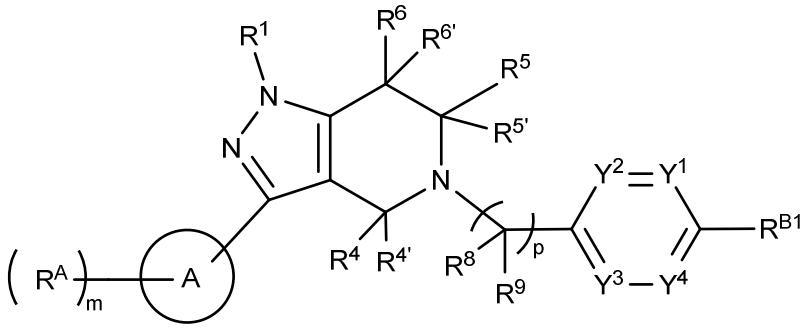
CLAIMS

WHAT IS CLAIMED IS:

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



Formula (IVa)

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};

R^1 is hydrogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, or optionally substituted C_{2-7} heterocycloalkyl;

each of R^4 and $R^{4'}$ is independently selected from hydrogen, halo, -CN, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, and optionally substituted C_{2-7} heterocycloalkyl; or R^4 and $R^{4'}$ taken together form an oxo; or R^4 and $R^{4'}$ taken together with the carbon to which they are attached form a 3-6 membered cycloalkyl or 3-6 membered heterocycloalkyl;

each of R^5 and $R^{5'}$ is independently selected from hydrogen, halo, -CN, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, and optionally substituted C_{2-7} heterocycloalkyl; or R^5 and $R^{5'}$ taken together form an oxo; or R^5 and $R^{5'}$ taken together with the carbon to which they are attached form a 3-6 membered cycloalkyl or 3-6 membered heterocycloalkyl;

each of R^6 and $R^{6'}$ is independently selected from hydrogen, halo, -CN, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, and optionally

substituted C_{2-7} heterocycloalkyl; or R^6 and $R^{6'}$ taken together form an oxo; or R^6 and $R^{6'}$ taken together with the carbon to which they are attached form a 3-6 membered cycloalkyl or 3-6 membered heterocycloalkyl;

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 with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or 3-6 membered heterocycloalkyl;

ring A is monocyclic heteroaryl, bicyclic heteroaryl, monocyclic heterocycloalkyl, or bicyclic heterocycloalkyl;

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;

R^{B1} is 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 of R^{Y1}, R^{Y2}, R^{Y3} and R^{Y4} is independently selected from hydrogen, halo, -CN, $-NO_2$, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, $-S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl,

optionally substituted phenyl, optionally substituted monocyclic heteroaryl, and optionally substituted bicyclic heteroaryl; or

R^{Y1} and R^{Y2} are taken together with the carbons to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl; or

R^{Y3} and R^{Y4} are taken together with the carbons to which they are attached to form an optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl;

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

p is 0 or 1.

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

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

wherein the alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl or heterocycloalkyl 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^4 and $R^{4'}$ is independently selected from hydrogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, and optionally substituted C_{2-7} heterocycloalkyl, or R^4 and $R^{4'}$ taken together form an oxo, or R^4 and $R^{4'}$ taken together with the carbon to which they are attached form a 3-6 membered cycloalkyl or 3-6 membered 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^5 and $R^{5'}$ is independently selected from hydrogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, and optionally substituted C_{2-7} heterocycloalkyl, or R^5 and $R^{5'}$ taken together form an oxo, or R^5 and $R^{5'}$ taken together with the carbon to which they are attached form a 3-6 membered cycloalkyl or 3-6 membered 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^6 and $R^{6'}$ is independently selected from hydrogen, halo, -CN, $-OR^{11}$, $-SR^{11}$, -

$N(R^{12})(R^{11})$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{3-8} cycloalkyl, and optionally substituted C_{2-7} heterocycloalkyl, or R^6 and $R^{6'}$ taken together form an oxo, or R^6 and $R^{6'}$ taken together with the carbon to which they are attached form a 3-6 membered cycloalkyl or 3-6 membered 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^8 and R^9 is independently selected from hydrogen, -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 with the carbon to which they are attached form an optionally substituted 3-6 membered cycloalkyl or 3-6 membered 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 monocyclic heteroaryl, bicyclic heteroaryl, monocyclic heterocycloalkyl, or bicyclic heterocycloalkyl;

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;

R^{B1} is 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 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 of R^{Y1}, R^{Y2}, R^{Y3} and R^{Y4} is independently selected from hydrogen, halo, -CN, $-NO_2$, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{12})(R^{11})$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-OC(O)N(R^{12})(R^{11})$, $-C(O)N(R^{12})(R^{11})$, $-N(R^{12})C(O)R^{12}$, $-N(R^{12})C(O)OR^{12}$, $-N(R^{12})C(O)N(R^{12})(R^{11})$, $-N(R^{12})S(O)_2(R^{12})$, $-S(O)R^{12}$, $-S(O)_2R^{12}$, $-S(O)_2N(R^{12})(R^{11})$, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-9} heterocycloalkyl, optionally substituted naphthyl, optionally substituted phenyl, optionally substituted monocyclic heteroaryl, and 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, -OH, $-NO_2$, amino, oxo, -CN, C_{1-3} alkoxy, C_{1-3} alkyl and C_{1-3} haloalkyl; or

R^{Y1} and R^{Y2} are taken together with the carbons to which they are attached to form an

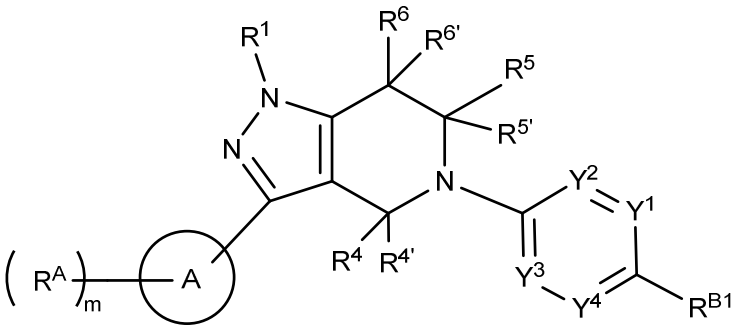
optionally substituted C_{3-8} cycloalkyl or optionally substituted C_{2-9} heterocycloalkyl, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from: halogen, -OH, amino, $-NO_2$, oxo, C_{1-6} alkoxy, -CN, C_{1-6} alkyl, and C_{1-6} haloalkyl; or

R^{Y3} and R^{Y4} are taken together with the carbons 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, and C_{1-6} haloalkyl;

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

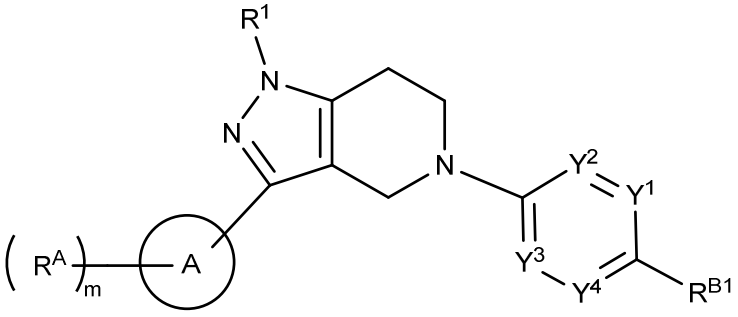
p is 0 or 1.

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



Formula (IVa-1).

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



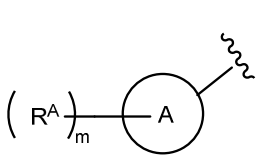
Formula (IVa-2).

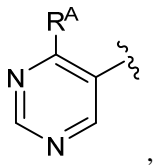
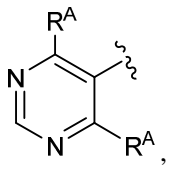
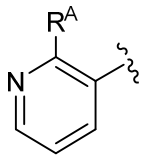
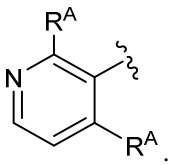
5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^1 is C_{1-3} alkyl; and/or

wherein each of R^{Y1}, R^{Y2}, R^{Y3} and R^{Y4} is hydrogen; and/or

wherein ring A is 5 or 6 membered monocyclic heteroaryl.

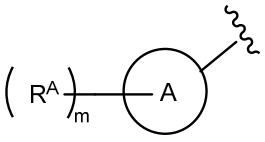
6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein

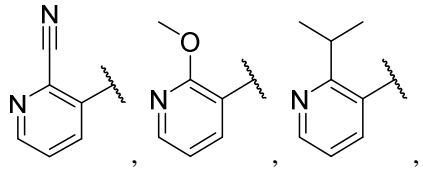
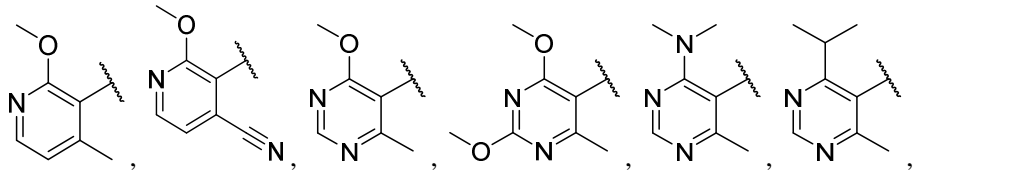
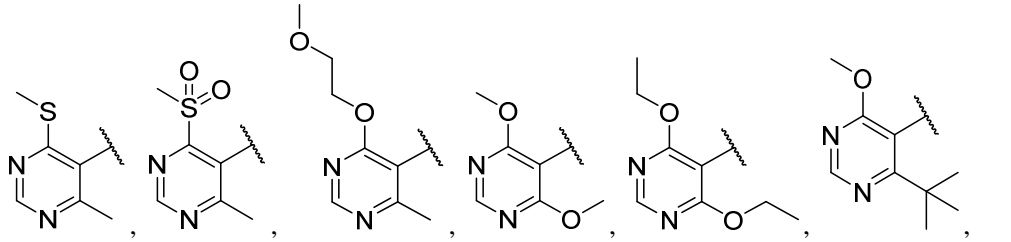
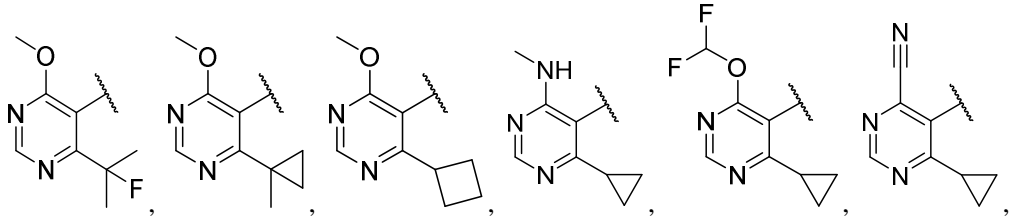


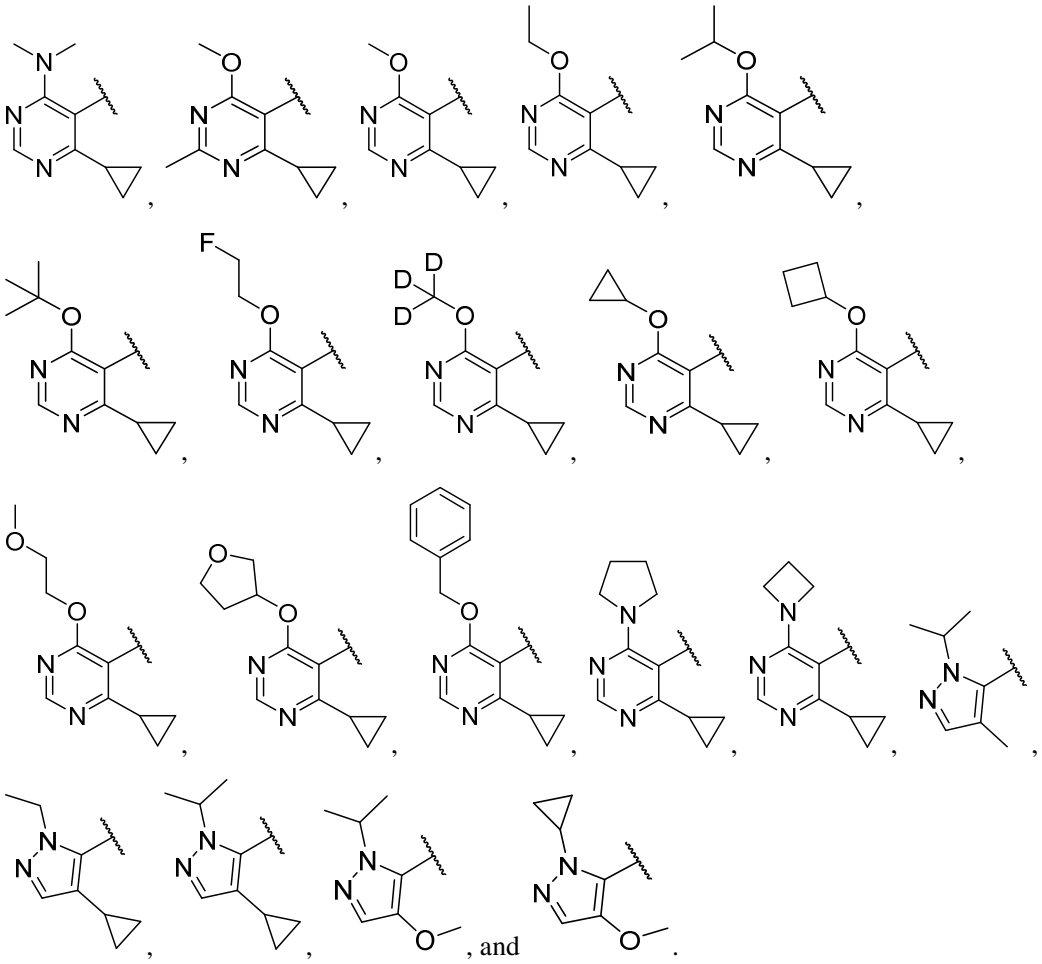
is , , , or .

7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, 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 $-S(O)_2N(R^{12})(R^{11})$.

8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof,

wherein 

is selected from: , , , .



9. The compound, or a pharmaceutically acceptable salt thereof, of any one of claims 1, 2, and 5 to 7 wherein p is 1.

10. The compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein each of R^8 and R^9 is independently selected from hydrogen, -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.

11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein each of R^8 and R^9 is hydrogen.

12. The compound of claim 9, 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.

13. The compound of any one of claims 1 to 12 or a pharmaceutically acceptable salt thereof, wherein R^{B1} is optionally substituted C_{3-8} cycloalkyl or optionally substituted phenyl.

14. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is optionally substituted C_{2-9} heterocycloalkyl, optionally substituted monocyclic heteroaryl, or optionally substituted bicyclic heteroaryl, each of which containing 1-4 heteroatoms selected from O, S, N, P, and Si.

15. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is optionally substituted 5 membered monocyclic heteroaryl with 1 to 4 heteroatoms selected from N, O, S and P.

16. The compound of claim 15, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is imidazole, pyrazole, triazole, or tetrazole, each of which optionally substituted.

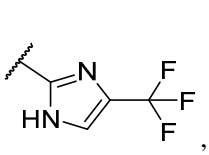
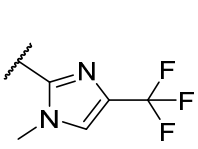
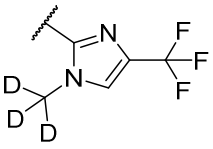
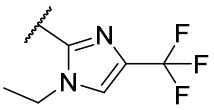
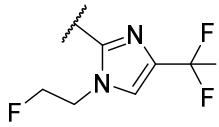
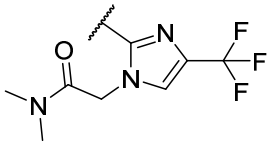
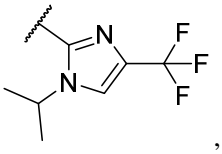
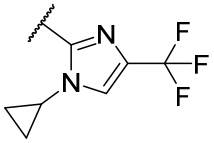
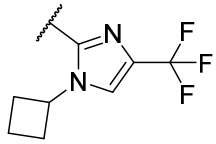
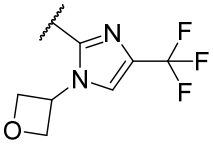
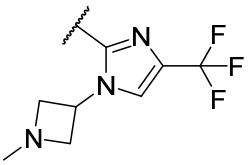
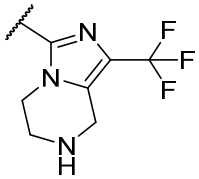
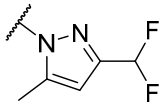
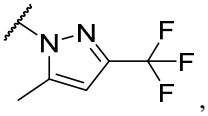
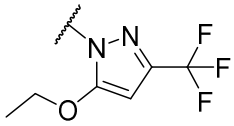
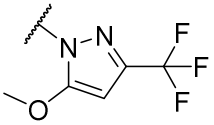
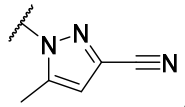
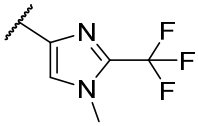
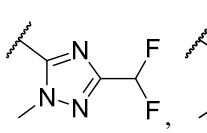
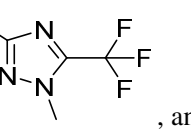
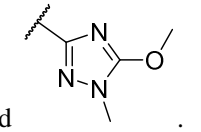
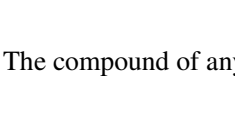
17. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is optionally substituted fused 5-6, 6-6 or 6-5 heteroaryl.

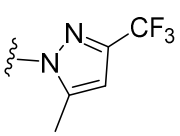
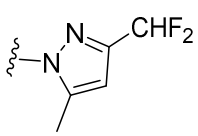
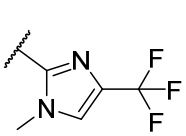
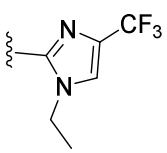
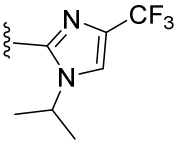
18. The compound of any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is optionally substituted with one or more substituents independently selected from halogen, $-NO_2$, oxo, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, 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, oxo, -CN, C_{1-3} alkoxy, C_{1-3} alkyl and C_{1-3} haloalkyl.

19. The compound of claim 18, 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.

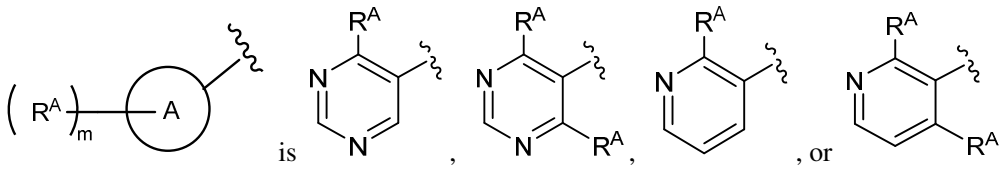
20. The compound of claim 18 or 19, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is

optionally substituted with one or more substituents independently selected from halogen, -OR^{11}, -NO_2, oxo, -CN, C_{1-3} haloalkyl, C_{1-3} alkyl, C_{1-3} aminoalkyl, C_{1-3} hydroxyalkyl, optionally substituted C_{1-4} heteroalkyl (e.g., -$CH_2C(=O)N(CH_3)_2$), optionally substituted C_{3-6} cycloalkyl, and optionally substituted C_{2-5} heterocycloalkyl.

21. The compound of any one of claims 14-16, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is selected from: , , , , , , , , , , , , , , , , , , , , , , , , , , and .

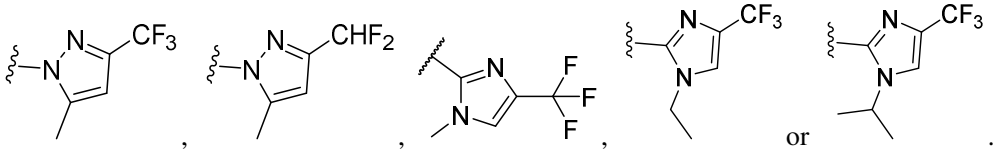
22. The compound of any one of claims 14-16, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is , , ,  or .

23. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein Y^1 is N or CR^{Y1}; Y^2 is N or CR^{Y2}; Y^3 is CR^{Y3}; Y^4 is CR^{Y4}; each of R^{Y1}, R^{Y2}, R^{Y3}, and R^{Y4} is independently hydrogen or C_1-C_6 alkyl; R^1 is hydrogen or C_1-C_6 alkyl;

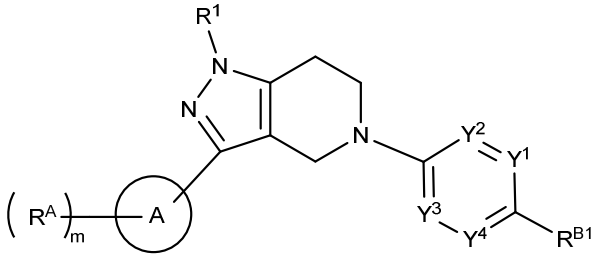


and each R^A is independently OH, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} haloalkyl, or C_3-C_6 cycloalkyl; and R^{B1} is 5 membered heteroaryl optionally substituted with one or more substituents selected from C_{1-3} haloalkyl and C_{1-3} alkyl.

24. The compound of claim 23, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is



25. A compound having the structure of Formula (IVa-2), or a pharmaceutically acceptable salt thereof,



Formula (IVa-2)

wherein

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

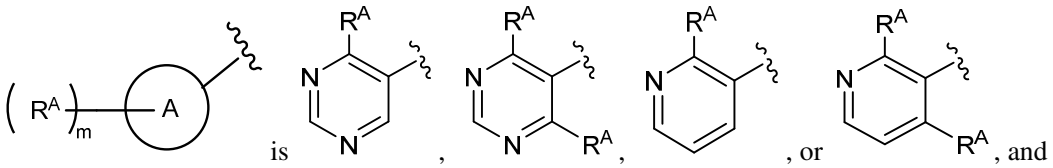
Y^2 is N or CR^{Y2};

Y^3 is CR^{Y3};

Y^4 is CR^{Y4};

each of R^{Y1}, R^{Y2}, R^{Y3}, and R^{Y4} is independently hydrogen or C_1-C_6 alkyl;

R^1 is hydrogen or C_1-C_6alkyl;

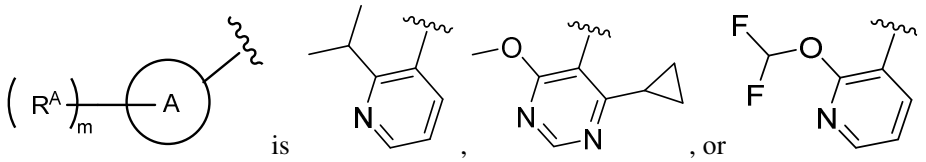


each R^A is independently OH, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} haloalkyl, or C_3-C_6 cycloalkyl; and R^{B1} is 5 membered heteroaryl optionally substituted with one or more substituents selected from C_{1-3} haloalkyl and C_{1-3} alkyl.

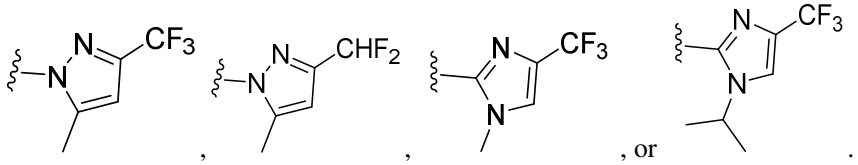
26. The compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein:
Y^1 is CH, Y^2 is CH, Y^3 is CH, and Y^4 is CH;
Y^1 is CH, Y^2 is N, Y^3 is CH, and Y^4 is CH; or
Y^1 is N, Y^2 is CH, Y^3 is CH, and Y^4 is CH.

27. The compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein R^1 is $-CH_3$.

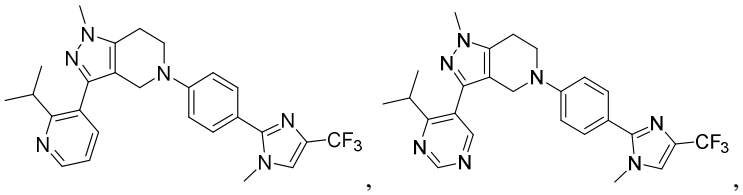
28. The compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein

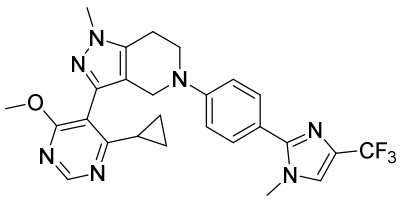


29. The compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein R^{B1} is



30. A compound or a pharmaceutically acceptable salt thereof, wherein the compound is

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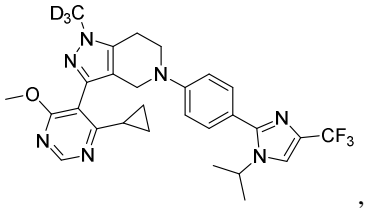
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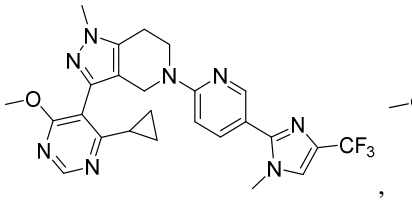
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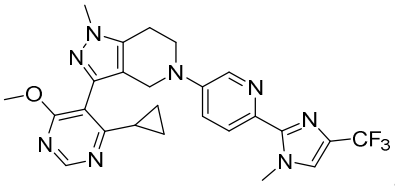
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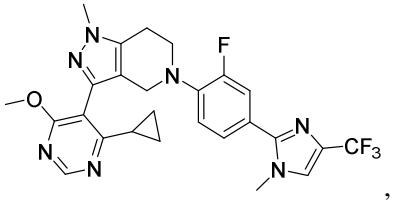
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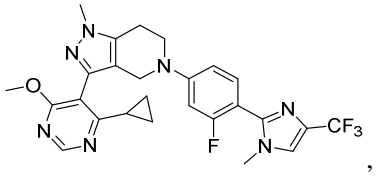
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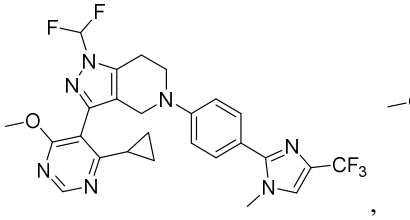
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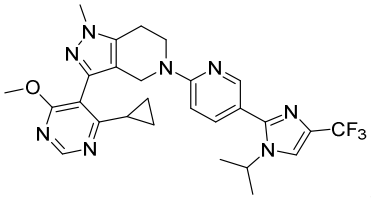
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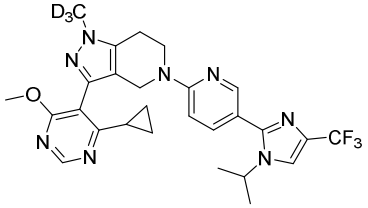
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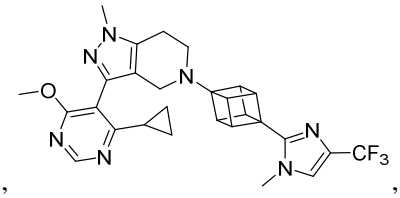
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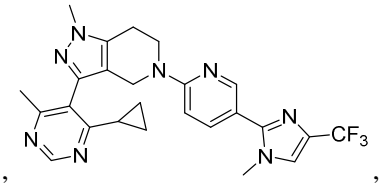
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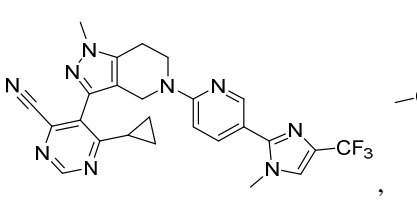
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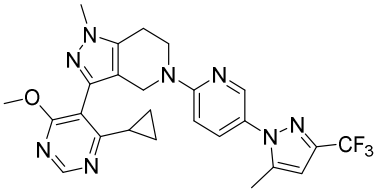
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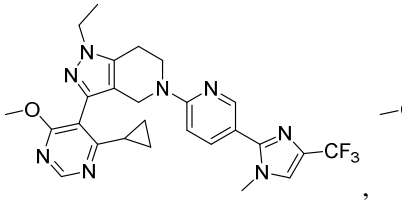
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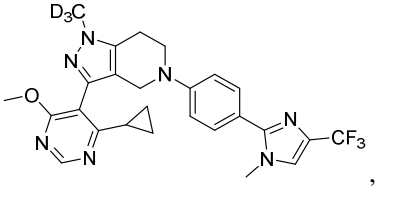
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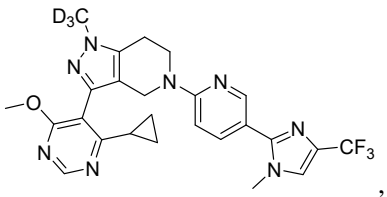
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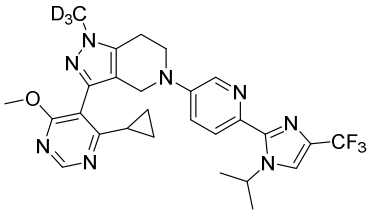
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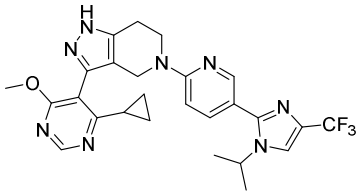
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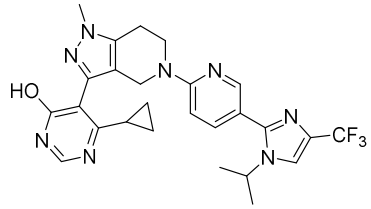
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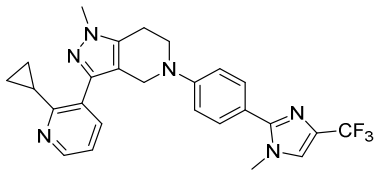
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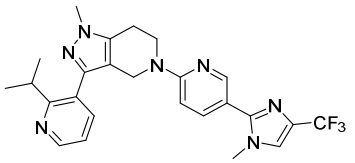
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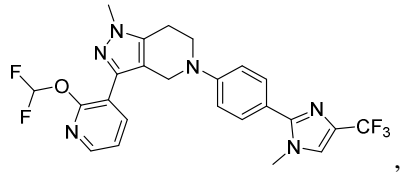
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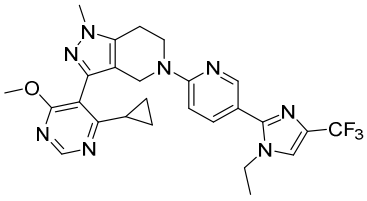
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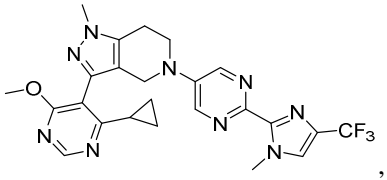
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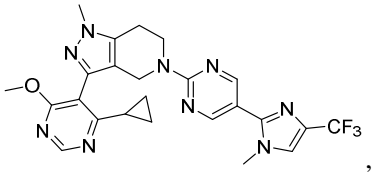
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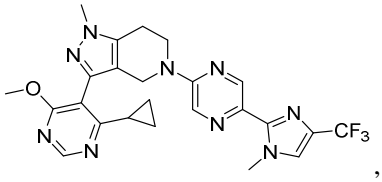
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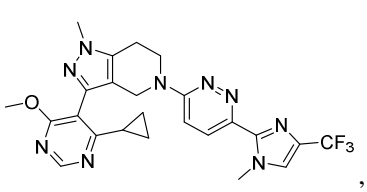
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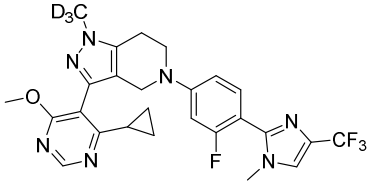
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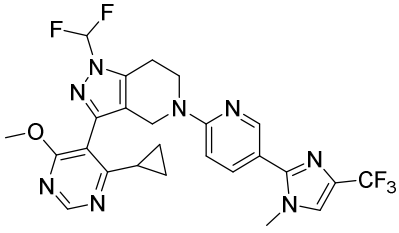
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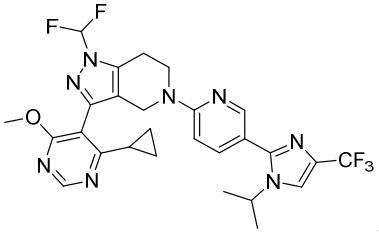
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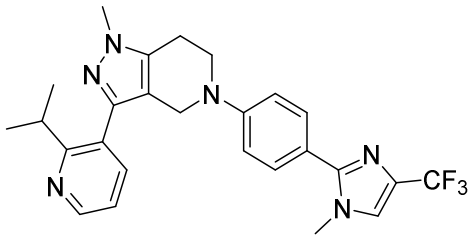
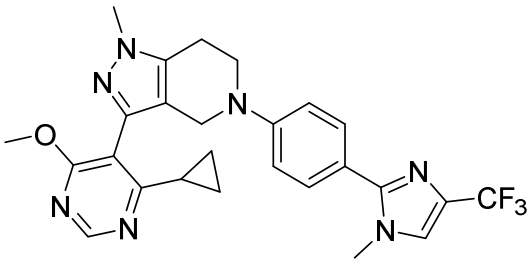
31. The compound of claim 25, which is:



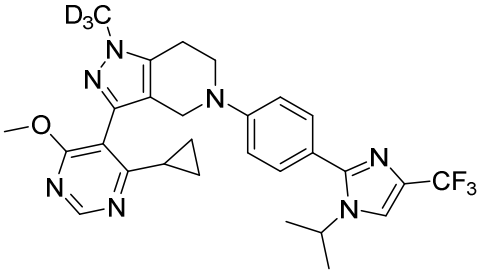
or a pharmaceutically acceptable salt thereof.

32. The compound of claim 25, which is:



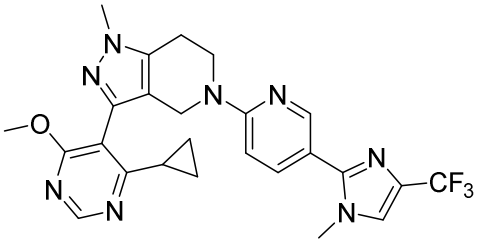
or a pharmaceutically acceptable salt thereof.

33. The compound of claim 25, which is:



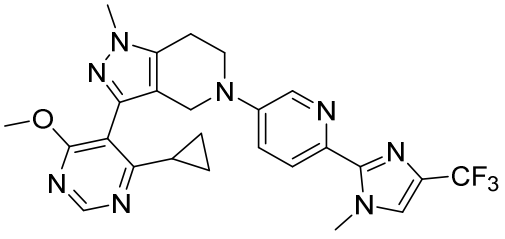
or a pharmaceutically acceptable salt thereof.

34. The compound of claim 25, which is:



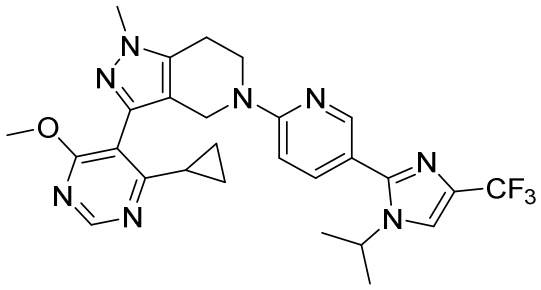
or a pharmaceutically acceptable salt thereof.

35. The compound of claim 25, which is:



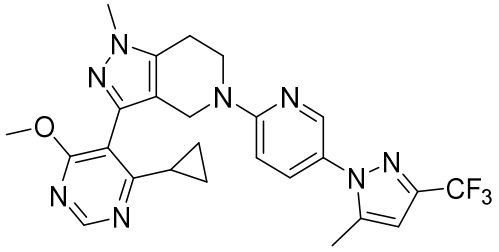
or a pharmaceutically acceptable salt thereof.

36. The compound of claim 25, which is:



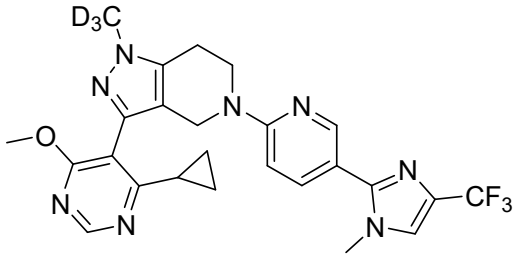
or a pharmaceutically acceptable salt thereof.

37. The compound of claim 25, which is:



or a pharmaceutically acceptable salt thereof.

38. The compound of claim 25, which is:



or a pharmaceutically acceptable salt thereof.

39. A pharmaceutical composition comprising a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

40. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for modulating or inhibiting ubiquitin specific protease 1 (USP1).

41. Use of a compound of any one of claims 1 to 38, 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).

42. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or disorder associated with ubiquitin specific protease (USP1) or associated with modulation of USP1.

43. The use of claim 42, wherein the disease or disorder is cancer.

44. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

45. The use of claim 43 or 44, 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.

46. The use of any one of claims 43 to 45, wherein the cancer comprises cancer cells with elevated levels of RAD 18.

47. The use of any one of claims 43 to 46, 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.