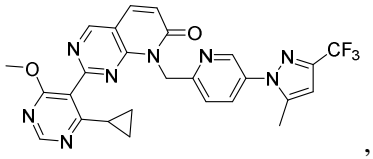
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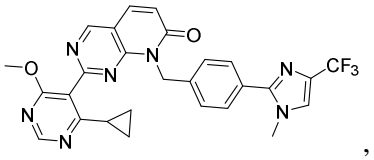
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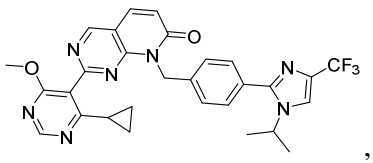
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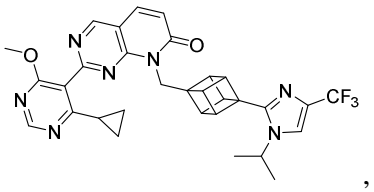
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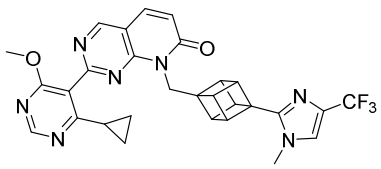
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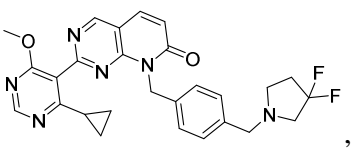
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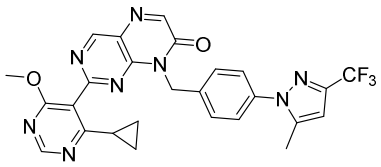
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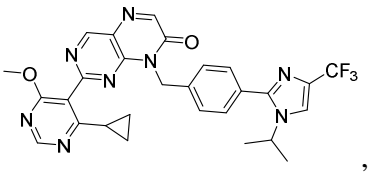
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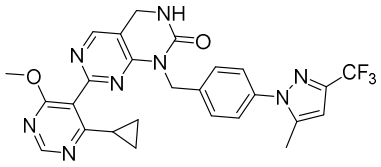
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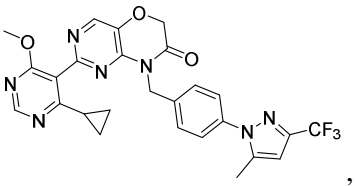
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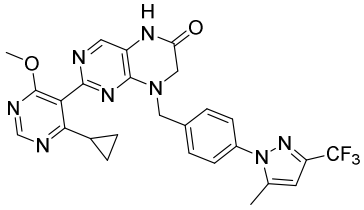
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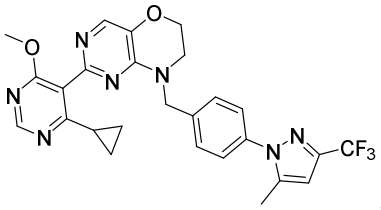
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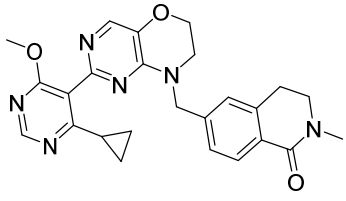
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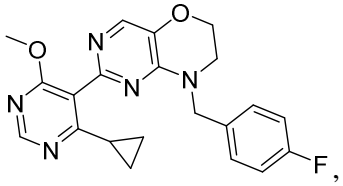
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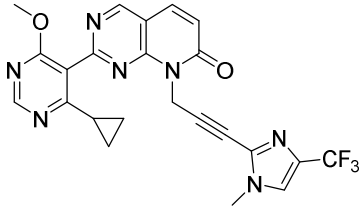
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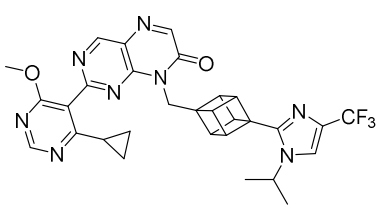
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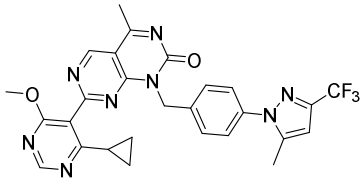
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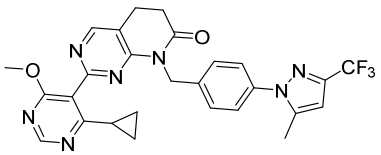
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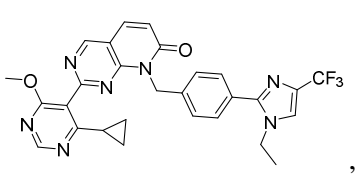
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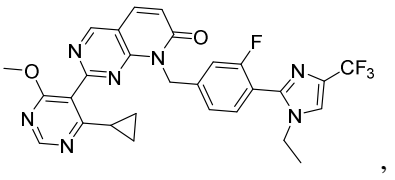
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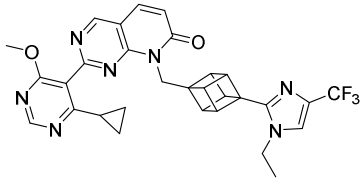
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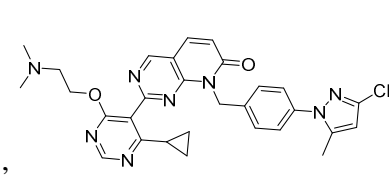
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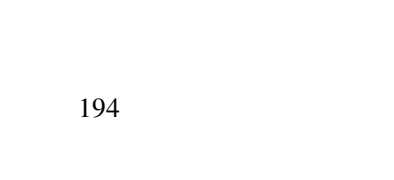
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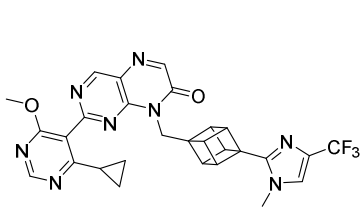
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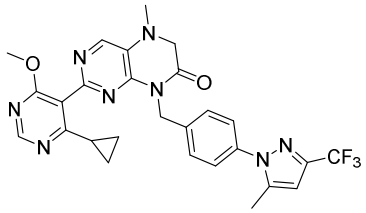
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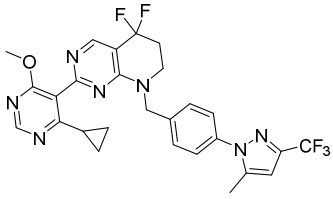
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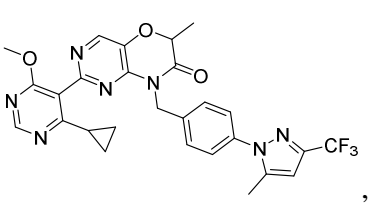
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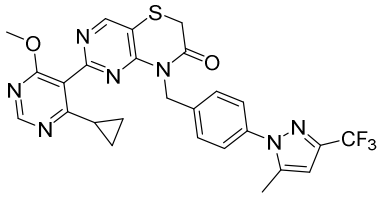
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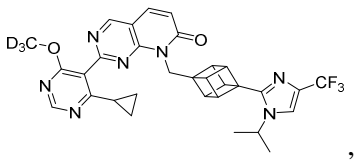
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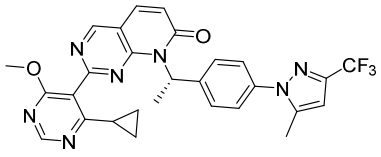
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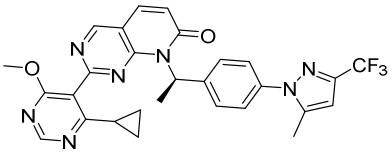
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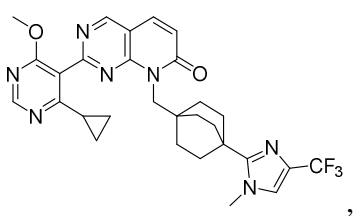
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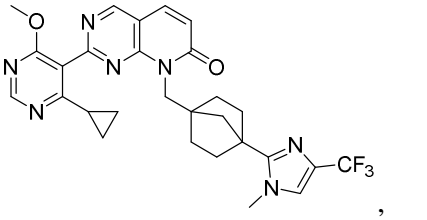
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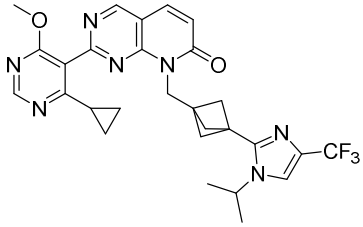
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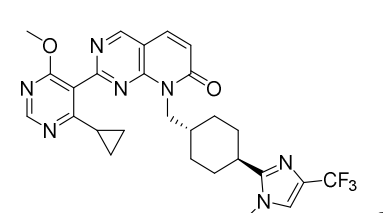
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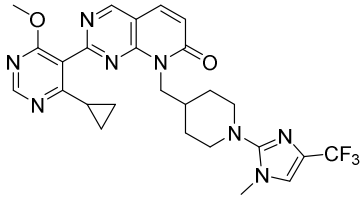
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36. A pharmaceutical composition comprising a compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

37. Use of a compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for modulating or inhibiting ubiquitin specific protease 1 (USP1).

38. Use of a compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for inhibiting or reducing DNA repair activity modulated by ubiquitin specific protease 1 (USP1).

39. Use of a compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or disorder associated with ubiquitin specific protease 1 (USP1) or associated with modulation of USP1.

40. The use of claim 39, wherein the disease or disorder is cancer.

41. Use of a compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

42. The use of claim 40 or 41, wherein the cancer is selected from the group consisting of lung cancer, non-small cell lung cancer (NSCLC), colon cancer, bladder cancer, osteosarcoma, ovarian cancer, skin cancer, and breast cancer.

43. The use of any one of claims 40 to 42, wherein the cancer comprises cancer cells with elevated levels of RAD 18.

44. The use of any one of claims 40 to 43, wherein the cancer is selected from the group consisting of a DNA damage repair pathway deficient cancer, a PARP inhibitor resistant or refractory cancer, a BRCA1 mutant cancer, a BRCA2 mutant cancer, and a BRCA1-deficient cancer.