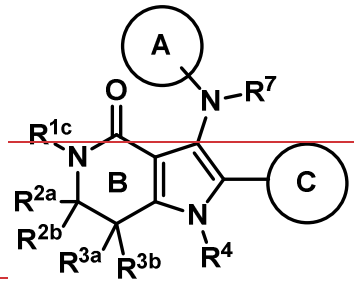
WHAT IS CLAIMED IS:

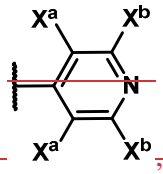
1. A compound of Formula (I):



Formula (I)

or a pharmaceutically acceptable salt thereof, wherein:

Ring C is selected from the group consisting of:



; wherein:

- each X^b is independently X^1, R^e, or H; and
- each X^a is independently selected from the group consisting of: H, halo; cyano; C_{1-10} alkyl which is optionally substituted with from 1-6 independently selected R^a; C_{2-6} alkenyl; $-S(O)_{1-2}(C_{1-4}$ alkyl); $-S(O)(=NH)(C_{1-4}$ alkyl); NR^eR^f; OH; $-S(O)_{1-2}NR'R''$; C_{1-4} thioalkoxy; NO_2; $C(=O)(C_{1-10}$ alkyl); $C(=O)O(C_{1-4}$ alkyl); $-C(=O)OH$; $-C(=O)NR'R''$; and $-SF_5$;

- 2-pyridyl or 3-pyridyl, each optionally substituted with X^1 and further optionally substituted with from 1-4 R^e;

- 2-pyridonyl or 4-pyridonyl, each optionally substituted with X^1 and further optionally substituted with from 1-4 R^e, wherein the ring nitrogen atom is optionally substituted with R^d;

- heteroaryl including 6 ring atoms, wherein from 2-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N(R^d),

and wherein the heteroaryl is optionally substituted with X^1 and further optionally substituted with from 1-4 R^e;

- heteroaryl including 5 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with X^1 and further optionally substituted with from 1-4 R^e;
- bicyclic heteroaryl including 7-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with X^1 and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e;
- C_{3-10} cycloalkyl or C_{3-10} cycloalkenyl, each of which is optionally substituted with X^1 and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e;
- heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with X^1 and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e; and
- C_{6-10} aryl optionally substituted with X^1 and further optionally substituted with from 1-4 R^e;

X^1 is $-(X^2)_m-L^1-R^5$, wherein: **m** is 0 or 1;

X^2 is selected from the group consisting of:

- -O-, -N(R^N)-, or -$S(O)_{0-2}$;
-  ;
- C_{2-6} alkenylene optionally substituted with from 1-3 R^a;
- C(=O)O *, -C(=O)N(R^N) *, or -$S(O)_{1-2}$N(R^N) *;
- -OC(=O) *, -N(R^N)C(=O) *, or -N(R^N)$S(O)_{1-2}$ *; and

- ~~$OC(=O)N(R^N)$ *, $N(R^N)C(=O)O$ *, $N(R^N)C(=O)N(R^N)$ *, or $N(R^N)S(O)_{1-2}N(R^N)$ *,~~

~~wherein the asterisk represents point of attachment to L^1;~~

~~L^1 is selected from the group consisting of: a bond and C_{1-10} alkylene optionally substituted with from 1-6 R^a;~~

~~R^5 is selected from the group consisting of:~~

- ~~H;~~
- ~~halo;~~
- ~~OH;~~
- ~~NR^eR^f;~~
- ~~C_{1-6} alkoxy or $S(O)_{0-2}(C_{1-6}$ alkyl), each optionally substituted with from 1-6 R^a;~~
- ~~R^g;~~
- ~~L^5-R^g;~~
- ~~R^{g2}-R^W or R^{g2}-R^Y; and~~
- ~~L^5-R^{g2}-R^W or L^5-R^{g2}-R^Y;~~

~~provided that:~~

~~when L^1 is a bond, then R^5 is selected from the group consisting of: H, R^g, R^{g2}-R^W, and R^{g2}-R^Y; and~~

~~X^1 is other than H, -OH, or NH_2;~~

~~L^5 is selected from the group consisting of: O, $S(O)_{0-2}$, NH, and $N(R^d)$;~~

~~R^W is L^W-W,~~

~~wherein L^W is C(=O), $S(O)_{1-2}$, OC(=O)*, NHC(=O)*, $NR^dC(=O)$*, $NHS(O)_{1-2}$*, or $NR^dS(O)_{1-2}$*, wherein the asterisk represents point of attachment to W, and~~

~~W is selected from the group consisting of:~~

- C_{2-6} alkenyl; C_{2-6} alkynyl; or C_{3-10} allenyl, each of which is optionally substituted with from 1-3 $\mathbf{R^a}$ and further optionally substituted with $\mathbf{R^g}$, wherein **W** is attached to $\mathbf{L^W}$ via an sp^2 or *sp* hybridized carbon atom, thereby providing an α, β-unsaturated system; and
- bicyclo[**x**.**y**.0]cycloalkyl optionally substituted with from 1-2 $\mathbf{R^e}$, wherein **x** is 1 or 2; and **y** is an integer from 1 to 6;

$\mathbf{R^Y}$ is selected from the group consisting of: $\mathbf{R^g}$ and $-(\mathbf{L^g})_g-\mathbf{R^g}$;

each of $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$ is independently selected from the group consisting of: H; halo; OH; C(O)OH or $C(O)NH_2$; CN; $\mathbf{R^b}$; $-\mathbf{L^b}-\mathbf{R^b}$; $N\mathbf{R^e}\mathbf{R^f}$; $\mathbf{R^g}$; $-(\mathbf{L^g})_g-\mathbf{R^g}$; $-(\mathbf{L^g})_g-\mathbf{R^W}$; $-(\mathbf{L^g})_g-\mathbf{R^{g2}}-\mathbf{R^W}$; and C_{1-6} alkoxy or C_{1-6} thioalkoxy, each optionally substituted with from 1-6 $\mathbf{R^a}$; provided that $\mathbf{R^{1c}}$ is other than halo, CN, or C(O)OH; or

two of variables $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$, together with the **Ring B** ring atoms to which each is attached, form a fused saturated or unsaturated ring of 3-12 ring atoms;

- wherein from 0-2 of the ring atoms are each an independently selected heteroatom (in addition to $N(\mathbf{R^{1c}})$ when $N(\mathbf{R^{1c}})$ forms part of the fused saturated or unsaturated ring), wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, $N(\mathbf{R^d})$, O, and $S(O)_{0-2}$; and
- wherein the fused saturated or unsaturated ring of 3-12 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo, $\mathbf{R^e}$, and $\mathbf{R^W}$; or

one of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ and one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ combine to form a double bond between the **Ring B** atoms to which each is attached;

Ring A is $\mathbf{R^g}$;

$\mathbf{R^4}$ and $\mathbf{R^7}$ are independently H or $\mathbf{R^d}$;

each occurrence of $\mathbf{R^a}$ is independently selected from the group consisting of: OH; halo; $N\mathbf{R^e}\mathbf{R^f}$; C_{1-4} alkoxy; C_{1-4} haloalkoxy; $-C(=O)O(C_{1-4}$ alkyl); $-C(=O)(C_{1-4}$ alkyl); $-C(=O)OH$; $-CON\mathbf{R'R''}$; $-S(O)_{1-2}N\mathbf{R'R''}$; $-S(O)_{1-2}(C_{1-4}$ alkyl); and cyano;

each occurrence of $\mathbf{R^b}$ is independently C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, each of which is optionally substituted with from 1-6 $\mathbf{R^a}$;

each occurrence of $\mathbf{L^b}$ is independently C(=O); C(=O)O; $S(O)_{1-2}$; C(=O)NH*; C(=O)N$\mathbf{R^d}$*; $S(O)_{1-2}$NH*; or $S(O)_{1-2}$N($\mathbf{R^d}$)*, wherein the asterisk represents point of attachment to $\mathbf{R^b}$;

each occurrence of $\mathbf{R^c}$ is independently selected from the group consisting of: halo; cyano; C_{1-10} alkyl which is optionally substituted with from 1-6 independently selected $\mathbf{R^a}$; C_{2-6} alkenyl; C_{2-6} alkynyl; C_{1-4} alkoxy optionally substituted with C_{1-4} alkoxy or C_{1-4} haloalkoxy; C_{1-4} haloalkoxy; $-S(O)_{1-2}(C_{1-4}$ alkyl); $-S(O)(=NH)(C_{1-4}$ alkyl); $-N\mathbf{R^e}\mathbf{R^f}$; -OH; $-S(O)_{1-2}N\mathbf{R'R''}$; $-C_{1-4}$ thioalkoxy; $-NO_2$; $-C(=O)(C_{1-10}$ alkyl); $-C(=O)O(C_{1-4}$ alkyl); -C(=O)OH; C(=O)N$\mathbf{R'R''}$; and SF_5;

each occurrence of $\mathbf{R^d}$ is independently selected from the group consisting of: C_{1-6} alkyl optionally substituted with from 1-3 independently selected $\mathbf{R^a}$; $-C(O)(C_{1-4}$ alkyl); $-C(O)O(C_{1-4}$ alkyl); $-CON\mathbf{R'R''}$; $-S(O)_{1-2}N\mathbf{R'R''}$; $-S(O)_{1-2}(C_{1-4}$ alkyl); -OH; and C_{1-4} alkoxy;

each occurrence of $\mathbf{R^e}$ and $\mathbf{R^f}$ is independently selected from the group consisting of: H; C_{1-6} alkyl optionally substituted with from 1-3 substituents each independently selected from the group consisting of $N\mathbf{R'R''}$, -OH, C_{1-6} alkoxy, C_{1-6} haloalkoxy, and halo; $-C(O)(C_{1-4}$ alkyl); $C(O)O(C_{1-4}$ alkyl); $CON\mathbf{R'R''}$; $S(O)_{1-2}N\mathbf{R'R''}$; $S(O)_{1-2}(C_{1-4}$ alkyl); -OH; and C_{1-4} alkoxy;

each occurrence of $\mathbf{R^g}$ is independently selected from the group consisting of:

- C_{3-10} cycloalkyl or C_{3-10} cycloalkenyl, each of which is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$;
- heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group

consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e;

- heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e; and
- C_{6-10} aryl optionally substituted with from 1-4 R^e;

each occurrence of L^g is independently selected from the group consisting of: -O-, -NH-, -NR^d-, $S(O)_{0-2}$, C(O), and C_{1-3} alkylene optionally substituted with from 1-3 R^a;

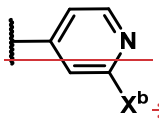
each **g** is independently 1, 2, or 3;

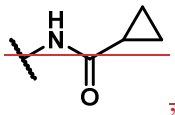
each R^{g2} is a divalent R^g group;

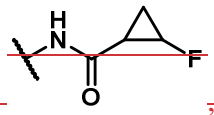
each occurrence of **R'** and **R''** is independently selected from the group consisting of: H; -OH; and C_{1-4} alkyl; and

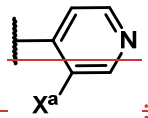
each occurrence of R^N is independently H, C_{1-3} alkyl, or C_{3-6} cycloalkyl,

provided that one or more of the following applies:

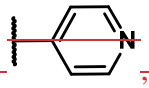
- when R^{2a} and R^{2b} are H or methyl; R^{3a} and R^{3b} are H; **Ring C** is 

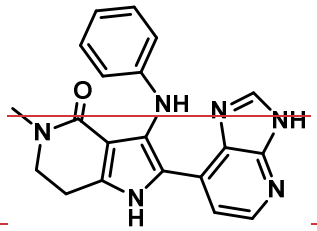
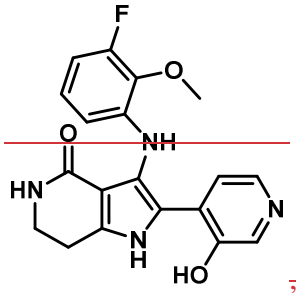
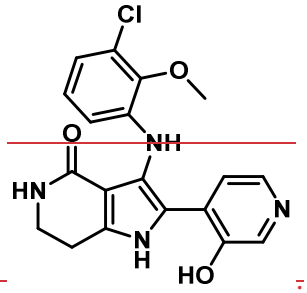
; and X^b is H, methyl, NH_2, NHC(=O)Me, NHC(=O)iPr, NHC(=O)NHEt, 

, 

, then **Ring A** is other than unsubstituted phenyl;
- when R^{2a}, R^{2b}, R^{3a}, and R^{3b} are each H; **Ring C** is 

; and X^a is methyl or F, then **Ring A** is other than unsubstituted phenyl;

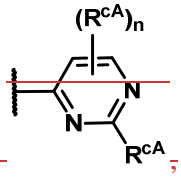
- when **R**^{1e}, **R**^{2a}, **R**^{2b}, **R**^{3a}, and **R**^{3b} are each H; **Ring C** is  , then **Ring A** is other than 4-fluorophenyl; and

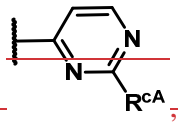
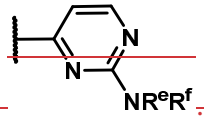
- the compound is other than:  ,  , or  .

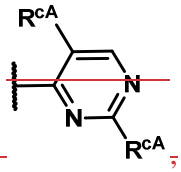
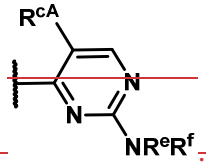
2. The compound of claim 1, wherein **Ring C** is heteroaryl including 6 ring atoms, wherein from 2-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N(**R**^{d}), and wherein the heteroaryl is optionally substituted with **X**^{1} and further optionally substituted with from 1-4 **R**^{eA}, wherein each **R**^{eA} is an independently selected **R**^{e}.

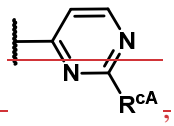
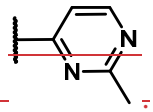
3. The compound of claims 1 or 2, wherein **Ring C** is heteroaryl including 6 ring atoms, wherein from 2-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N(**R**^{d}), and wherein the heteroaryl is optionally substituted with from 1-3 **R**^{eA}, wherein each **R**^{eA} is an independently selected **R**^{e}.

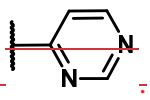
4. The compound of any one of claims 1-3, wherein **Ring C** is pyrimidyl optionally substituted with from 1-3 **R**^{eA}, such as pyrimidyl substituted with from 1-2 **R**^{eA}, wherein each **R**^{eA} is an independently selected **R**^{e}.

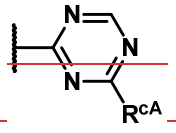
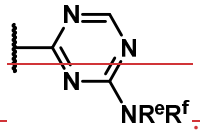
5. The compound of any one of claims 1-4, wherein **Ring C** is  ; wherein each R^{cA} is an independently selected R^{c}; and **n** is 0, 1, or 2.

6. The compound of any one of claims 1-5, wherein **Ring C** is  ; such as  .

7. The compound of any one of claims 1-5, wherein **Ring C** is  ; such as  .

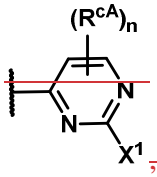
8. The compound of any one of claims 1-6, wherein **Ring C** is  ; wherein R^{cA} is C_{1-3} alkyl optionally substituted with from 1-3 independently selected halo. For example, **Ring C** is  .

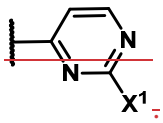
9. The compound of any one of claims 1-4, wherein **Ring C** is  .

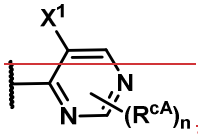
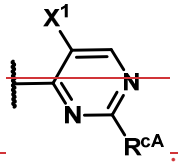
10. The compound of any one of claims 1-3, wherein **Ring C** is triazinyl optionally substituted with from 1-2 R^{cA}, wherein each R^{cA} is an independently selected R^e, such as wherein **Ring C** is  , such as  .

11. The compound of claims 1 or 2, wherein **Ring C** is heteroaryl including 6 ring atoms, wherein from 2-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N(R^d), and wherein the heteroaryl is substituted with X^1 and further optionally substituted with from 1-2 R^{cA}, wherein each R^{cA} is an independently selected R^e.

12. The compound of any one of claims 1-2 or 11, wherein **Ring C** is pyrimidyl substituted with X^1 and further optionally substituted with from 1-2 R^{cA}, wherein each R^{cA} is an independently selected R^e.

13. The compound of any one of claims 1-2 or 11-12, wherein **Ring C** is  , wherein each R^{cA} is an independently selected R^e; and **n** is 0, 1, or 2.

14. The compound of any one of claims 1-2 or 11-13, wherein **Ring C** is  .

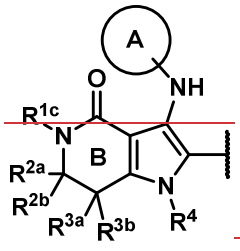
15. The compound of any one of claims 1-2 or 11-12, wherein **Ring C** is  , wherein **n** is 0, 1, or 2; and each R^{cA} is an independently selected R^{e}, such as wherein **Ring C** is  .

16. The compound of claim 1, wherein **Ring C** is bicyclic heteroaryl including 7-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, and wherein the heteroaryl is optionally substituted with X^{1} and further optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^{e}.

17. The compound of claims 1 or 16, wherein **Ring C** is bicyclic heteroaryl including 9-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, and wherein the heteroaryl is optionally substituted with X^{1} and further optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^{e}.

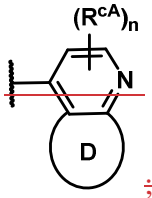
18. The compound of any one of claims 1 or 16-17, wherein **Ring C** is bicyclic heteroaryl including 9-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^{e}.

19. The compound of claims 17 or 18, wherein **Ring C** is connected to



via a 6-membered ring.

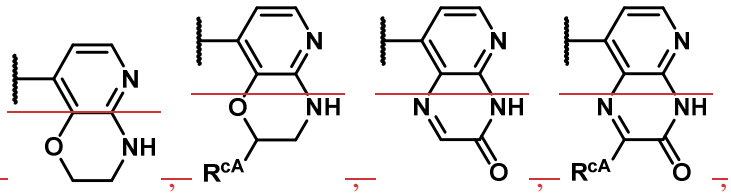
20. The compound of any one of claims 1 or 16-19, wherein **Ring C** is

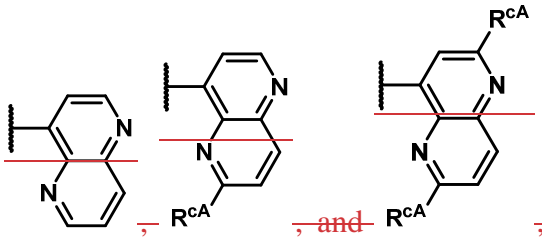


; **Ring D** is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}; **n** is 0, 1, or 2; and each **R**^{cA} is an independently selected **R**^{e}.

21. The compound of claim 20, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}.

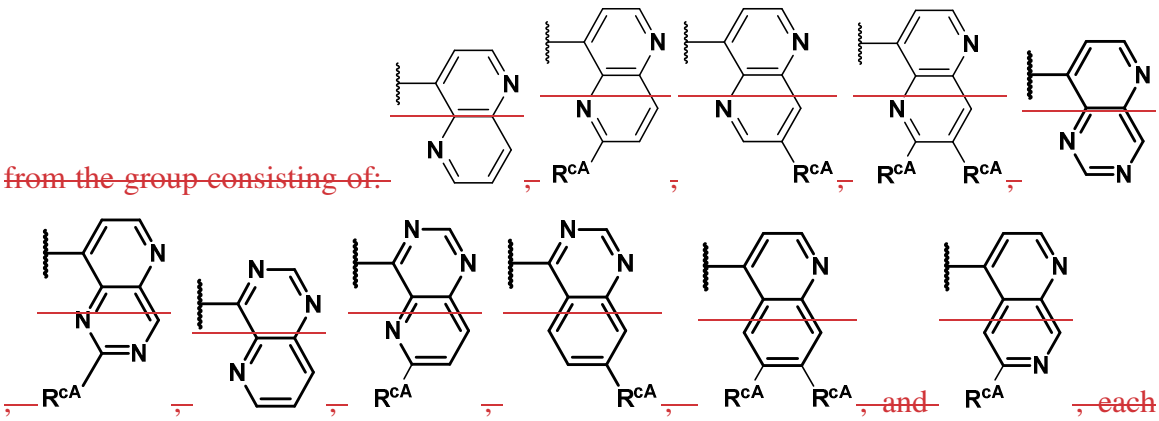
22. The compound of any one of claims 1 or 16-21, wherein **Ring C** is selected from the group consisting of:





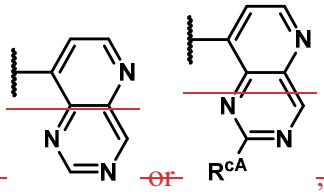
, each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.

23. The compound of any one of claims 1 or 16-21, wherein **Ring C** is selected from the group consisting of:



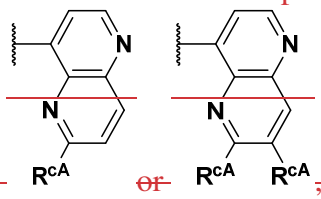
, each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.

24. The compound of any one of claims 1, 16-21, or claim 23, wherein **Ring C** is

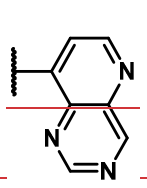
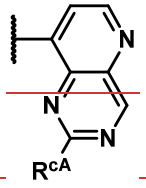
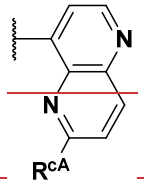
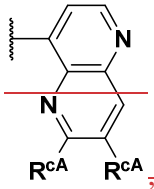


, wherein R^{cA} is an independently selected R^{c}.

25. The compound of any one of claims 1, 16-21, or claim 23, wherein **Ring C** is



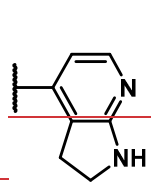
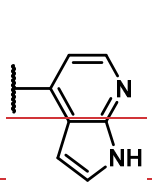
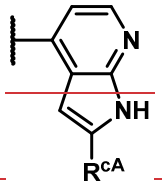
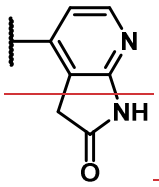
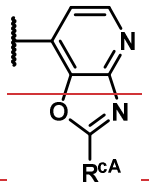
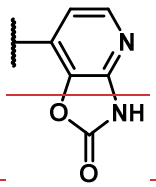
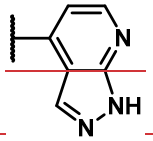
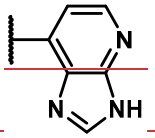
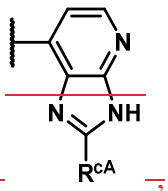
, wherein each R^{cA} is an independently selected R^{c}.

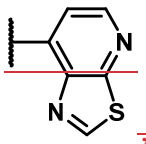
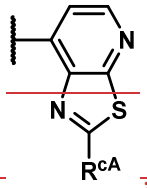
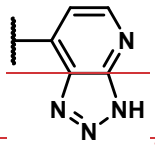
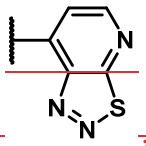
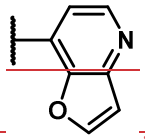
26. The compound of any one of claims 1, 16-21, or claim 23, wherein **Ring C** is selected from the group consisting of:  ,  ,  , and  , wherein:

each occurrence of $\mathbf{R}^{eA}$ is independently selected from the group consisting of: halo; $N\mathbf{R}^{e}\mathbf{R}^{f}$; C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; C_{1-3} alkyl substituted with from 1-3 independently selected halo; C_{1-3} alkyl substituted with C_{1-4} alkoxy; and C_{1-4} alkoxy substituted with C_{1-4} alkoxy;

such as wherein each occurrence of $\mathbf{R}^{eA}$ is independently selected from the group consisting of: C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-3 independently selected halo.

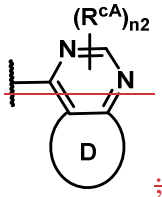
27. The compound of claim 20, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), $N(\mathbf{R}^{d})$, O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R}^{eA}$.

28. The compound of any one of claims 1, 16-20, or 27, wherein **Ring C** is selected from the group consisting of:  ,  ,  , (e.g., ),  (e.g., ),  ,  ,  ,

, each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.

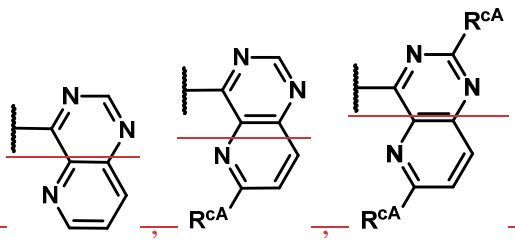
29. The compound of any one of claims 1 or 16-19, wherein **Ring C** is



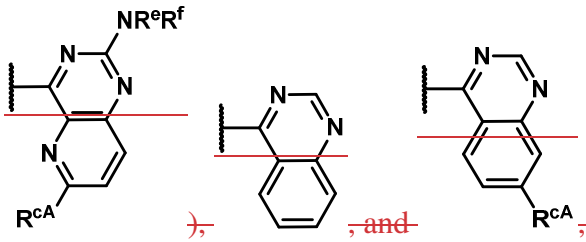
; **Ring D** is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}; **n2** is 0 or 1; and each R^{cA} is an independently selected R^{c}.

30. The compound of claim 29, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.

31. The compound of any one of claims 1, 16-19, or 29-30, wherein **Ring C** is selected from the group consisting of:

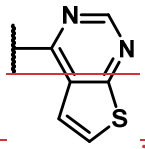
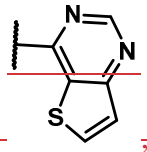
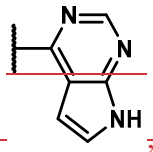
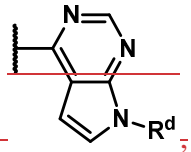
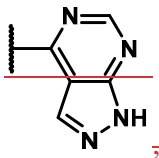
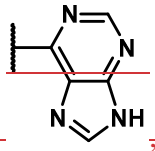


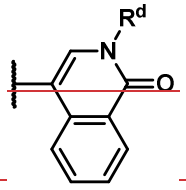
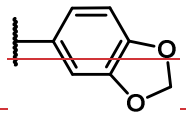
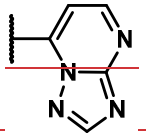
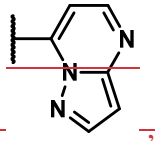
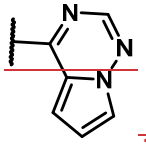
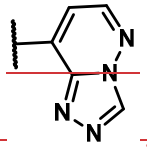
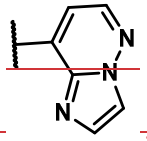
(e.g.,

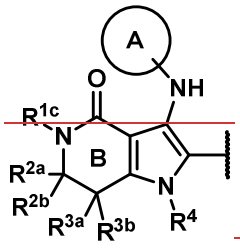


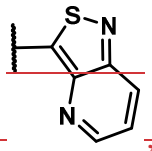
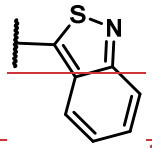
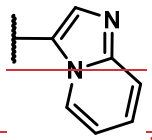
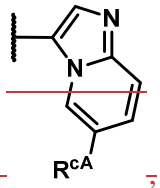
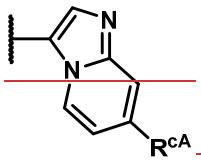
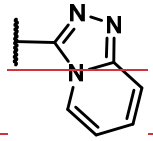
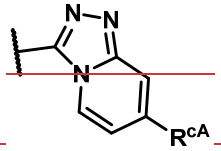
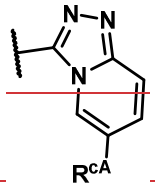
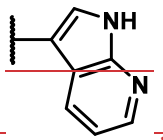
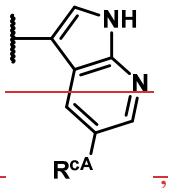
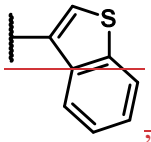
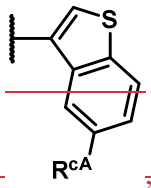
), and , each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.

32. The compound of claim 29, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{eA}.

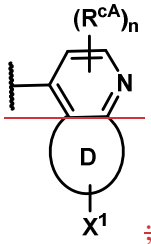
33. The compound of any one of claims 1, 16-19, 29, or 32, wherein **Ring C** is selected from the group consisting of:  ,  ,  ,  ,  , and  , each further optionally substituted with **R**^{eA}, wherein each **R**^{eA} is an independently selected **R**^{e}.

34. The compound of any one of claims 1 or 16-19, wherein **Ring C** is selected from the group consisting of:  ,  ,  ,  ,  ,  , and  , each further optionally substituted with **R**^{eA}, wherein each **R**^{eA} is an independently selected **R**^{e}.

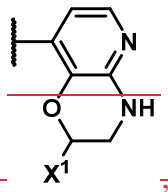
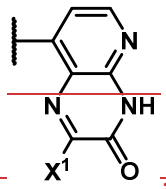
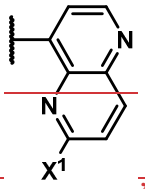
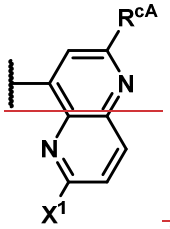
35. The compound of claims 17 or 18, wherein **Ring C** is connected to  via a 5-membered ring.

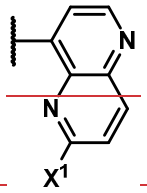
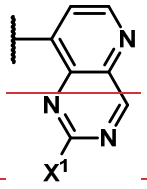
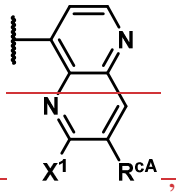
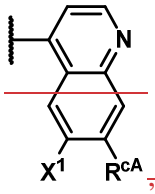
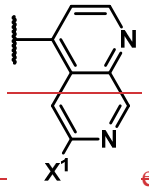
36. The compound of any one of claims 1, 16-18, or 35, wherein **Ring C** is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  , each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{e}.

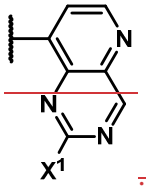
37. The compound of any one of claims 1 or 16-17, wherein **Ring C** is bicyclic heteroaryl including 9-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, and wherein the heteroaryl is substituted with X^{1} and further optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^{e}.

38. The compound of any one of claims 1, 16-17, 19, or 37, wherein **Ring C** is  ; **Ring D** is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}; **n** is 0, 1, or 2; and each R^{cA} is an independently selected R^{e}.

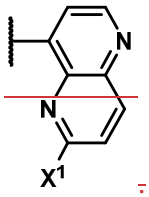
39. The compound of claim 38, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}.

40. The compound of any one of claims 1, 16-17, 19, or 37-39, wherein **Ring C** is selected from the group consisting of:  ,  ,  , and  , each further optionally substituted with **R**^{cA}, wherein each **R**^{cA} is an independently selected **R**^{e}.

41. The compound compound of any one of claims 1, 17, or 37, wherein **Ring C** is selected from the group consisting of:  ,  ,  ,  , and  each of which is further optionally substituted with from 1-2 **R**^{cA}, wherein each **R**^{cA} is an independently selected **R**^{e}.

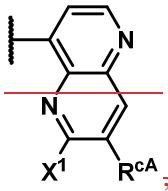
42. The compound of any one of claims 1, 17, 37, or 41, wherein **Ring C** is  .

43. The compound of any one of claims 1, 17, 37, or 41, wherein **Ring C** is



.

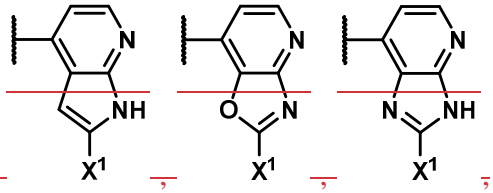
44. The compound of any one of claims 1, 17, 37, or 41, wherein **Ring C** is

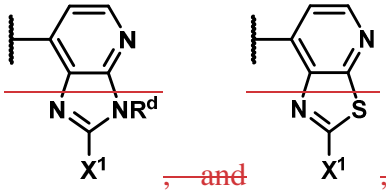


, wherein $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

45. The compound of claim 38, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R}^{d}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R}^{cA}$.

46. The compound of any one of claims 1, 16-17, 19, 37-38, or 45, wherein **Ring C** is selected from the group consisting of:

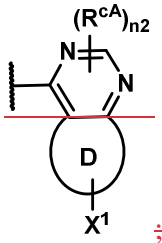




, and

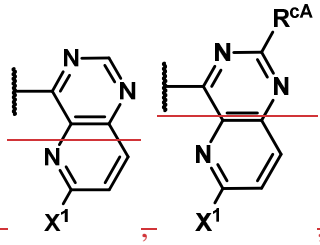
, each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

47. The compound of any one of claims 1, 16-17, 19, or 37, wherein **Ring C** is



; **Ring D** is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}; **n2** is 0 or 1; and each **R**^{cA} is an independently selected **R**^{c}.

48. The compound of claim 47, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}.

49. The compound of any one of claims 1, 16-17, 19, or 47-48, wherein **Ring C** is selected from the group consisting of:  , each further optionally substituted with **R**^{cA}, wherein each **R**^{cA} is an independently selected **R**^{c}.

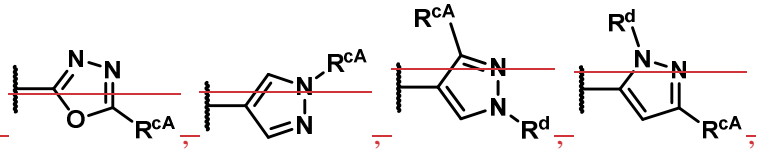
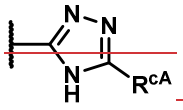
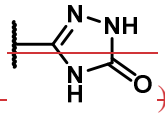
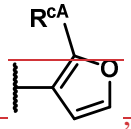
50. The compound of claim 47, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}.

51. The compound of claim 1, wherein **Ring C** is heteroaryl including 5 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, and wherein the heteroaryl is

optionally substituted with X^1 and further optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^c.

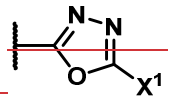
52. The compound of claims 1 or 51, wherein **Ring C** is heteroaryl including 5 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^c.

53. The compound of any one of claims 1 or 51-52, wherein **Ring C** is selected from the group consisting of: pyrazolyl, imidazolyl, thiazolyl, oxazolyl, triazolyl, furanyl, thiophenyl, oxadiazolyl, and thiadiazolyl, each optionally substituted with from 1-2 R^{cA}, wherein a ring nitrogen atom is optionally substituted with R^d, and each R^{cA} is an independently selected R^c.

54. The compound of any one of claims 1 or 51-53, wherein **Ring C** is selected from the group consisting of:   (e.g., ),  , and  .

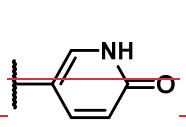
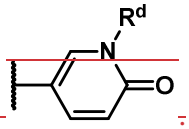
55. The compound of claims 1 or 51, wherein **Ring C** is heteroaryl including 5 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, and wherein the heteroaryl is substituted with X^1 and further optionally substituted with from 1-2 R^{cA}, wherein each R^{cA} is an independently selected R^c.

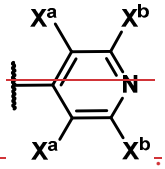
56. The compound of any one of claims 1, 51, or 55, wherein **Ring C** is selected from the group consisting of: pyrazolyl, imidazolyl, thiazolyl, oxazolyl, triazolyl, furanyl, thiophenyl, oxadiazolyl, and thiadiazolyl, each substituted with X^1 and further optionally

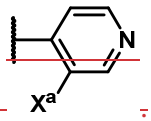
substituted with from 1-2 R^{eA}, wherein a ring nitrogen atom is optionally substituted with R^d, and each R^{eA} is an independently selected R^e, such as wherein **Ring C** is  .

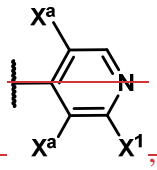
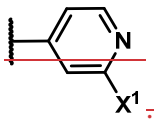
57. The compound of claim 1, wherein **Ring C** is 2-pyridonyl or 4-pyridonyl, each optionally substituted with X^1 and further optionally substituted with from 1-4 R^{eA}, wherein the ring nitrogen atom is optionally substituted with R^d, wherein each R^{eA} is an independently selected R^e.

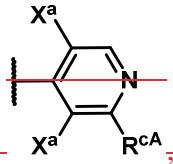
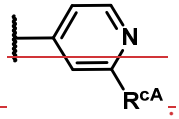
58. The compound of claims 1 or 57, wherein **Ring C** is 2-pyridonyl which is optionally substituted with X^1 and further optionally substituted with from 1-4 R^{eA}, wherein the ring nitrogen atom is optionally substituted with R^d, wherein each R^{eA} is an independently selected R^e.

59. The compound of any one of claims 1 or 57-58, wherein **Ring C** is 2-pyridonyl which is optionally substituted with from 1-4 R^{eA}, wherein the ring nitrogen atom is optionally substituted with R^d, wherein each R^{eA} is an independently selected R^e, such as wherein **Ring C** is  or  .

60. The compound of claim 1, wherein **Ring C** is  .

61. The compound of claim 1 or 60, wherein **Ring C** is  .

62. The compound of claim 1 or 60, wherein **Ring C** is  , such as  .

63. The compound of claim 1 or 60, wherein **Ring C** is  , wherein **R**^{cA} is an independently selected **R**^{c}, such as wherein **Ring C** is  .

64. The compound of any one of claims 1 or 63, wherein each **X**^{a} is selected from the group consisting of: H; halo; and C_{1-6} alkyl optionally substituted with from 1-6 **R**^{a}.

65. The compound of any one of claims 1 or 63-64, wherein from 1-2, such as 1, occurrence of **X**^{a} is independently a substituent other than H.

66. The compound of any one of claims 1 or 63-64, wherein one occurrence of **X**^{a} is halo, such as –F or –Cl.

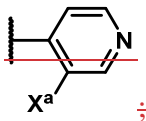
67. The compound of any one of claims 1 or 63-66, wherein one occurrence of **X**^{a} is –F.

68. The compound of any one of claims 1 or 63-65, wherein one occurrence of **X**^{a} is C_{1-3} alkyl optionally substituted with from 1-6 **R**^{a}.

69. The compound of any one of claims 1 or 63-65, or 68, wherein one occurrence of X^a is C_{1-3} alkyl substituted with from 1-3 independently selected halo, such as $-CF_3$ or $-CHF_2$.

70. The compound of any one of claims 1 or 63-64, wherein each X^a is –H.

71. The compound of any one of claims 1 or 60-61, wherein **Ring C** is



; wherein X^a is selected from the group consisting of: –F; –Cl; –H; and C_{1-3} alkyl optionally substituted with from 1-3 independently selected halo.

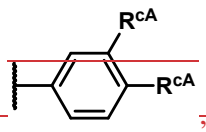
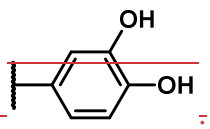
72. The compound of claim 71, wherein X^a is –F.

73. The compound of claim 71, wherein X^a is –Cl.

74. The compound of claim 71, wherein X^a is –H.

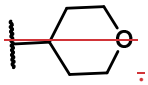
75. The compound of claim 71, wherein X^a is C_{1-3} alkyl substituted with from 1-3 independently selected halo, such as $-CF_3$ or $-CHF_2$.

76. The compound of claim 1, wherein **Ring C** is C_{6-10} aryl optionally substituted with X^1 and further optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^c.

77. The compound of claims 1 or 76, wherein **Ring C** is phenyl optionally substituted with from 1-4 R^{cA}, wherein each R^{cA} is an independently selected R^c, such as wherein **Ring C** is  , such as  .

78. The compound of claim 1, wherein **Ring C** is heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with **X**^{1} and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and **R**^{eA}, wherein each **R**^{eA} is an independently selected **R**^{e}.

79. The compound of claims 1 or 78, wherein **Ring C** is heterocyclyl including from 4-8, such as 5-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, and wherein the heterocyclyl is optionally substituted with **X**^{1} and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and **R**^{eA}, wherein each **R**^{eA} is an independently selected **R**^{e}, such as wherein **Ring C** is



.

80. The compound of any one of claims 1-79, wherein **m** is 1.

81. The compound of any one of claims 1-80, wherein **X**^{2} is selected from the group consisting of: -O-, -N(**R**^{N})-, and -S(O)$_{0-2}$-.

82. The compound of any one of claims 1-81, wherein **X**^{2} is -N(**R**^{N})-.

83. The compound of any one of claims 1-82, wherein **X**^{2} is -N(H)-.

84. The compound of any one of claims 1-81, wherein **X**^{2} is -O-.

85. The compound of any one of claims 1-80, wherein **X**^{2} is selected from the group consisting of: -OC(=O)-*, -N(**R**^{N})C(=O)-*, and -N(**R**^{N})S(O)$_{1-2}$-*.

86. The compound of any one of claims 1-80 or 85, wherein **X**^{2} is -N(**R**^{N})C(=O)-*.

87. The compound of any one of claims 1-80 or 85-86, wherein $\mathbf{X^2}$ is –N(H)C(=O)-*.

88. The compound of any one of claims 1-80 or 85, wherein $\mathbf{X^2}$ is –N($\mathbf{R^N}$)S(O)$_2$-*, such as –NHS(O)$_2$-.

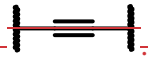
89. The compound of any one of claims 1-57, wherein $\mathbf{X^2}$ is selected from the group consisting of: –OC(=O)N($\mathbf{R^N}$)-*, –N($\mathbf{R^N}$)C(=O)O-*, –N($\mathbf{R^N}$)C(=O)N($\mathbf{R^N}$)-*, and –N($\mathbf{R^N}$)S(O)$_{1-2}$N($\mathbf{R^N}$)-*.

90. The compound of any one of claims 1-80 or 89, wherein $\mathbf{X^2}$ is –N($\mathbf{R^N}$)C(=O)O-*, such as –N(H)C(=O)O-*.

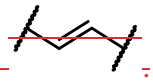
91. The compound of any one of claims 1-80 or 89, wherein $\mathbf{X^2}$ is –N($\mathbf{R^N}$)C(=O)N($\mathbf{R^N}$)-*, such as –N(H)C(=O)N(H)-*.

92. The compound of any one of claims 1-80 or 89, wherein $\mathbf{X^2}$ is –C(=O)O-*, –C(=O)N($\mathbf{R^N}$)-*, or –S(O)$_{1-2}$N($\mathbf{R^N}$)-*.

93. The compound of any one of claims 1-80 or 92, wherein $\mathbf{X^2}$ is –C(=O)N($\mathbf{R^N}$)-*, such as –C(=O)N(H)-*.

94. The compound of any one of claims 1-80, wherein $\mathbf{X^2}$ is  .

95. The compound of any one of claims 1-80, wherein $\mathbf{X^2}$ is C$_{2-6}$ alkenylene optionally substituted with from 1-3 $\mathbf{R^a}$.

96. The compound of any one of claims 1-80 or 95, wherein $\mathbf{X^2}$ is  .

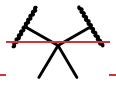
97. The compound of any one of claims 1-79, wherein **m** is 0.

98. The compound of any one of claims 1-97, wherein $\mathbf{L^1}$ is a bond.

99. The compound of any one of claims 1-97, wherein $\mathbf{L^1}$ is C_{1-10} alkylene optionally substituted with from 1-6 $\mathbf{R^a}$.

100. The compound of any one of claims 1-97 or 99, wherein $\mathbf{L^1}$ is C_{1-3} alkylene optionally substituted with from 1-6 $\mathbf{R^a}$, such as wherein $\mathbf{L^1}$ is unsubstituted C_{1-3} alkylene.

101. The compound of any one of claims 1-97 or 99-100, wherein $\mathbf{L^1}$ is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CF_2-$, or $-CH(Me)-$, such as wherein $\mathbf{L^1}$ is $-CH_2-$, $-CH_2CH_2-$, or $-CH(Me)-$.

102. The compound of any one of claims 1-97 or 99, wherein $\mathbf{L^1}$ is branched C_{3-6} alkylene optionally substituted with from 1-6 $\mathbf{R^a}$, such as wherein $\mathbf{L^1}$ is  or 

, wherein ***aa*** is the point of attachment to $\mathbf{R^5}$.

103. The compound of any one of claims 1-97 or 99-102, wherein $\mathbf{R^5}$ is $-C_{1-6}$ alkoxy or $-S(O)_{0-2}(C_{1-6}$ alkyl), each optionally substituted with from 1-6 $\mathbf{R^a}$.

104. The compound of any one of claims 1-97 or 99-103, wherein $\mathbf{R^5}$ is $-C_{1-6}$ alkoxy optionally substituted with from 1-6 $\mathbf{R^a}$.

105. The compound of any one of claims 1-97 or 99-104, wherein $\mathbf{R^5}$ is $-C_{1-3}$ alkoxy, such as methoxy.

106. The compound of any one of claims 1-102, wherein $\mathbf{R^5}$ is H or halo, such as wherein $\mathbf{R^5}$ is H or -F.

107. The compound of any one of claims 1-102 or 106, wherein $\mathbf{R^5}$ is H.

108. The compound of any one of claims 1-97 or 99-102, wherein $\mathbf{R^5}$ is -OH or $-N\mathbf{R^e}\mathbf{R^f}$.

109. The compound of any one of claims 1-97, 99-102, or 108, wherein R^5 is –OH.

110. The compound of any one of claims 1-97, wherein R^5 is $-R^g$.

111. The compound of any one of claims 1-97 or 110, wherein R^5 is selected from the group consisting of:

- heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e; and
- C_{6-10} aryl optionally substituted with from 1-4 R^e.

112. The compound of any one of claims 1-97 or 110-111, wherein R^5 is C_{6-10} aryl optionally substituted with from 1-4 R^e.

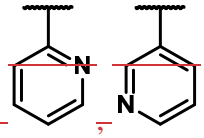
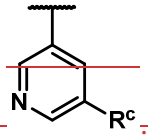
113. The compound of any one of claims 1-97 or 110-112, wherein R^5 is phenyl optionally substituted with from 1-4 R^e.

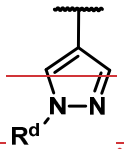
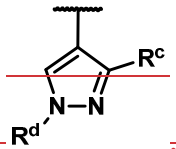
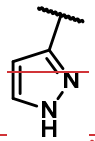
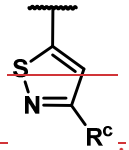
114. The compound of any one of claims 1-102 or 110-113, wherein R^5 is phenyl optionally substituted with from 1-2 independently selected halo, such as –F.

115. The compound of any one of claims 1-97 or 110-111, wherein R^5 is heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e.

116. The compound of any one of claims 1-97, 110-111, or 115, wherein R^5 is heteroaryl including from 5-6 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e.

117. The compound of any one of claims 1-97, 110-111, or 115-116, wherein R^5 is heteroaryl including 6 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each

independently selected from the group consisting of N, N(H), and N(R^d), and wherein the heteroaryl is optionally substituted with from 1-4 R^e, such as wherein R^5 is  ,  , or .

118. The compound of any one of claims 1-97, 110-111, or 115-116, wherein R^5 is heteroaryl including 5 ring atoms, wherein from 1-4, such as 2-4, ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e, such as wherein R^5 is  ,  ,  , or  .

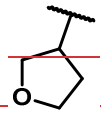
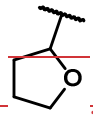
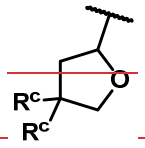
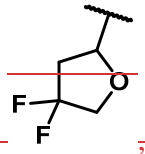
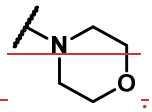
119. The compound of any one of claims 1-97 or 110, wherein R^5 is selected from the group consisting of:

- C_{3-10} cycloalkyl or C_{3-10} cycloalkenyl, each of which is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e; and
- heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e.

120. The compound of any one of claims 1-97, 110, or 119, wherein R^5 is C_{3-10} cycloalkyl or C_{3-10} cycloalkenyl, each of which is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e.

121. The compound of any one of claims 1-97, 110, or 119-120, wherein R^5 is C_{3-10} cycloalkyl, such as C_{3-6} cycloalkyl, optionally substituted with from 1-4 R^e, such as wherein R^5 is cyclopropyl.

122. The compound of any one of claims 1-97, 110, or 119, wherein R^5 is heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e.

123. The compound of any one of claims 1-97, 110, 119, or 122, wherein R^5 is heterocyclyl including from 4-8, such as 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e, such as wherein R^5 is  ,  ,  , such as  , or  .

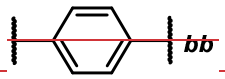
124. The compound of any one of claims 1-97, wherein R^5 is selected from the group consisting of: $-R^{g2}-R^W$ and $-R^{g2}-R^Y$.

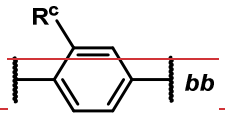
125. The compound of any one of claims 1-97, or 124, wherein R^5 is $-R^{g2}-R^Y$.

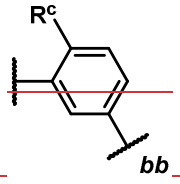
126. The compound of claims 124 or 125, wherein the $-R^{g2}-$ group present in R^5 is C_{6-10} arylene optionally substituted with from 1-4 R^e.

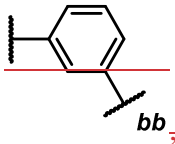
127. The compound of any one of claims 124-126, wherein the $-R^{g2}-$ group present in R^5 is phenylene optionally substituted with from 1-4 R^e.

128. The compound of any one of claims 124-127, wherein the $-R^{g2}-$ group present in R^5 is 1,3-phenylene or 1,4-phenylene, each optionally substituted with from 1-4

R^e, such as wherein $-R^{g2}$ is 

, 

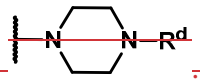
, 

, or 

, wherein ***bb*** is the point of attachment to $R^{¥}$.

129. The compound of any one of claims 101-105, wherein the $R^{¥}$ group present in R^5 is $-R^g$.

130. The compound of any one of claims 124-129, wherein the $R^{¥}$ group present in R^5 is heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e.

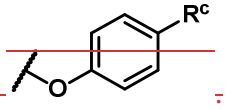
131. The compound of any one of claims 124-130, wherein the $R^{¥}$ group present in R^5 is heterocyclyl including from 4-8, such as 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e, such as wherein $R^{¥}$ is 

.

132. The compound of any one of claims 1-97 or 99-102, wherein R^5 is $-L^5-R^g$.

133. The compound of any one of claims 1-97, 99-102, or 132, wherein R^5 is $-O-R^g$.

134. The compound of any one of claims 1-97, 99-102, or 132-133, wherein R^5 is $-O-(C_{6-10}$ aryl) wherein the C_{6-10} aryl is optionally substituted with from 1-4 R^e.

135. The compound of any one of claims 1-97, 99-102, or 132-134, wherein R^5 is –O-phenyl wherein the phenyl is optionally substituted with from 1-2 R^e, such as wherein R^5 is  .

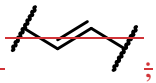
136. The compound of any one of claims 1-79, wherein X^1 is $-(X^2)_m-L^1-R^5$, wherein:

- **m** is 0 or 1;
- X^2 is $N(R^N)$- or –O-;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is R^g.

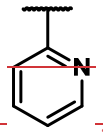
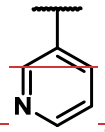
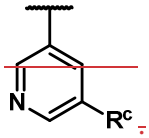
137. The compound of any one of claims 1-79, wherein X^1 is $-X^2-L^1-R^5$, wherein:

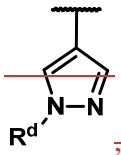
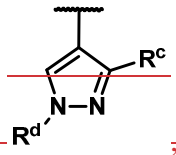
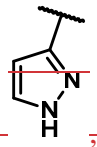
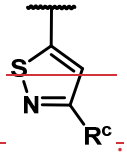
- X^2 is $N(R^N)C(=O)$ *, $N(R^N)S(O)_2$ *, $N(R^N)C(=O)O$ *, or $N(R^N)C(=O)N(R^N)$*;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is R^g.

138. The compound of any one of claims 1-79, wherein X^1 is $-X^2-L^1-R^5$, wherein:

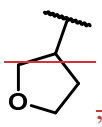
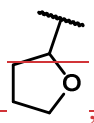
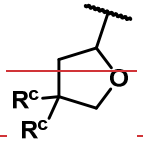
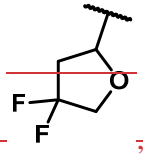
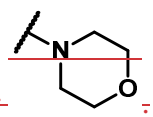
- X^2 is  or  ;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is R^g.

139. The compound of any one of claims 136-138, wherein R^5 is phenyl optionally substituted with from 1-4 R^e, such as wherein R^5 is phenyl optionally substituted with from 1-2 independently selected halo, such as –F.

140. The compound of any one of claims 136-138, wherein R^5 is heteroaryl including 6 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N(R^d), and wherein the heteroaryl is optionally substituted with from 1-4 R^e, such as wherein R^5 is  ,  , or  .

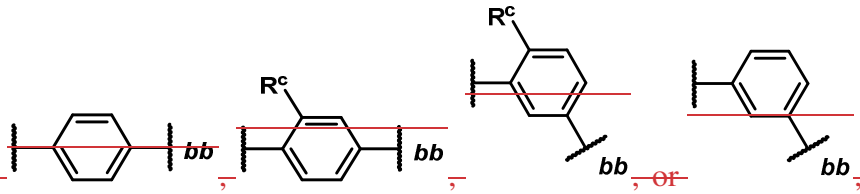
141. The compound of any one of claims 136-138, wherein R^5 is heteroaryl including 5 ring atoms, wherein from 1-4, such as 2-4, ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e, such as wherein R^5 is  ,  ,  , or  .

142. The compound of any one of claims 136-138, wherein R^5 is C_{3-10} cycloalkyl, such as C_{3-6} cycloalkyl, optionally substituted with from 1-4 R^e, such as wherein R^5 is cyclopropyl.

143. The compound of any one of claims 136-138, wherein R^5 is heterocyclyl including from 4-8, such as 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e, such as wherein R^5 is  ,  ,  such as  , or  .

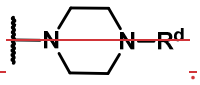
144. The compound of any one of claims 1-79, wherein X^1 is $-(X^2)_m-L^1-R^5$, wherein:

- **m** is 0 or 1;
- X^2 is $N(R^N)$ or O;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is $-R^{g2}-R^Y$.

145. The compound of claim 144, wherein the R^{g2} group present in R^5 is 1,3-phenylene or 1,4-phenylene, each optionally substituted with from 1-4 R^c, such as wherein $-R^{g2}-$ is 

, wherein ***bb*** is the point of attachment to R^Y.

146. The compound of claims 144 or 145, wherein the R^Y group present in R^5 is $-R^g$.

147. The compound of any one of claims 144-146, wherein the R^Y group present in R^5 is heterocyclyl including from 4-8, such as 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), $N(R^d)$, O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e, such as wherein R^Y is 

.

148. The compound of any one of claims 1-79, wherein X^1 is $-X^2-L^1-R^5$, wherein:

- X^2 is $N(R^N)$, O, $N(R^N)C(=O)$ *, $N(R^N)S(O)_2$, $N(R^N)C(=O)O$ *, or $N(R^N)C(=O)N(R^N)$ *;
- L^1 is C_{1-6} alkylene optionally substituted with from 1-3 R^a; and

- **R^5** is H, halo, C_{1-6} alkoxy optionally substituted with from 1-3 **R^a**, or –OH.

149. The compound of claim 148, wherein **R^5** is H.

150. The compound of claim 148, wherein **R^5** is halo, such as –F.

151. The compound of claim 148, wherein **R^5** is C_{1-6} alkoxy optionally substituted with from 1-3 **R^a**, such as wherein **R^5** is C_{1-3} alkoxy such as methoxy.

152. The compound of claim 148, wherein **R^5** is –OH.

153. The compound of any one of claims 136 or 139-147, wherein **m** is 0.

154. The compound of any one of claims 136 or 139-147, wherein **m** is 1.

155. The compound of any one of claims 136, 139-152, or 154, wherein **X^2** is –$N(R^N)$–, such as N(H).

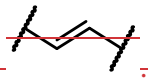
156. The compound of any one of claims 136, 139-152, or 154, wherein **X^2** is –O–.

157. The compound of any one of claims 137, 139-143, or 148-152, wherein **X^2** is $N(R^N)C(=O)$–*, such as –N(H)C(=O)–*.

158. The compound of any one of claims 137, 139-143, or 148-152, wherein **X^2** is $N(R^N)S(O)_2$–, such as –$N(H)S(O)_2$–*.

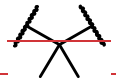
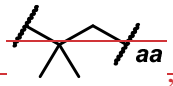
159. The compound of any one of claims 137, 139-143, or 148-152, wherein **X^2** is –$N(R^N)C(=O)O$–*, or –$N(R^N)C(=O)N(R^N)$–*, such as –N(H)C(=O)O–* or –N(H)C(=O)N(H)–*.

160. The compound of any one of claims 138-143, wherein **X^2** is  .

161. The compound of any one of claims 138-143, wherein X^2 is  .

162. The compound of any one of claims 136-147 or 153-161, wherein L^1 is a bond.

163. The compound of any one of claims 136-161, wherein L^1 is C_{1-3} alkylene, such as CH_2, CH_2CH_2, or CH(Me).

164. The compound of any one of claims 136-161, wherein L^1 is branched C_{3-6} alkylene, such as  or  , wherein ***aa*** is the point of attachment to R^5.

165. The compound of any one of claims 1-79, wherein X^1 is $-L^1-R^5$, wherein L^1 is C_{1-6} alkylene optionally substituted with from 1-3 R^a; and R^5 is $-L^5-R^g$.

166. The compound of claim 165, wherein R^5 is $-O-R^g$.

167. The compound of claims 165 or 166, wherein R^5 is -O-(phenyl), wherein the phenyl is optionally substituted with from 1-2 R^e.

168. The compound of any one of claims 165-167, wherein L^1 is C_{1-3} alkylene, such as CH_2, CH_2CH_2, or CH(Me).

169. The compound of any one of claims 2-168, wherein each occurrence of R^{cA} is independently selected from the group consisting of: halo; cyano; C_{1-10} alkyl which is optionally substituted with from 1-6 independently selected R^a; C_{1-4} alkoxy optionally substituted with C_{1-4} alkoxy or C_{1-4} haloalkoxy; C_{1-4} haloalkoxy; $S(O)_{1-2}(C_{1-4}$ alkyl); NR^eR^f; OH; $S(O)_{1-2}NR'R''$; C_{1-4} thioalkoxy; $C(=O)(C_{1-10}$ alkyl); $C(=O)O(C_{1-4}$ alkyl); C(=O)OH; and $C(=O)NR'R''$.

170. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is $-NR^eR^f$.

171. The compound of any one of claims 2-170, wherein one occurrence of R^{cA} is $-NH_2$.

172. The compound of any one of claims 2-170, wherein one occurrence of R^{cA} is $-NH(C_{1-6}$ alkyl), wherein the C_{1-6} alkyl is optionally substituted with from 1-3 substituents each independently selected from the group consisting of N**R'R''**, -OH, C_{1-6} alkoxy, C_{1-6} haloalkoxy, and halo.

173. The compound of any one of claims 2-170 or 172, wherein one occurrence of R^{cA} is -NHMe, $-NHCH_2CF_3$, $-NHCH_2CH_2OH$, or -NHiPr.

174. The compound of any one of claims 2-170, wherein one occurrence of R^{cA} is $-NHC(=O)C_{1-4}$ alkyl, such as $NHC(=O)CH_3$; or wherein one occurrence of R^{cA} is $N(C_{1-3}$ alkyl$)_2$ such as NMe_2.

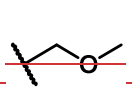
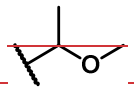
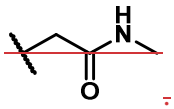
175. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is C_{1-4} alkoxy optionally substituted with C_{1-4} alkoxy or C_{1-4} haloalkoxy, such as wherein one occurrence of R^{cA} is OMe or OCH_2CH_2OMe.

176. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is C_{1-4} haloalkoxy, such as $-OCH_2CF_3$.

177. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is C_{1-4} thioalkoxy, such as $-SCH_3$.

178. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is C_{1-6} alkyl, such as methyl; or wherein one occurrence of R^{cA} is C_{1-6} alkyl substituted with from 1-6 independently selected halo, such as $-CF_3$.

179. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is C_{1-6} alkyl substituted with R^a, such as C_{1-6} alkyl substituted with C_{1-3} alkoxy or

C(=O)N**R'R"**, such as wherein one occurrence of R^{cA} is  ,  , or  .

180. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is halo, such as F.

181. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is OH.

182. The compound of any one of claims 2-169, wherein one occurrence of R^{cA} is C(=O)N**R'R"**, such as C(=O)NHMe.

183. The compound of any one of claims 1-182, wherein R^{1c} is H.

184. The compound of any one of claims 1-183, wherein R^{2a} and R^{2b} are both H.

185. The compound of any one of claims 1-183, wherein from 1-2 of R^{2a} and R^{2b} is an independently selected substituent that is other than H.

186. The compound of any one of claims 1-183 or 185, wherein one of R^{2a} and R^{2b}, such as R^{2a}, is a substituent that is other than H.

187. The compound of any one of claims 1-183 or 185-186, wherein one of R^{2a} and R^{2b}, such as R^{2a}, is R^{b}.

188. The compound of any one of claims 1-183 or 185-187, wherein one of R^{2a} and R^{2b}, such as R^{2a}, is C_{1-6} alkyl, which is optionally substituted with from 1-6 R^{a}.

189. The compound of any one of claims 1-183 or 185-188, wherein one of R^{2a} and R^{2b}, such as R^{2a}, is C_{1-3} alkyl, such as methyl or ethyl.

190. The compound of any one of claims 186-189, wherein the other of R^{2a} and R^{2b}, such as R^{2b}, is H.

191. The compound of any one of claims 1-190, wherein R^{3a} and R^{3b} are both H.

192. The compound of any one of claims 1-190, wherein from 1-2 of R^{3a} and R^{3b} is an independently selected substituent that is other than H.

193. The compound of any one of claims 1-190 or 192, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is a substituent that is other than H.

194. The compound of any one of claims 1-190 or 192-193, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is R^{b}.

195. The compound of any one of claims 1-190 or 192-194, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is C_{1-6} alkyl which is optionally substituted with from 1-6 R^{a}.

196. The compound of any one of claims 1-190 or 192-194, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is C_{1-3} alkyl, such as methyl or ethyl.

197. The compound of any one of claims 1-190 or 192-195, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is C_{1-3} alkyl substituted with from 1-3 independently selected halo.

198. The compound of any one of claims 1-190, 192-195, or 197, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CHF_2$, or $-CH_2CH_2F$.

199. The compound of any one of claims 1-190 or 192-195, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is C_{1-3} alkyl substituted with C_{1-4} alkoxy, C_{1-4} haloalkoxy, or $NR^{e}R^{f}$.

200. The compound of any one of claims 1-190, 192-195, or 199, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, -

$CH_2CH(Me)OMe$, $-CH_2OEt$, $-CH_2CH_2OCHF_2$, $-CH_2N\mathbf{R^e R^f}$ (e.g., $-CH_2N(CF_3)Me$), or $-CH_2CH_2N\mathbf{R^e R^f}$ (e.g., $-CH_2CH_2NMe_2$).

201. The compound of any one of claims 1-190, 192-195, or 199-200, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is C_{1-3} alkyl substituted with C_{1-4} alkoxy.

202. The compound of any one of claims 1-190, 192-195, or 199-201 wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $-CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, $-CH_2CH(Me)OMe$, or $-CH_2OEt$, such as $-CH_2OMe$; such as $-CH_2CH_2OMe$; optionally the other one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3b}}$ is H.

203. The compound of any one of claims 1-190 or 192-193, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $\mathbf{R^g}$ or $(\mathbf{L^g})_g\text{-}\mathbf{R^g}$.

204. The compound of any one of claims 1-190, 192-193, or 203, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is selected from the group consisting of:

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), $N(\mathbf{R^d})$, O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^e}$; and

C_{3-6} cycloalkyl optionally substituted with from 1-4 $\mathbf{R^e}$.

205. The compound of any one of claims 1-190, 192-193, or 203-204, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is selected from the group consisting of: cyclopropyl, cyclobutyl, oxetanyl, and azetidinyl, each of which is optionally substituted with from 1-2 substituents independently selected from the group consisting of: C_{1-3} alkyl and halo, wherein the ring nitrogen of the azetidinyl is optionally substituted with $\mathbf{R^d}$.

206. The compound of any one of claims 1-190, 192-193, or 203, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $(C_{1-3}$ alkylene$)\ \mathbf{R^g}$ or $(C_{1-3}$ alkylene$)\text{-}O\text{-}\mathbf{R^g}$, and optionally the $\mathbf{R^g}$ group of $\mathbf{R^{3a}}$ or $\mathbf{R^{3b}}$ is:

C_{3-6}-cycloalkyl optionally substituted with from 1-4 R^e, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e.

207. The compound of any one of claims 1-190, 192-193, 203, or 206, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2-R^g$, $-CH_2CH_2R^g$, or $-CH_2-O-R^g$, wherein the R^g group of R^{3a} or R^{3b} is:

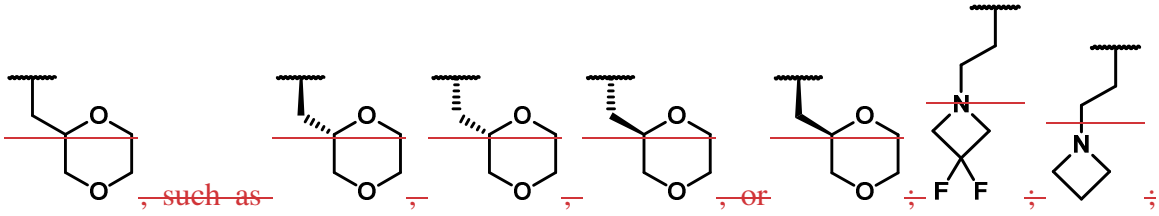
C_{3-6}-cycloalkyl optionally substituted with from 1-4 R^e, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e.

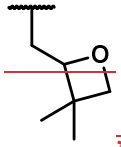
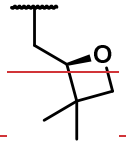
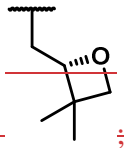
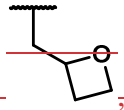
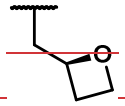
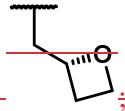
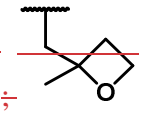
208. The compound of any one of claims 1-190, 192-193, 203, or 206-207, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2-R^g$, $-CH_2CH_2R^g$, or $-CH_2-O-R^g$, wherein the R^g group of R^{3a} or R^{3b} is selected from the group consisting of:

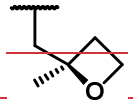
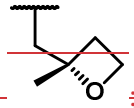
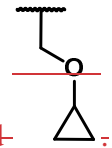
cyclopropyl, cyclobutyl, oxetanyl, 1,4-dioxanyl, and azetidinyl, each of which is optionally substituted with from 1-2 substituents independently selected from the group consisting of: C_{1-3}-alkyl and halo, wherein the ring nitrogen of the azetidinyl is optionally substituted with R^d.

209. The compound of any one of claims 1-190, 192-193, 203 or 206-208, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is selected from the group consisting of:



, such as , , , , or ; ; ; ;

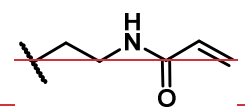
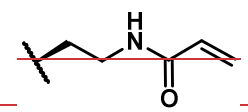
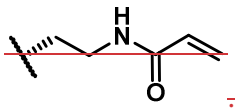
 , such as  or  ;  , such as  or  ; 

, such as  or  ;  ; and  .

210. The compound of any one of claims 1-190, 192-193 wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $(\mathbf{L^g})_g$-$\mathbf{R^W}$.

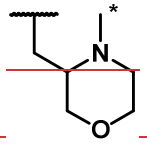
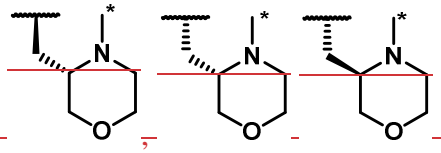
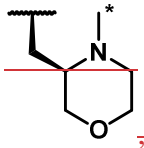
211. The compound any one of claim 1-190, 192-193 or 210, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $-(C_{1-3}$-alkylene)-$\mathbf{R^W}$; optionally one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $-CH_2$-$\mathbf{R^W}$, or $-CH_2CH_2$-$\mathbf{R^W}$.

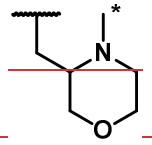
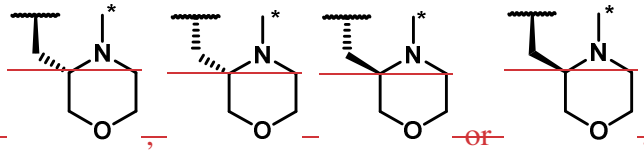
212. The compound of claim 1-190, 192-193 or 210-211, wherein the $\mathbf{R^W}$ group of $\mathbf{R^{3a}}$ or $\mathbf{R^{3b}}$ is: $C(=O)$-$CH=CH_2$, or $-NHC(=O)$-$CH=CH_2$.

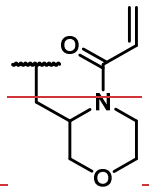
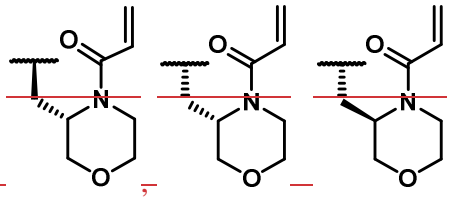
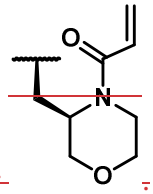
213. The compound of any claims of 1-190, 192-193 or 210-212, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is  , such as  or  .

214. The compound of any one of claims 1-190 or 192-193, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $(\mathbf{L^g})_g$-$\mathbf{R^{g2}}$-$\mathbf{R^W}$.

215. The compound of any one of claims 1-190, 192-193 or 214, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $-(C_{1-3}$-alkylene)-$\mathbf{R^{g2}}$-$\mathbf{R^W}$, and optionally one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $-CH_2$-$\mathbf{R^{g2}}$-$\mathbf{R^W}$, or $-CH_2CH_2$-$\mathbf{R^{g2}}$-$\mathbf{R^W}$.

216. The compound of any one of claims 1-190, 192-193 or 214-215, wherein the R^{g2} group of R^{3a} or R^{3b} is  , such as  ,  , wherein the waveline represents the point of attachment to L^g (e.g., CH_2 or CH_2CH_2) and the asterisk represents the point of attachment to R^W; and wherein the R^W group of R^{3a} or R^{3b} is $-C(=O)-CH=CH_2$, or $-NHC(=O)-CH=CH_2$.

217. The compound of any one of claims 1-190, 192-193 or 214-216, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2-R^{g2}-R^W$, and wherein the R^{g2} group of R^{3a} or R^{3b} is  , such as  , wherein the waveline represents the point of attachment to L^g (e.g., $-CH_2-$ or $-CH_2CH_2-$) and the asterisk represents the point of attachment to R^W; and wherein the R^W group of R^{3a} or R^{3b} is $-C(=O)-CH=CH_2$, or $-NHC(=O)-CH=CH_2$.

218. The compound of any one of claims 1-190, 192-193 or 214-217, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is  , such as  , or  .

219. The compound of any one of claims 1-190 or 193-218 wherein the other of R^{3a} and R^{3b} is H.

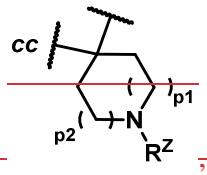
220. The compound of any one of claims 1-190 or 193-218, wherein the other of R^{3a} and R^{3b} is C_{1-3} alkyl, such as methyl; or wherein the other of R^{3a} and R^{3b} is halo, such as -F.

221. The compound of any one of claims 1-190, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused saturated or unsaturated ring of 3-12 ring atoms;

- wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^{d}), O, and $S(O)_{0-2}$; and
- wherein the fused saturated or unsaturated ring of 3-12 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo, R^{e}, and R^{w}.

222. The compound of any one of claims 1-190 or 221, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-8 ring atoms;

- wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^{d}), O, and $S(O)_{0-2}$; and
- wherein the fused saturated ring of 4-8 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo, R^{e}, and R^{w}.

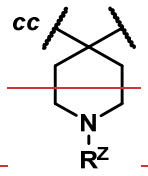
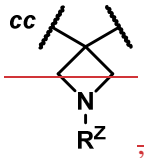
223. The compound of any one of claims 1-190 or 221-222, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form: 

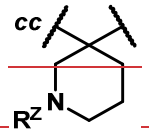
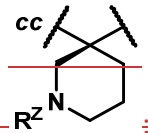
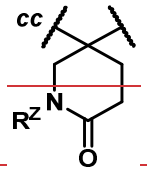
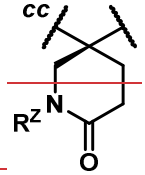
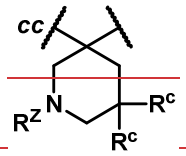
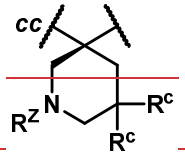
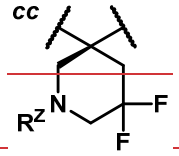
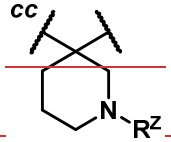
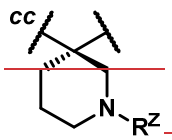
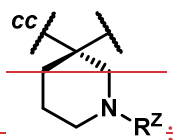
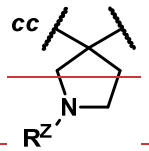
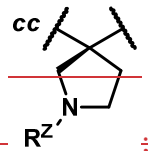
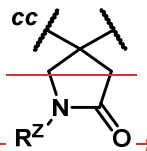
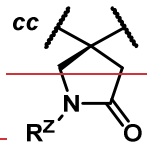
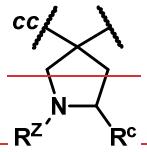
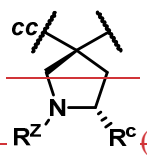
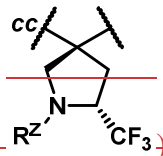
, which is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and R^{e}, wherein:

p1 and **p2** are independently 0, 1, or 2;

R^Z is H, R^d, C(=O)-**W**, or $S(O)_2$**W**; and

cc represents the point of attachment to C($R^{2a}R^{2b}$).

224. The compound of any one of claims 1-190 or 221-223, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form  or  , wherein R^Z is H, R^d, C(=O)-**W**, or $S(O)_2$**W**; and *cc* represents the point of attachment to C($R^{2a}R^{2b}$).

225. The compound of any one of claims 1-190 or 221-223, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused ring selected from the group consisting of:  such as  ;  such as  ;  such as  (e.g., );  such as  or  ;  such as  ;  such as  ; and  such as  (e.g., ), wherein R^Z is H, R^d, C(=O)-**W**, or $S(O)_2$**W**; and *cc* represents the point of attachment to C($R^{2a}R^{2b}$).

226. The compound of any one of claims 223-225, wherein R^Z is H.

227. The compound of any one of claims 223-225, wherein R^Z is R^d.

228. The compound of any one of claims 223-225 or 227, wherein R^Z is C_{1-6} alkyl optionally substituted with from 1-3 independently selected R^a.

229. The compound of any one of claims 223-225, wherein R^Z is C(=O)-**W** or $S(O)_2$-**W**.

230. The compound of any one of claims 223-225 or 229, wherein **W** is C_{2-4} alkenyl.

231. The compound of any one of claims 223-225 or 229-230, wherein R^Z is C(=O)-CH_2=CH_2.

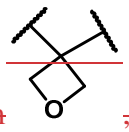
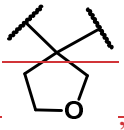
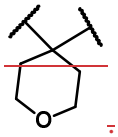
232. The compound of any one of claims 1-190, wherein R^{3a} and R^{3b} together with the **Ring B** ring atom to which each is attached form a fused C_{3-6} cycloalkyl, wherein the fused C_{3-6} cycloalkyl is optionally substituted with from 1-2 R^e.

233. The compound of any one of claims 1-190 or 232, wherein R^{3a} and R^{3b} together with the **Ring B** ring atom to which each is attached form a fused cyclopropyl or cyclobutyl.

234. The compound of any one of claims 1-190, wherein R^{3a} and R^{3b} together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-6 ring atoms;

wherein from 1-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^d), O, and $S(O)_{0-2}$; and

wherein the fused saturated ring of 4-6 ring atoms is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and R^e.

235. The compound of any one of claims 1-190 or 234, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form  ,  , or  .

236. The compound of any one of claims 1-183, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) taken together with the **Ring B** ring atoms to which each is attached, form a fused saturated or unsaturated ring of 3-12 ring atoms;

wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^{d}), O, and $S(O)_{0-2}$; and

wherein the fused saturated or unsaturated ring of 3-12 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^{e}.

237. The compound of any one of claims 1-183 or 236, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) taken together with the **Ring B** ring atoms to which each is attached, form a fused saturated ring of 3-8 ring atoms;

wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^{d}), O, and $S(O)_{0-2}$; and

wherein the fused saturated ring of 3-8 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^{e}.

238. The compound of any one of claims 1-183 or 236-237, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) taken together with the **Ring B** ring atoms to which each is attached, form a fused C_{3-6} cycloalkyl which is optionally substituted with from 1-2 R^{e}.

239. The compound of any one of claims 1-183 or 236-238, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) taken together with the **Ring B** ring atoms to which each is attached, form a fused cyclopropyl or cyclobutyl.

240. The compound of any one of claims 1-183, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) combine to form a double bond between the **Ring B** atoms to which each is attached.

241. The compound of any one of claims 236-240, wherein the other of R^{2a} and R^{2b} and the other of R^{3a} and R^{3b} are each H.

242. The compound of any one of claims 1-183 or 240, wherein the other one of R^{3a} and R^{3b} is R^{g} or $-(L^{g})_{g}-R^{g}$.

243. The compound of any one of claims 1-183, 240 or 242, wherein the other one of R^{3a} and R^{3b} is $-(L^{g})_{g}-R^{g}$.

244. The compound of any one of claims 1-183, 240 or 242-243, wherein the other one of R^{3a} and R^{3b} is $-(C_{1-3}\text{ alkylene})-R^{g}$ or $-(C_{1-3}\text{ alkylene})-O-R^{g}$, and optionally the R^{g} group of R^{3a} or R^{3b} is:

C_{3-6} cycloalkyl optionally substituted with from 1-4 R^{e}, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^{e}.

245. The compound of any one of claims 1-183, 240 or 242-244, wherein the other one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2-R^{g}$, $-CH_2CH_2R^{g}$, or $-CH_2-O-R^{g}$, wherein the R^{g} group of R^{3a} or R^{3b} is:

C_{3-6} cycloalkyl optionally substituted with from 1-4 R^{e}, or

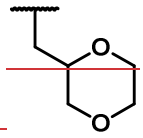
heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O,

and $S(O)_{0-2}$; and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e.

246. The compound of any one of claims 1-183, 240 or 242-245, wherein the other one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2-R^g$, $-CH_2CH_2R^g$, or $-CH_2-O-R^g$, wherein the R^g group of R^{3a} or R^{3b} is selected from the group consisting of:

cyclopropyl, cyclobutyl, oxetanyl, 1,4-dioxanyl, and azetidinyl, each of which is optionally substituted with from 1-2 substituents independently selected from the group consisting of: C_{1-3} alkyl and halo, wherein the ring nitrogen of the azetidinyl is optionally substituted with R^d.

247. The compound of any one of claims 1-183, 240 or 242-245, wherein the other one of R^{3a} and R^{3b}, such as R^{3a}, is selected from the group consisting of:



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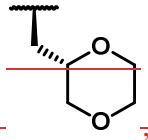

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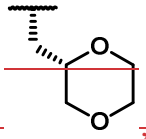

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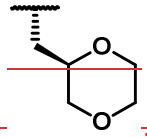

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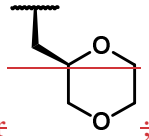

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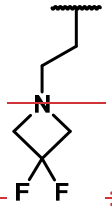

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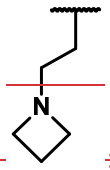

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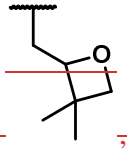

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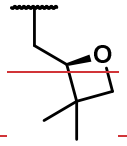

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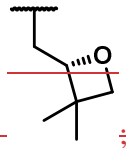

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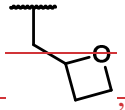

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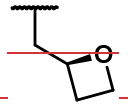

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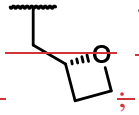

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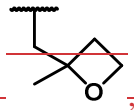

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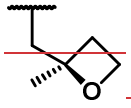

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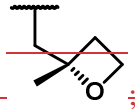

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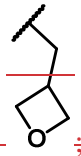

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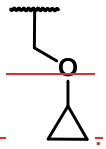


.

248. The compound of any one of claims 1-183, wherein R^{1c}, R^{2a}, and R^{2b} are each H; one of R^{3a} and R^{3b}, such as R^{3a}, is C_{1-3} alkyl optionally substituted with from 1-3 R^a; and the other of R^{3a} and R^{3b} is H, optionally each R^a substituent present in R^{3a} or R^{3b}

is independently selected from the group consisting of: halo, C_{1-4} alkoxy, and C_{1-4} haloalkoxy.

249. The compound of any one of claims 1-183, wherein R^{1c}, R^{2a}, and R^{2b} are each H; one of R^{3a} and R^{3b}, such as R^{3a}, is C_{1-3} alkyl optionally substituted with from C_{1-4} alkoxy; optionally one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2CH_2$-OMe; and the other of R^{3a} and R^{3b} is H.

250. The compound of any one of claims 1-183, wherein R^{1c}, R^{2a}, and R^{2b} are each H; and R^{3a} and R^{3b} are independently selected C_{1-3} alkyl.

251. The compound of any one of claims 1-183, wherein R^{1c}, R^{2a}, and R^{2b} are each H; one of R^{3a} and R^{3b}, such as R^{3a}, is $-R^g$, $-(C_{1-3}$ alkylene)-R^g, or $-(C_{1-3}$ alkylene)-O-R^g,

optionally wherein the R^g group of R^{3a} or R^{3b} is:

C_{3-6} cycloalkyl optionally substituted with from 1-4 R^e, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e; and

the other of R^{3a} and R^{3b} is H.

252. The compound of any one of claims 1-183, wherein R^{1c}, R^{2a}, and R^{2b} are each H; and R^{3a} and R^{3b} taken together with the **Ring B** ring carbon atom to which each is attached form a fused C_{3-6} (such as C_3 or C_4) cycloalkyl, wherein the fused cycloalkyl ring is optionally substituted with from 1-2 R^e.

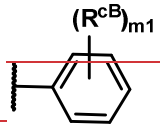
253. The compound of any one of claims 1-183, wherein R^{1c}, R^{2a}, and R^{2b} are each H; and R^{3a} and R^{3b} together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-6 ring atoms;

- wherein from 1-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N($\mathbf{R^d}$), O, and S(O)$_{0-2}$; and
- wherein the fused saturated ring of 4-6 ring atoms is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and $\mathbf{R^e}$.

254. The compound of any one of claims 1-183, wherein $\mathbf{R^{1e}}$ is H; one of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ (such as $\mathbf{R^{2a}}$) and one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ (such as $\mathbf{R^{3a}}$) taken together with the **Ring B** ring atoms to which each is attached, form a fused C$_{3-6}$ (such as C$_3$ or C$_4$) cycloalkyl which is optionally substituted with from 1-2 $\mathbf{R^e}$; and the other of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ and the other of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are each H.

255. The compound of any one of claims 1-183, wherein $\mathbf{R^{1e}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$ are each H.

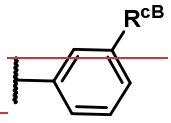
256. The compound of any one of claims 1-238, wherein $\mathbf{R^4}$ is H; and $\mathbf{R^7}$ is H.

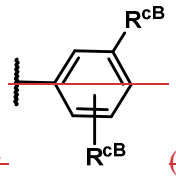
257. The compound of any one of claims 1-256, wherein **Ring A** is 

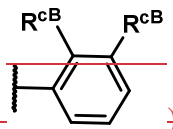
, wherein each $\mathbf{R^{eB}}$ is an independently selected $\mathbf{R^e}$; and **m1** is 0, 1, 2, 3, or 4.

258. The compound of claim 257, wherein **m1** is 1, 2, or 3.

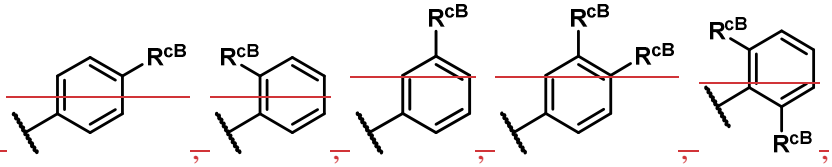
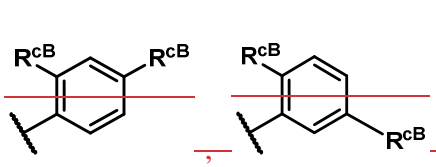
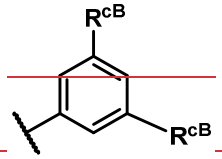
259. The compound of claims 257 or 258, wherein **m1** is 1 or 2, such as 2.

260. The compound of any one of claims 1-259, wherein **Ring A** is 

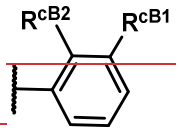


or 

(e.g.,), wherein each $\mathbf{R^{eB}}$ is an independently selected $\mathbf{R^e}$.

261. The compound of any one of claims 1-259, wherein **Ring A** is selected from the group consisting of:  ,  , and  , wherein each R^{cB} is an independently selected R^{c}.

262. The compound of any one of claims 257-261, wherein each R^{cB} is independently selected from the group consisting of: halo, such as -Cl and -F; -CN; C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-6 independently selected halo.

263. The compound of any one of claims 1-256, wherein **Ring A** is  , wherein R^{cB1} is R^{c}; and R^{cB2} is H or R^{c}, optionally wherein R^{cB1} and R^{cB2} are each independently selected from the group consisting of: halo, such as -Cl and -F; -CN; C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-6 independently selected halo.

264. The compound of claim 263, wherein R^{cB1} is halo, such as -F or -Cl, such as -F.

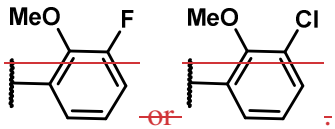
265. The compound of claim 263, wherein R^{cB1} is C_{1-3} alkyl or C_{1-3} alkyl substituted with from 1-6 independently selected halo, such as wherein R^{cB1} is methyl, CHF_2, or CF_3.

266. The compound of any one of claims 263-265, wherein R^{eB2} is selected from the group consisting of: halo; -CN; C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-6 independently selected halo.

267. The compound of any one of claims 263-266, wherein R^{eB2} is C_{1-4} alkoxy or C_{1-4} haloalkoxy.

268. The compound of any one of claims 263-267, wherein R^{eB2} is selected from the group consisting of cyano; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-6 independently selected halo, such as wherein R^{eB2} is cyano, methyl, ethyl, $-CHF_2$, $-CF_3$, or $-CH_2CHF_2$.

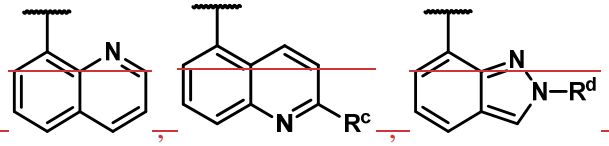
269. The compound of any one of claims 1-256, or 263-268, wherein **Ring A** is



or .

270. The compound of any one of claims 1-256, wherein **Ring A** is heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e.

271. The compound of any one of claims 1-256 or 270, wherein **Ring A** is bicyclic heteroaryl including from 9-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e.

272. The compound of any one of claims 1-256 or 270-271, wherein **Ring A** is selected from the group consisting of: 

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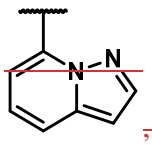
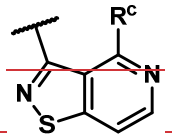
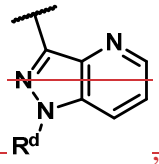
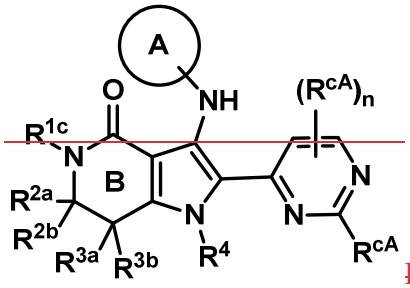
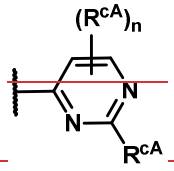
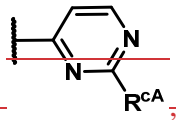
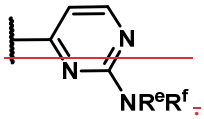



, and , each of which is further optionally substituted with R^e.

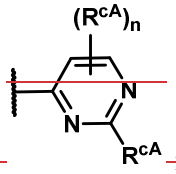
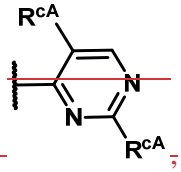
273. The compound of claim 1, wherein the compound is a compound of Formula (**I-a**):

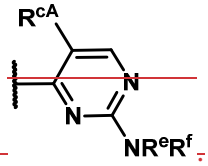

Formula (**I-a**)

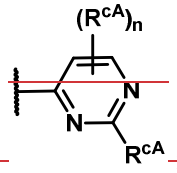
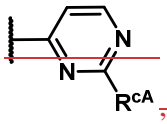
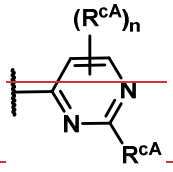
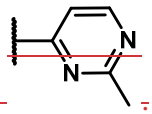
or a pharmaceutically acceptable salt thereof,

wherein: each R^{cA} is an independently selected R^c; and **n** is 0, 1, or 2.

274. The compound of claim 273, wherein  is  , such as  .

275. The compound of claims 273 or 274, wherein  is  ,

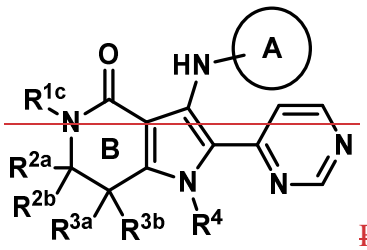
such as  .

276. The compound of any one of claims 273 or 274, wherein  is  , wherein R^{cA} is C_{1-3} alkyl optionally substituted with from 1-3 independently selected halo; optionally wherein  is  .

277. The compound of any one of claims 273-276, wherein one of R^{3a} and R^{3b}, such as R^{3a}, is C_{1-3} alkyl substituted with C_{1-4} alkoxy; optionally wherein the other one of of R^{3a} and R^{3b}, such as R^{3b} is H.

278. The compound of any one of claims 276 wherein one of R^{3a} and R^{3b}, such as R^{3a}, is $-CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, $-CH_2CH(Me)OMe$, or $-CH_2OEt$; optionally wherein one of R^{3a} and R^{3b}, such as R^{3a} is $-CH_2CH_2OMe$.

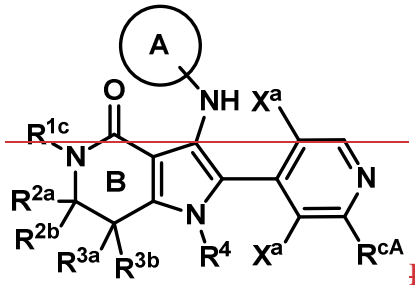
279. The compound of claim 1, wherein the compound is a compound of Formula (I-b):



Formula (I-b)

or a pharmaceutically acceptable salt thereof.

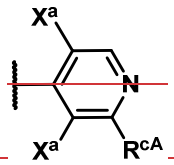
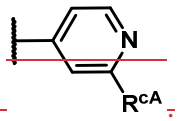
280. The compound of claim 1, wherein the compound is a compound of Formula (I-c):



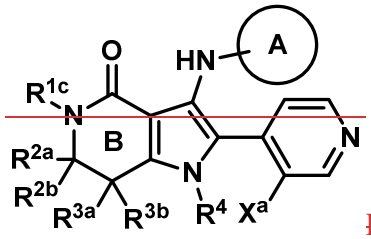
Formula (I-c)

or a pharmaceutically acceptable salt thereof,

wherein: R^{cA} is an independently selected R^{c}.

281. The compound of claim 280, wherein  is  .

282. The compound of claim 1, wherein the compound is a compound of Formula (I-d):



Formula (I-d)

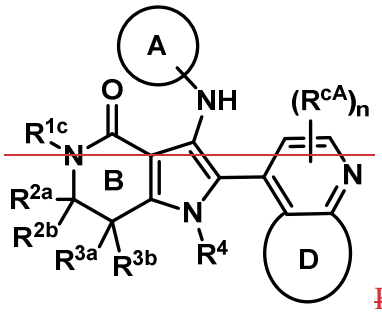
or a pharmaceutically acceptable salt thereof, wherein:

X^a is selected from the group consisting of: H; -F; -Cl; C_{1-6} alkyl; and C_{1-3} alkyl substituted with from 1-3 independently selected halo.

283. The compound of claim 282, wherein X^a is -F.

284. The compound of claim 82, wherein X^a is C_{1-3} substituted with from 1-3 independently selected halo, such as $-CF_2H$ or $-CF_3$.

285. The compound of claim 1, wherein the compound is a compound of Formula (I-e):



~~Formula (I-e)~~

~~or a pharmaceutically acceptable salt thereof,~~

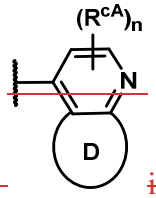
~~wherein:~~

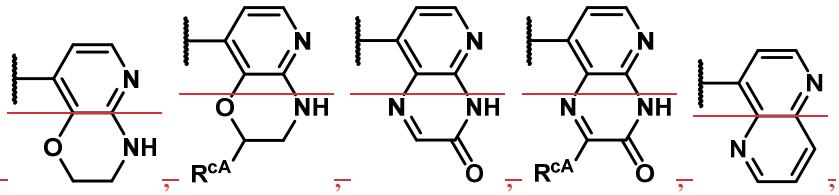
~~each R^{cA} is an independently selected R^c;~~

~~n is 0, 1, or 2; and~~

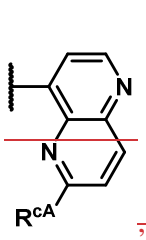
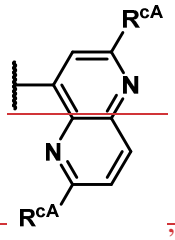
~~**Ring D** is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.~~

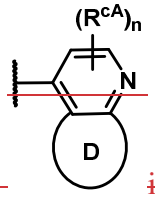
~~**286.** The compound of claim 285, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.~~

~~**287.** The compound of claims 285 or 286, wherein~~ 

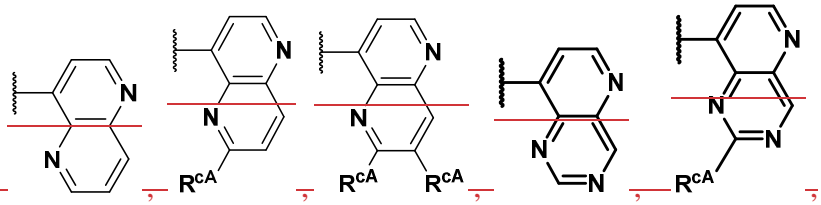
~~is selected from the group consisting of:~~ 

~~,~~ ~~,~~ ~~,~~ ~~,~~ ~~,~~ ~~,~~

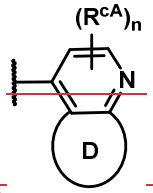


, and , each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.



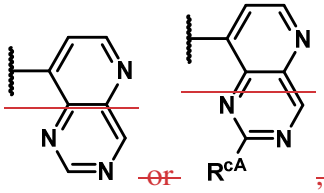
288. The compound of claims 285 or 286, wherein is selected from the group consisting of:



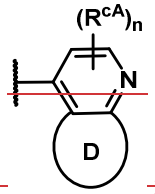
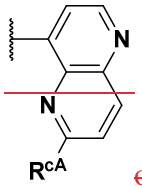
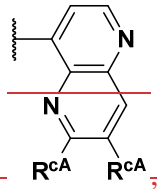
, each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.

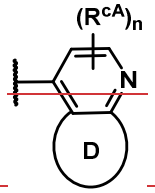
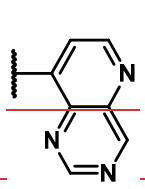
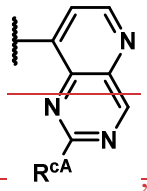
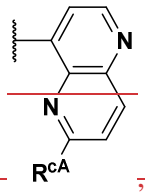
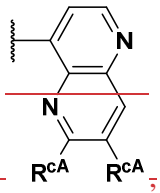


289. The compound of any one of claims 285-288, wherein is



or , wherein R^{cA} is an independently selected R^{c}.

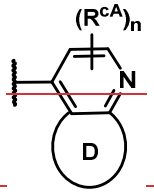
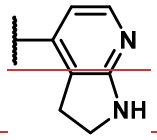
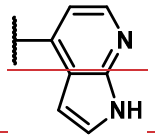
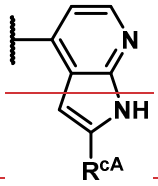
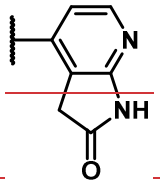
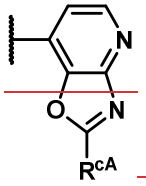
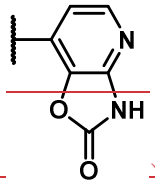
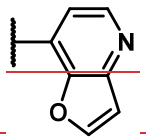
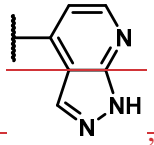
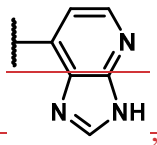
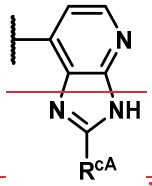
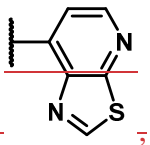
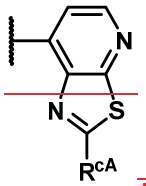
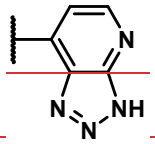
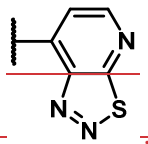
290. The compound of any one of claims 285-288, wherein  is  or  , wherein each R^{cA} is an independently selected R^{e}.

291. The compound of any one of claims 285-288, wherein  is selected from the group consisting of:  ,  ,  , and  ; wherein:

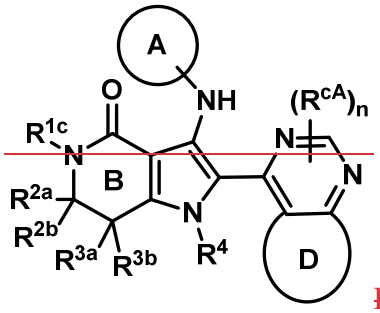
each occurrence of R^{cA} is independently selected from the group consisting of: halo; $NR^{e}R^{f}$; C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; C_{1-3} alkyl substituted with from 1-3 independently selected halo; C_{1-3} alkyl substituted with C_{1-4} alkoxy; and C_{1-4} alkoxy substituted with C_{1-4} alkoxy;

such as wherein each occurrence of R^{cA} is independently selected from the group consisting of: C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-3 independently selected halo.

292. The compound of claim 285, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), $N(R^{d})$, O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.

293. The compound of claims 285 or 292, wherein  is selected from the group consisting of:  ,  ,   ,   ,         , and , each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.

294. The compound of claim 1, wherein the compound is a compound of Formula (I-f):



Formula (I-f)

or a pharmaceutically acceptable salt thereof,

wherein:

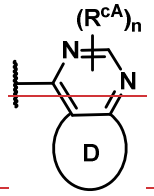
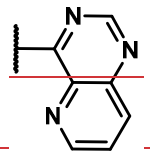
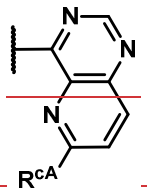
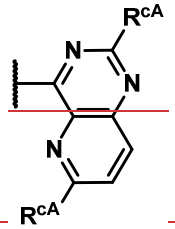
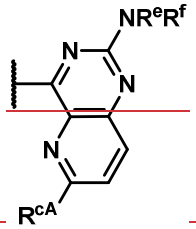
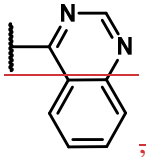
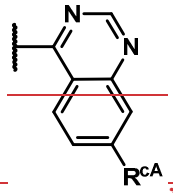
each R^{cA} is an independently selected R^{c};

n is 0 or 1; and

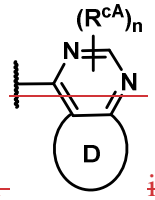
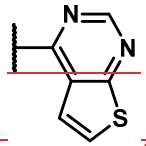
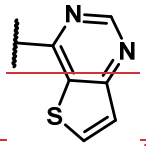
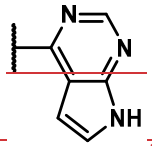
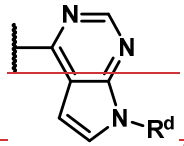
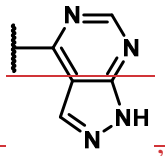
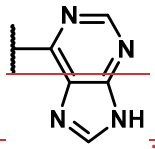
Ring D is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the

group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.

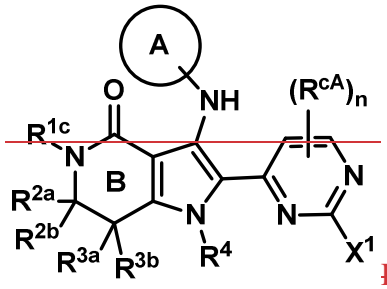
295. The compound of claim 294, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.

296. The compound of claims 294 or 295, wherein  is selected from the group consisting of:  ,  ,  (e.g., ),  , and  , each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^e.

297. The compound of claim 294, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.

298. The compound of claims 294 or 297, wherein  is selected from the group consisting of:  ,  ,  ,  ,  , and  , each further optionally substituted with R^{cA}, wherein each R^{cA} is an independently selected R^{c}.

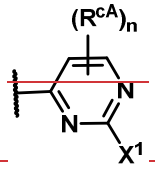
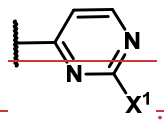
299. The compound of claim 1, wherein the compound is a compound of Formula (**I-g**):



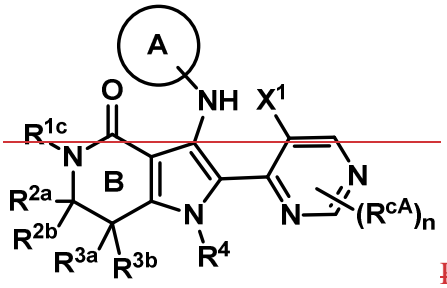
Formula (**I-g**)

or a pharmaceutically acceptable salt thereof,

wherein: each R^{cA} is an independently selected R^{c}; and **n** is 0, 1, or 2.

300. The compound of claim 299, wherein  is  .

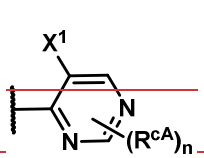
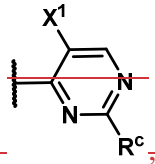
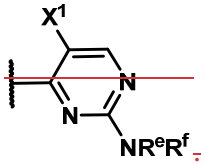
301. The compound of claim 1, wherein the compound is a compound of Formula (**I-h**):



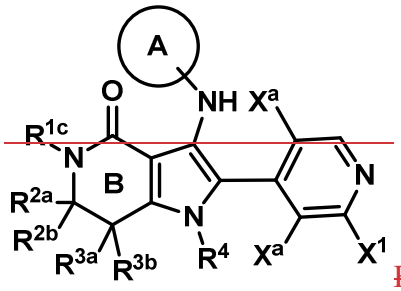
Formula (I-h)

or a pharmaceutically acceptable salt thereof,

wherein: each R^{cA} is an independently selected R^c; and **n** is 0, 1, or 2.

302. The compound of claim 301, wherein  is  , such as  .

303. The compound of claim 1, wherein the compound is a compound of Formula (I-i):

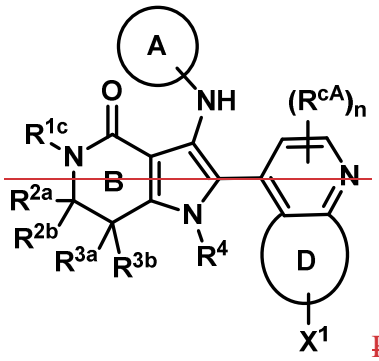


Formula (I-i)

or a pharmaceutically acceptable salt thereof.

304. The compound of claim 303, wherein each X^a is H.

305. The compound of claim 1, wherein the compound is a compound of Formula (I-j):



Formula (I-j)

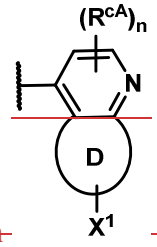
or a pharmaceutically acceptable salt thereof;

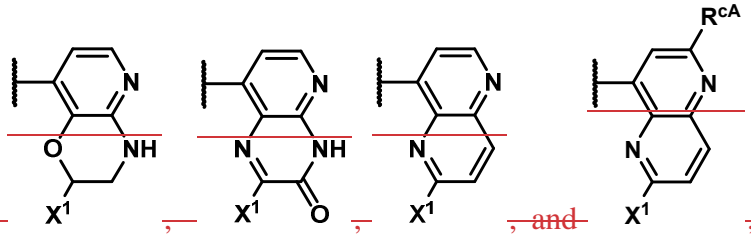
wherein **n** is 0, 1, or 2;

each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$; and

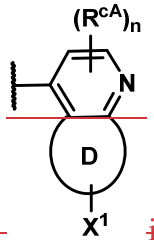
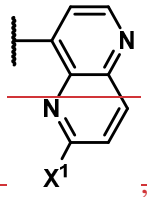
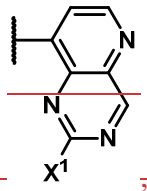
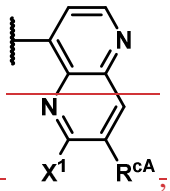
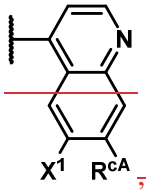
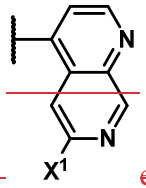
Ring D is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R}^{d}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R}^{cA}$.

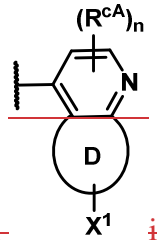
306. The compound of claim 305, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R}^{d}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R}^{cA}$.

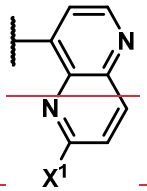
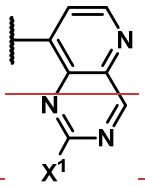
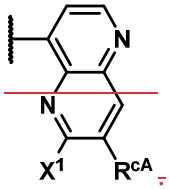
307. The compound of claims 305 or 306, wherein  is selected from



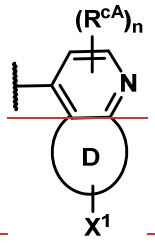
the group consisting of: , , , , and , each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

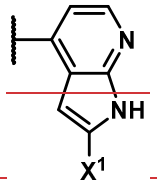
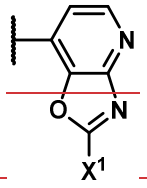
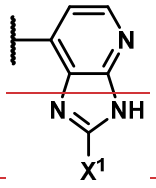
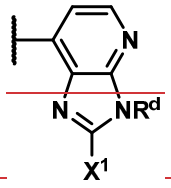
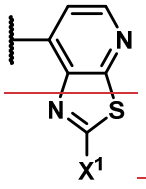
308. The compound of any one of claims 305 or 306, wherein  is selected from the group consisting of: consisting of:  ,  ,  ,  , and  each of which is further optionally substituted with from 1-2 R^{cA}, wherein each R^{cA} is an independently selected R^{c}.



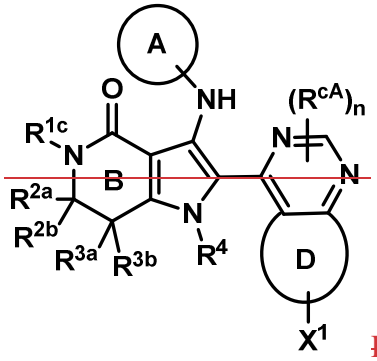
309. The compound of any one of claims 305, 306 or 308, wherein is selected from the group consisting of: consisting of:  ,  , and  .

310. The compound of claim 305, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{cA}.



311. The compound of claims 305 or 310, wherein is selected from the group consisting of:  ,  ,  ,  , and  , each further optionally substituted with R^{eA}, wherein each R^{eA} is an independently selected R^{e}.

312. The compound of claim 1, wherein the compound is a compound of Formula (**I-k**):



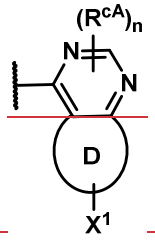
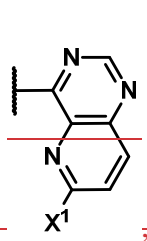
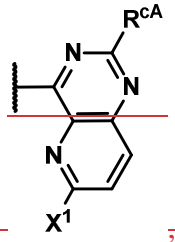
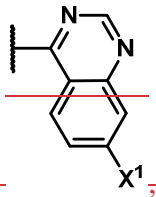
or a pharmaceutically acceptable salt thereof;

wherein **n** is 0 or 1;

each R^{eA} is an independently selected R^{e}; and

Ring D is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(R^{d}), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 R^{eA}.

313. The compound of claim 312, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}.

314. The compound of claims 312 or 313, wherein  is selected from the group consisting of:  ,  , and  , each further optionally substituted with **R**^{cA}, wherein each **R**^{cA} is an independently selected **R**^{e}.

315. The compound of claim 312, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}.

316. The compound of any one of claims 273-315, wherein each occurrence of **R**^{cA} is independently selected from the group consisting of: halo; cyano; C$_{1-10}$ alkyl which is optionally substituted with from 1-6 independently selected **R**^{a}; C$_{1-4}$ alkoxy optionally substituted with C$_{1-4}$ alkoxy or C$_{1-4}$ haloalkoxy; C$_{1-4}$ haloalkoxy; S(O)$_{1-2}$(C$_{1-4}$ alkyl); N**R**^{e}**R**^{f}; OH; S(O)$_{1-2}$N**R'R''**; C$_{1-4}$ thioalkoxy; C(=O)(C$_{1-10}$ alkyl); C(=O)O(C$_{1-4}$ alkyl); C(=O)OH; and C(=O)N**R'R''**.

317. The compound of any one of claims 273-316, wherein one occurrence of **R**^{cA} is N**R**^{e}**R**^{f}.

318. The compound of any one of claims 273-317, wherein one occurrence of R^{cA} is $-NH_2$.

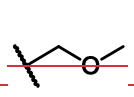
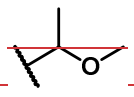
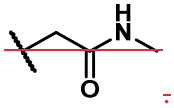
319. The compound of any one of claims 273-317, wherein one occurrence of R^{cA} is $-NH(C_{1-6}$ alkyl), wherein the C_{1-6} alkyl is optionally substituted with from 1-3 substituents each independently selected from the group consisting of N**R'R''**, OH, C_{1-6} alkoxy, C_{1-6} haloalkoxy, and halo, such as wherein one occurrence of R^{cA} is $-NHMe$, $-NHCH_2CF_3$, $-NHCH_2CH_2OH$, or $-NHiPr$.

320. The compound of any one of claims 273-317, wherein one occurrence of R^{cA} is $-NHC(=O)C_{1-4}$ alkyl, such as $NHC(=O)CH_3$; or wherein one occurrence of R^{cA} is $N(C_{1-3}$ alkyl$)_2$ such as NMe_2.

321. The compound of any one of claims 273-316, wherein one occurrence of R^{cA} is C_{1-4} alkoxy optionally substituted with C_{1-4} alkoxy or C_{1-4} haloalkoxy, such as wherein one occurrence of R^{cA} is OMe or OCH_2CH_2OMe; or wherein one occurrence of R^{cA} is C_{1-4} haloalkoxy, such as $-OCH_2CF_3$.

322. The compound of any one of claims 273-316, wherein one occurrence of R^{cA} is C_{1-4} thioalkoxy, such as $-SCH_3$.

323. The compound of any one of claims 273-316, wherein one occurrence of R^{cA} is C_{1-6} alkyl, such as methyl; or wherein one occurrence of R^{cA} is C_{1-6} alkyl substituted with from 1-6 independently selected halo, such as $-CF_3$.

324. The compound of any one of claims 273-316, wherein one occurrence of R^{cA} is C_{1-6} alkyl substituted with R^a, such as C_{1-6} alkyl substituted with C_{1-3} alkoxy or C(=O)N**R'R"**, such as wherein one occurrence of R^{cA} is  ,  , or  .

325. The compound of any one of claims 273-316, wherein one occurrence of R^{cA} is halo, such as –F.

326. The compound of any one of claims 273-316, wherein one occurrence of R^{cA} is –OH.

327. The compound of any one of claims 273-316, wherein one occurrence of R^{cA} is C(=O)N**R'R"**, such as C(=O)NHMe.

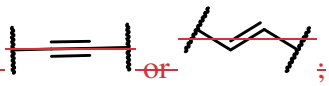
328. The compound of any one of claims 299-327, wherein X^1 is $-(X^2)_m-L^1-R^5$, wherein:

- **m** is 0 or 1;
- X^2 is $N(R^N)$ or O ;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is R^g.

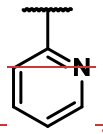
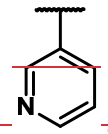
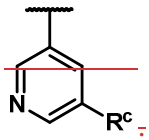
329. The compound of any one of claims 299-327, wherein X^1 is X^2-L^1-R^5, wherein:

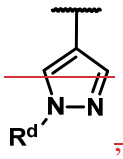
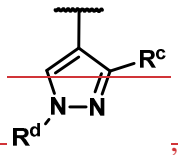
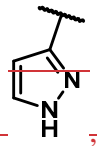
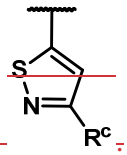
- X^2 is $N(R^N)C(=O)*$, $N(R^N)S(O)_2*$, $N(R^N)C(=O)O*$, or $N(R^N)C(=O)N(R^N)*$;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is R^g.

330. The compound of any one of 299-327, wherein X^1 is X^2-L^1-R^5, wherein:

- X^2 is  ;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is R^g.

331. The compound of any one of claims 328-330, wherein R^5 is phenyl optionally substituted with from 1-4 R^e, such as wherein R^5 is phenyl optionally substituted with from 1-2 independently selected halo, such as F.

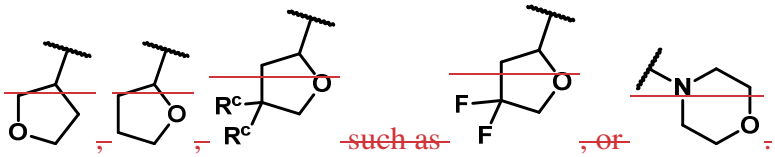
332. The compound of any one of claims 328-330, wherein R^5 is heteroaryl including 6 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N(R^d), and wherein the heteroaryl is optionally substituted with from 1-4 R^e, such as wherein R^5 is  ,  , or  .

333. The compound of any one of claims 328-330, wherein R^5 is heteroaryl including 5 ring atoms, wherein from 1-4, such as 2-4, ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e, such as wherein R^5 is  ,  ,  , or  .

334. The compound of any one of claims 328-330, wherein R^5 is C_{3-10} cycloalkyl, such as C_{3-6} cycloalkyl, optionally substituted with from 1-4 R^e, such as wherein R^5 is cyclopropyl.

335. The compound of any one of claims 328-330, wherein R^5 is heterocyclyl including from 4-8, such as 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents

independently selected from the group consisting of oxo and R^e, such as wherein R^5 is



such as

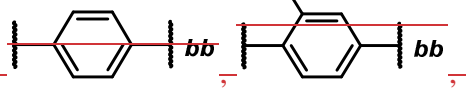
, or

.

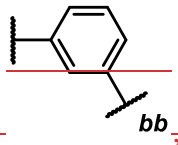
336. The compound of any one of claims 299-327, wherein X^1 is $-(X^2)_m-L^1-R^5$, wherein:

- **m** is 0 or 1;
- X^2 is $-N(R^N)-$ or $-O-$;
- L^1 is a bond or C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is $-R^{g2}-R^Y$.

337. The compound of claim 336, wherein the R^{g2} group present in R^5 is 1,3-phenylene or 1,4-phenylene, each optionally substituted with from 1-4 R^e, such as wherein $-R^{g2}-$ is



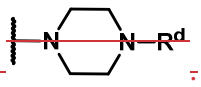
, or



, wherein ***bb*** is the point of attachment to R^Y.

338. The compound of claims 336 or 337, wherein the R^Y group present in R^5 is $-R^g$.

339. The compound of any one of claims 336-338, wherein the R^Y group present in R^5 is heterocyclyl including from 4-8, such as 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), $N(R^d)$, O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e, such as wherein R^Y is



.

340. The compound of any one of claims 329-337, wherein X^1 is $-X^2-L^1-R^5$, wherein:

- X^2 is $-N(R^N)-$, $-O-$, $-N(R^N)C(=O)-*$, $-N(R^N)S(O)_2-$, $-N(R^N)C(=O)O-*$, or $-N(R^N)C(=O)N(R^N)-*$;
- L^1 is C_{1-6} alkylene optionally substituted with from 1-3 R^a; and
- R^5 is H, halo, C_{1-6} alkoxy optionally substituted with from 1-3 R^a, or –OH.

341. The compound of claim 340, wherein R^5 is H.

342. The compound of claim 340, wherein R^5 is halo, such as –F.

343. The compound of claim 340, wherein R^5 is C_{1-6} alkoxy optionally substituted with from 1-3 R^a, such as wherein R^5 is C_{1-3} alkoxy such as methoxy.

344. The compound of claim 340, wherein R^5 is –OH.

345. The compound of any one of claims 329 or 331-339, wherein **m** is 0.

346. The compound of any one of claims 329 or 331-339, wherein **m** is 1.

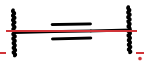
347. The compound of any one of claims 329, 331-334 or 346 wherein X^2 is $N(R^N)-$, such as N(H).

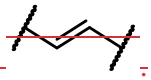
348. The compound of any one of claims 329, 331-334 or 346, wherein X^2 is –O–.

349. The compound of any one of claims 329, 331-335 or 340-344, wherein X^2 is $N(R^N)C(=O)-*$, such as $N(H)C(=O)-*$.

350. The compound of any one of claims 329, 331-335 or 340-344, wherein X^2 is $N(R^N)S(O)_2-$, such as $N(H)S(O)_2-*$.

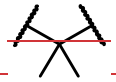
351. The compound of any one of claims 329, 331-335 or 340-344, wherein X^2 is $N(R^N)C(=O)O$ *, or $N(R^N)C(=O)N(R^N)$ *, such as N(H)C(=O)O * or N(H)C(=O)N(H) *.

352. The compound of any one of claims 330-335, wherein X^2 is  .

353. The compound of any one of claims 330-335, wherein X^2 is  .

354. The compound of any one of claims 263-274 or 280-288, wherein L^1 is a bond.

355. The compound of any one of claims 328-353, wherein L^1 is C_{1-3} alkylene, such as $-CH_2-$, $-CH_2CH_2-$, or $-CH(Me)-$.

356. The compound of any one of claims 328-353, wherein L^1 is branched C_{3-6} alkylene, such as  or  , wherein ***aa*** is the point of attachment to R^5.

357. The compound of any one of claims 299-327, wherein X^1 is $-L^1-R^5$, wherein L^1 is C_{1-6} alkylene optionally substituted with from 1-3 R^a; and R^5 is $-L^5-R^g$.

358. The compound of claim 357, wherein R^5 is $-O-R^g$.

359. The compound of claims 357 or 358, wherein R^5 is -O-(phenyl), wherein the phenyl is optionally substituted with from 1-2 R^e.

360. The compound of any one of claims 357-359, wherein L^1 is C_{1-3} alkylene, such as $-CH_2-$, $-CH_2CH_2-$, or $-CH(Me)-$.

361. The compound of any one of claims 273-360, wherein R^{1c} is H.

362. The compound of any one of claims 273-361, wherein R^{2a} and R^{2b} are both H.

363. The compound of any one of claims 273-361, wherein R^{2a} is a substituent that is other than H.

364. The compound of any one of claims 273-361 or 363, wherein R^{2a} is C_{1-6} alkyl which is optionally substituted with from 1-6 R^a, such as wherein R^{2a} is C_{1-3} alkyl, such as methyl or ethyl.

365. The compound of claims 363 or 364, wherein R^{2b} is H.

366. The compound of any one of claims 273-365, wherein R^{3a} and R^{3b} are both H.

367. The compound of any one of claims 273-365, wherein R^{3a} is a substituent that is other than H.

368. The compound of any one of claims 273-365 or 367, wherein R^{3a} is C_{1-6} alkyl which is optionally substituted with from 1-6 R^a, such as wherein R^{3a} is C_{1-3} alkyl, such as methyl or ethyl.

369. The compound of any one of claims 273-365 or 367, wherein R^{3a} is C_{1-3} alkyl substituted with from 1-3 independently selected halo, such as wherein R^{3a} is $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CHF_2$, or $-CH_2CH_2F$.

370. The compound of any one of claims 273-365 or 367, wherein R^{3a} is C_{1-3} alkyl substituted with C_{1-4} alkoxy, C_{1-4} haloalkoxy, or NR^eR^f, such as wherein R^{3a} is $-CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, $-CH_2CH(Me)OMe$, $-CH_2OEt$, $-CH_2NR^eR^f$ (e.g., $-CH_2N(CF_3)Me$), or $-CH_2CH_2NR^eR^f$ (e.g., $-CH_2CH_2NMe_2$).

371. The compound of any one of claims 273-365 or 367, wherein R^{3a} is selected from the group consisting of:

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^{e}; and

C_{3-6} cycloalkyl optionally substituted with from 1-4 R^{e}.

372. The compound of any one of claims 273-365 or 367, wherein R^{3a} is $(C_{1-3}$ alkylene) R^{g} or $(C_{1-3}$ alkylene) O R^{g}, and optionally the R^{g} group of R^{3a} is:

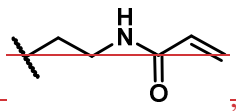
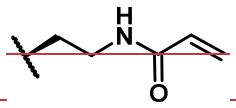
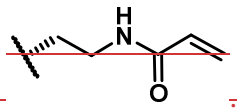
C_{3-6} cycloalkyl optionally substituted with from 1-4 R^{e}, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^{d}), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^{e}.

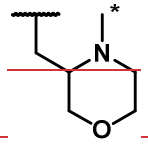
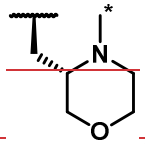
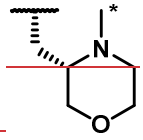
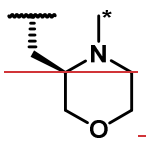
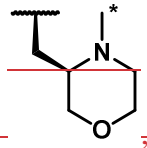
373. The compound of claims 273-365, 367 or 372, wherein R^{3a} is $-CH_2-R^{g}$, or $-CH_2CH_2R^{g}$, wherein R^{g} is 1,4-dioxanyl.

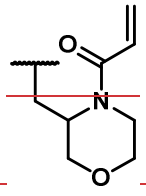
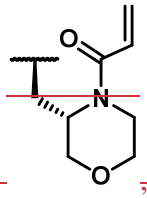
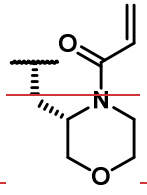
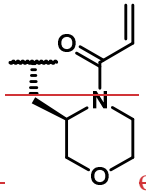
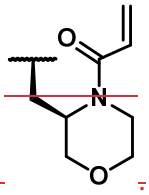
374. The compound of any one of claims 273-365 or 367, wherein R^{3a} is $(L^{g})_{g}$-R^{W}.

375. The compound of any one of claims 273-365, 367 or 374, wherein R^{3a} is CH_2CH_2-R^{W}, wherein the R^{W} group is $C(=O)$-$CH=CH_2$, or $-NHC(=O)$-$CH=CH_2$.

376. The compound of any one of claims 273-365, 367 or 374-375, wherein R^{3a} is  , such as  or  .

377. The compound of any one of claims 273-365, or 367, wherein R^{3a} is $-(L^{g})_{g}$-R^{g2}-R^{W}.

378. The compound of any one of claims 273-365, 367 or 377, wherein R^{3a} is CH_2-R^{g2}-R^W, wherein the R^{g2} group is  , such as  ,  ,  or  , wherein the waveline represents the point of attachment to CH_2 and the asterisk represents the point of attachment to R^W; and optionally the R^W group is $C(=O)$-$CH=CH_2$.

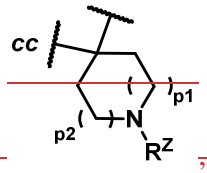
379. The compound of any one of claims 273-365, 367 or 377-378, wherein R^{3a} is  , such as  ,  ,  or  .

380. The compound of claims 273-365, or 367-379, wherein R^{3b} is H.

381. The compound of any one of claims 273-365, or 367-379, wherein R^{3b} is C_{1-3}-alkyl, such as methyl.

382. The compound of any one of claims 273-365, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-8 ring atoms;

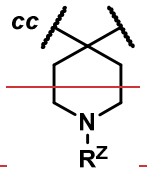
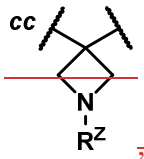
- wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^d), O, and $S(O)_{0-2}$; and
- wherein the fused saturated ring of 4-8 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo, R^e, and R^W.

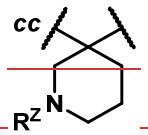
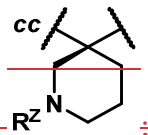
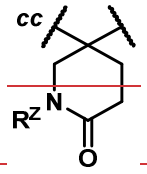
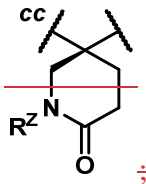
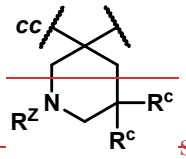
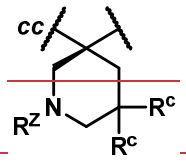
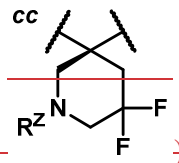
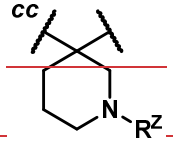
383. The compound of any one of claims 273-365 or 382, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form:  , which is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and R^e, wherein:

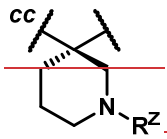
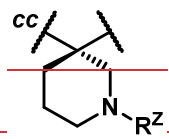
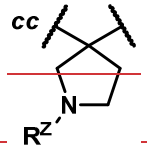
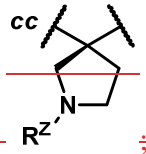
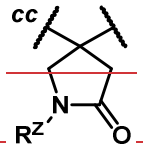
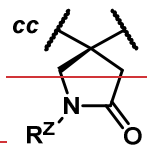
p1 and **p2** are independently 0, 1, or 2;

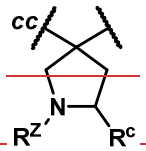
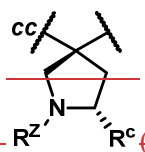
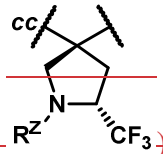
R^Z is H, R^d, C(=O)-**W**, or $S(O)_2$**W**; and

cc represents the point of attachment to $C(R^{2a}R^{2b})$.

384. The compound of any one of claims 273-365 or 382-383, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form  or  , wherein R^Z is H, R^d, C(=O)-**W**, or $S(O)_2$**W**; and *cc* represents the point of attachment to $C(R^{2a}R^{2b})$.

385. The compound of any one of claims 273-365 or 382-383, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused ring selected from the group consisting of:  such as  ;  such as  ;  such as  (e.g., );  such as

 ~~or~~  ~~;~~  ~~such as~~  ~~;~~  ~~such as~~ 

~~; and~~  ~~such as~~  ~~(e.g.,~~  ~~),wherein~~ $\cancel{\mathbf{R^Z}}$ ~~is H,~~ $\cancel{\mathbf{R^d}}$~~, C(=O)-W, or~~ $\cancel{S(O)_2\mathbf{W}}$~~; and~~ ***cc*** ~~represents the point of attachment to~~ $\cancel{C(\mathbf{R^{2a}R^{2b}})}$~~.~~

~~**386.** The compound any one of claims 383-385, wherein~~ $\cancel{\mathbf{R^Z}}$ ~~is H.~~

~~**387.** The compound of any one of claims 383-385, wherein~~ $\cancel{\mathbf{R^Z}}$ ~~is~~ $\cancel{C_{1-6}}$ ~~alkyl optionally substituted with from 1-3 independently selected~~ $\cancel{\mathbf{R^a}}$~~.~~

~~**388.** The compound of any one of claims 383-385, wherein~~ $\cancel{\mathbf{R^Z}}$ ~~is C(=O)-W or~~ $\cancel{S(O)_2\mathbf{W}}$~~, optionally wherein W is~~ $\cancel{C_{2-4}}$ ~~alkenyl.~~

~~**389.** The compound of any one of claims 273-365, wherein~~ $\cancel{\mathbf{R^{3a}}}$ ~~and~~ $\cancel{\mathbf{R^{3b}}}$ ~~together with the Ring B ring atom to which each is attached form a fused~~ $\cancel{C_{3-6}}$ ~~cycloalkyl, wherein the fused~~ $\cancel{C_{3-6}}$ ~~cycloalkyl is optionally substituted with from 1-2~~ $\cancel{\mathbf{R^c}}$~~.~~

~~**390.** The compound of any one of claims 273-365, wherein~~ $\cancel{\mathbf{R^{3a}}}$ ~~and~~ $\cancel{\mathbf{R^{3b}}}$ ~~together with the Ring B ring atom to which each is attached, form a fused saturated ring of 4-6 ring atoms;~~

- ~~wherein from 1-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(~~$\cancel{\mathbf{R^d}}$~~), O, and~~ $\cancel{S(O)_{0-2}}$~~; and~~
- ~~wherein the fused saturated ring of 4-6 ring atoms is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and~~ $\cancel{\mathbf{R^c}}$~~.~~

391. The compound of any one of claims 273-361, wherein R^{2a} and R^{3a} taken together with the **Ring B** ring atoms to which each is attached, form a fused C_{3-6} (e.g., C_3 or C_4) cycloalkyl which is optionally substituted with from 1-2 R^e.

392. The compound of any one of claims 273-362, wherein R^{2b} and R^{3b} are each H.

393. The compound of any one of claims 273-362, wherein R^{1c}, R^{2a}, and R^{2b} are each H; R^{3a} is C_{1-3} alkyl optionally substituted with from 1-3 R^a; and R^{3b} is H, optionally each R^a substituent present in R^{3a} is independently selected from the group consisting of: halo, C_{1-4} alkoxy, and C_{1-4} haloalkoxy.

394. The compound of any one of claims 273-362 or 393, wherein R^{1c}, R^{2a}, and R^{2b} are each H; and R^{3a} and R^{3b} are independently selected C_{1-3} alkyl.

395. The compound of any one of claims 273-362, wherein R^{1c}, R^{2a}, and R^{2b} are each H; R^{3a}, is R^g, $(C_{1-3}$ alkylene$)$ R^g, or $(C_{1-3}$ alkylene$)$-O-R^g,

optionally wherein the R^g group of R^{3a} is:

C_{3-6} cycloalkyl optionally substituted with from 1-4 R^e, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^e; and

R^{3b} is H.

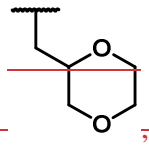
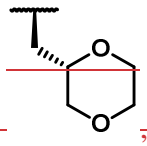
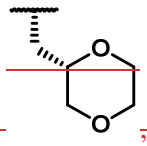
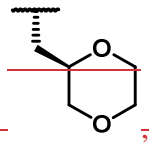
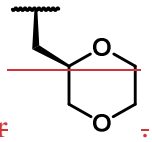
396. The compound of any one of claims 273-362, wherein R^{1c}, R^{2a}, and R^{2b} are each H; and R^{3a} and R^{3b} taken together with the **Ring B** ring carbon atom to which each is attached form a fused C_{3-6} (such as C_3 or C_4) cycloalkyl, wherein the fused cycloalkyl ring is optionally substituted with from 1-2 R^e.

397. The compound of any one of claims 273-362, wherein R^{1e}, R^{2a}, and R^{2b} are each H; and R^{3a} and R^{3b} together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-6 ring atoms;

- wherein from 1-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^{d}), O, and $S(O)_{0-2}$; and
- wherein the fused saturated ring of 4-6 ring atoms is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and R^{e}.

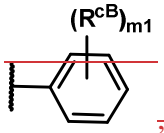
398. The compound of any one of claims 273-361, wherein R^{1e} is H; R^{2a} and R^{3a} taken together with the **Ring B** ring atoms to which each is attached, form a fused C_{3-6} (e.g., C_3 or C_4) cycloalkyl which is optionally substituted with from 1-2 R^{e}; and R^{2b} and R^{3b} are each H.

399. The compound of any one of claims 273-361, wherein R^{1e} is H; R^{2a} and R^{3a} combine to form a double bond between the **Ring B** atoms to which each is attached; and R^{2b} is H; and R^{3b} is $-(L^{g})_{g}-R^{g}$.

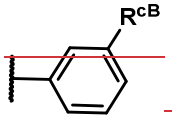
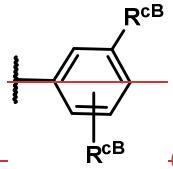
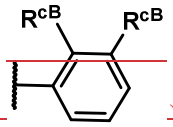
400. The compound of any one of claims 273-361 or 399, wherein R^{1e} is H; R^{2a} and R^{3a} combine to form a double bond between the **Ring B** atoms to which each is attached; and R^{2b} is H; and R^{3b} is  , such as  ,  ,  ,  or .

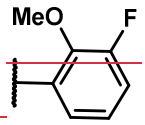
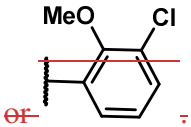
401. The compound of any one of claims 273-362, wherein R^{1e}, R^{2a}, R^{2b}, R^{3a}, and R^{3b} are each H.

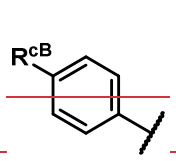
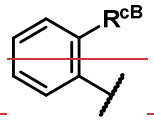
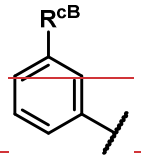
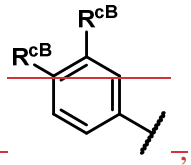
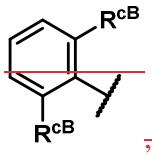
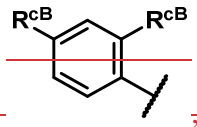
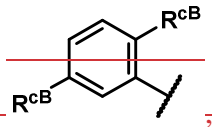
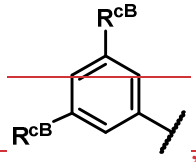
402. The compound of any one of claims 273-401, wherein **R^4** is H.

403. The compound of any one of claims 273-402, wherein **Ring A** is  , wherein each **R^{cB}** is an independently selected **R^e**; and **m1** is 0, 1, 2, 3, or 4.

404. The compound of claim 403, wherein **m1** is 1, 2, or 3, such as 1 or 2.

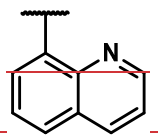
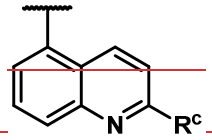
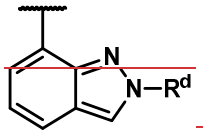
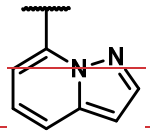
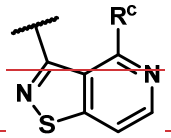
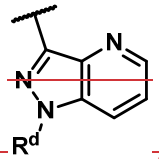
405. The compound of any one of claims 273-404, wherein **Ring A** is  or  (e.g., ), wherein each **R^{cB}** is an independently selected **R^e**.

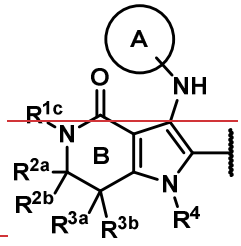
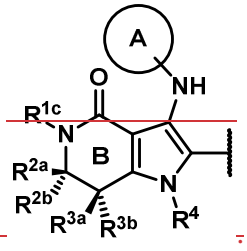
406. The compound of any one of claims 273-405, wherein **Ring A** is  or  .

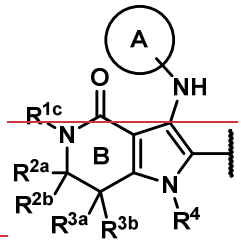
407. The compound of any one of claims 273-404, wherein **Ring A** is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  , and  , wherein each **R^{cB}** is an independently selected **R^e**.

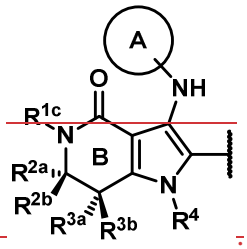
408. The compound of any one of claims 403-407, wherein each R^{cB} is independently selected from the group consisting of: -halo, such as -Cl and -F; -CN; C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-6 independently selected halo.

409. The compound of any one of claims 273-402, wherein **Ring A** is bicyclic heteroaryl including from 9-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(R^d), O, and S(O)$_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 R^e, such as wherein:

Ring A is selected from the group consisting of:  ,  ,  ,  ,  , and  , each of which is further optionally substituted with R^e.

410. The compound of any one of claims 1-409, wherein the 
moiety is  .

411. The compound of any one of claims 1-409, wherein the 

moiety is 

.

412. The compound of claim 1, wherein the compound is selected from the group consisting of the compounds delineated in **Table C1**, or a pharmaceutically acceptable salt thereof.

413. A pharmaceutical composition comprising a compound of any one of claims 1-412, or a pharmaceutically acceptable salt thereof, and pharmaceutically acceptable diluent or carrier.

414. A method for treating cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound of any one of claims 1-412, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

415. A method for treating cancer in a subject in need thereof, the method comprising (a) determining that the cancer is associated with a dysregulation of an *EGFR* gene, an EGFR kinase, or expression or activity or level of any of the same; and (b) administering to the subject a therapeutically effective amount of a compound of any one of claims 1-412, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

416. A method of treating an EGFR associated cancer in a subject, the method

~~comprising administering to a subject identified or diagnosed as having an EGFR-associated cancer a therapeutically effective amount of a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 383.~~

~~**417.** A method of treating an EGFR-associated cancer in a subject, the method comprising:~~

~~(a) determining that the cancer in the subject is an EGFR-associated cancer; and~~

~~(b) administering to the subject a therapeutically effective amount of a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.~~

~~**418.** A method of treating a subject, the method comprising administering a therapeutically effective amount of a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413, to a subject having a clinical record that indicates that the subject has a dysregulation of an *EGFR* gene, an EGFR kinase, or expression or activity or level of any of the same.~~

~~**419.** The method of any one of claims 415 and 417, wherein the step of determining that the cancer in the subject is an EGFR-associated cancer includes performing an assay to detect dysregulation in an *EGFR* gene, an EGFR kinase protein, or expression or activity or level of any of the same in a sample from the subject.~~

~~**420.** The method of claim 419, further comprising obtaining a sample from the subject.~~

~~**421.** The method of claim 420, wherein the sample is a biopsy sample.~~

~~**422.** The method of any one of claims 419-421, wherein the assay is selected~~

from the group consisting of sequencing, immunohistochemistry, enzyme-linked immunosorbent assay, and fluorescence in situ hybridization (FISH).

423. The method of claim 422, wherein the FISH is break apart FISH analysis.

424. The method of claim 422, wherein the sequencing is pyrosequencing or next generation sequencing.

425. The method of any one of claims 415, 418, and 419, wherein the dysregulation in an *EGFR* gene, an EGFR kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *EGFR* gene.

426. The method of claim 425, wherein the one or more point mutations in an *EGFR* gene results in the translation of an EGFR protein having one or more amino acid substitutions at one or more of the following amino acid positions exemplified in **Table 1a** and **1b**.

427. The method of claim 426, wherein the one or more point mutations is selected from the mutations in **Table 1a** and **1b** (e.g., L858R, G719S, G719C, G719A, L861Q, a deletion in exon 19 and/or an insertion in exon 20).

428. The method of claim 426, wherein the one or more point mutations is an EGFR inhibitor resistance mutation (e.g., L718Q, L747S, D761Y, T790M, C797S, T854A).

429. The method of claim 426, wherein the one or more point mutations in an *EGFR* gene include a deletion in exon 19 of a human *EGFR* gene.

430. The method of claim 426, wherein the one or more mutations is an EGFR insertion in exon 20 of a human *EGFR* gene.

431. The method of claim 428, wherein the insertion in exon 20 of a human EGFR gene is selected from: V769_D770insX, D770_N771insX, N771_P772insX, P772_H773insX, and H773_V774insX.

432. The method of claims 428 or 429, wherein the insertion in exon 20 of a human *EGFR* gene is selected from: Y772_A775dup, A775_G776insYVMA, G776delinsVC, G776delinsVV, V777_G778insGSP, and P780_Y781insGSP.

433. The method of any one of claims 426, 427 and 329-432, wherein the EGFR-associated cancer is selected from the group consisting of: oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer, a hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytomaLi-Fraumeni tumor, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer and skin cancer.

434. The method of any one of claims 417 and 419-433, wherein the EGFR-associated cancer is selected from the group consisting of: lung cancer, pancreatic cancer, head and neck cancer, melanoma, colon cancer, renal cancer, leukemia, glioblastoma, or breast cancer.

435. The method of claim 433 or 434, wherein the lung cancer is non-small cell lung cancer.

436. The method of any one of claims 414-435, wherein the cancer is a HER2-associated cancer.

437. The method of claim 436, wherein the HER2-associated cancer is associated with a dysregulation of a *HER2* gene, a HER2 kinase, or expression or activity or level of any of the same.

438. The method of any one of claims 436 and 437, wherein determining that the cancer in the subject is a HER2-associated cancer includes performing an assay to detect dysregulation in a *HER2* gene, a HER2 kinase protein, or expression or activity or level of any of the same in a sample from the subject.

439. The method of claim 438, further comprising obtaining a sample from the subject.

440. The method of claim 439, wherein the sample is a biopsy sample.

441. The method of any one of claims 438-440, wherein the assay is selected from the group consisting of sequencing, immunohistochemistry, enzyme-linked immunosorbent assay, and fluorescence in situ hybridization (FISH).

442. The method of claim 441, wherein the sequencing is pyrosequencing or next generation sequencing.

443. The method of any one of claims 437-442, wherein the dysregulation in a *HER2* gene, a HER2 kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *HER2* gene.

444. The method of claim 443, wherein the one or more point mutations in a *HER2* gene results in the translation of a HER2 protein having one or more amino acid substitutions at one or more of the following amino acid positions exemplified in **Table 3**.

445. The method of claim 444, wherein the one or more point mutations is selected from the mutations in **Table 3** (e.g., S310F, S310Y, R678Q, R678W, R678P,

~~I767M, V773M, V777L, and V842I).~~

~~**446.** The method of any one of claims 414-445, wherein the cancer is selected from the group consisting of: non-small cell lung cancer, pancreatic cancer, and colorectal cancer.~~

~~**447.** The method of any one of claims 414-446, further comprising administering an additional therapy or therapeutic agent to the subject.~~

~~**448.** The method of claim 447, wherein the additional therapy or therapeutic agent is selected from radiotherapy, cytotoxic chemotherapeutics, kinase targeted-therapeutics, apoptosis modulators, signal transduction inhibitors, immune-targeted therapies, and angiogenesis-targeted therapies.~~

~~**449.** The method of claim 448, wherein said additional therapeutic agent is selected from one or more kinase targeted therapeutics.~~

~~**450.** The method of claim 449, wherein said additional therapeutic agent is a tyrosine kinase inhibitor.~~

~~**451.** The method of claim 450, wherein said additional therapeutic agent is a second EGFR inhibitor.~~

~~**452.** The method of claim 447, wherein said additional therapeutic agent is selected from osimertinib, gefitinib, erlotinib, afatinib, lapatinib, neratinib, AZD-9291, CL-387785, CO-1686, WZ4002, and combinations thereof.~~

~~**453.** The method of claim 447, wherein said additional therapeutic agent is a second compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.~~

454. The method of claim 447, wherein said additional therapeutic agent is a HER2 inhibitor.

455. The method of claim 454, wherein the HER2 inhibitor is selected from trastuzumab, pertuzumab, trastuzumab emtansine, lapatinib, KU004, neratinib, dacomitinib, afatinib, tucatinib, erlotinib, pyrotinib, poziotinib, CP-724714, CUDC-101, sapitinib (AZD8931), tanespimycin (17-AAG), IPI-504, PF299, pelitinib, S- 22261-1, and AEE-788.

456. The method of any one of claims 447-455, wherein the compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413, and the additional therapeutic agent are administered simultaneously as separate dosages.

457. The method of any one of claims 447-455, wherein the compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413, and the additional therapeutic agent are administered as separate dosages sequentially in any order.

458. A method of treating a subject having a cancer, wherein the method comprises:

(a) administering one or more doses of a first EGFR inhibitor to the subject for a period of time;

(b) after (a), determining whether a cancer cell in a sample obtained from the subject has at least one EGFR inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with the first EGFR inhibitor of step (a); and

(c) administering a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, as a monotherapy or in conjunction with another anticancer agent to the subject if the subject has been determined to have a cancer cell that has at least one

EGFR inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with the first EGFR inhibitor of step (a); or

(d) administering additional doses of the first EGFR inhibitor of step (a) to the subject if the subject has not been determined to have a cancer cell that has at least one EGFR inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with the first EGFR inhibitor of step (a).

459. The method of claim 458, wherein the anticancer agent in step (c) is a second EGFR inhibitor, an immunotherapy, a HER2 inhibitor, or a combination thereof.

460. The method of claim 458, wherein the anticancer agent in step (c) is the first EGFR inhibitor administered in step (a).

461. The method of claim 458, wherein the subject is administered additional doses of the first inhibitor of EGFR of step (a), and the method further comprises (e) administering another anticancer agent to the subject.

462. The method of claim 461, wherein the anticancer agent of step (e) is a second EGFR inhibitor, an immunotherapy, or a combination thereof.

463. The method of claim 461, wherein the anticancer agent of step (e) is a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof.

464. The method of any one of claims 458-463, wherein the EGFR inhibitor resistance mutation is a substitution at amino acid position 718, 747, 761, 790, 797, or 854 (e.g., L718Q, L747S, D761Y, T790M, C797S, T854A).

465. A method of treating an EGFR-associated cancer in a subject, the method comprising administering to a subject identified or diagnosed as having an EGFR-associated cancer that has one or more EGFR inhibitor resistance mutations a therapeutically effective amount of a compound of any one of claims 1-412 or a

pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

466. A method of treating an EGFR-associated cancer in a subject, the method comprising:

(a) determining that the cancer in the subject has one or more EGFR inhibitor resistance mutations; and

(b) administering to the subject a therapeutically effective amount of a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

467. A method of treating a subject having a cancer, wherein the method comprises:

(a) determining whether a cancer cell in a sample obtained from a subject having a cancer and previously administered one or more doses of a first EGFR inhibitor has one or more EGFR inhibitor resistance mutations that confer increased resistance to a cancer cell or tumor to treatment with the first EGFR inhibitor that was previously administered to the subject; and

(b) administering a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, as a monotherapy or in conjunction with another anticancer agent to the subject if the subject has been determined to have a cancer cell that has at least one EGFR inhibitor resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with the first modulator of EGFR that was previously administered to the subject; or

(c) administering additional doses of the first modulator of EGFR to the subject if the subject has not been determined to have a cancer cell that has at least one EGFR modulator resistance mutation that confers increased resistance to a cancer cell or tumor to treatment with the first modulator of EGFR previously administered to the subject.

468. The method of claim 467, wherein the anticancer agent of step (b) is a second EGFR innhibitor, an immunotherapy, a HER2 inhibitor, or a combination thereof.

469. The method of claim 467, wherein the anticancer agent of step (b) is the first EGFR inhibitor previously administered to the subject.

470. The method of claim 467, wherein the subject is administered additional doses of the first EGFR inhibitor previously administered to the subject, and the method further comprises (d) administering another anticancer agent to the subject.

471. The method of claim 470, wherein the anticancer agent of step (d) is a second EGFR inhibitor, an immunotherapy, or a combination thereof.

472. The method of claim 470, wherein the anticancer agent of step (d) is a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof.

473. The method of claim 472, wherein the second EGFR inhibitor is selected from osimertinib, gefitinib, erlotinib, afatinib, lapatinib, neratinib, AZD-9291, CL-387785, CO-1686, WZ4002, and combinations thereof.

474. The method of any one of claims 465-473, wherein the cancer is selected from the group consisting of: non-small cell lung cancer, pancreatic cancer, and colorectal cancer.

475. The method of any one of claims 465-474, wherein the cancer is associated with a dysregulation of a *HER2* gene, a HER2 kinase, or expression or activity or level of any of the same.

476. The method of claim 475, wherein the dysregulation in a *HER2* gene, a HER2 kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *HER2* gene.

477. The method of claim 476, wherein the one or more point mutations in a

HER2 gene results in the translation of a HER2 protein having one or more amino acid substitutions at one or more of the following amino acid positions exemplified in **Table 3**.

478. The method of claim 477, wherein the one or more point mutations is selected from the mutations in **Table 3** (e.g., S310F, S310Y, R678Q, R678W, R678P, I767M, V773M, V777L, and V842I).

479. A method for modulating EGFR in a mammalian cell, the method comprising contacting the mammalian cell with an effective amount of a compound of any one of claims 1-412, or a pharmaceutically acceptable salt thereof.

480. The method of claim 479, wherein the contacting occurs in vivo.

481. The method of claim 479, wherein the contacting occurs in vitro.

482. The method of any one of claims 479-481, wherein the mammalian cell is a mammalian cancer cell.

483. The method of claim 482, wherein the mammalian cancer cell is a mammalian EGFR-associated cancer cell.

484. The method of any one of claims 479-483, wherein the cell has a dysregulation of an *EGFR* gene, an EGFR kinase protein, or expression or activity or level of any of the same.

485. The method of claim 484, wherein the dysregulation in an *EGFR* gene, an EGFR kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *EGFR* gene.

486. The method of claim 485, wherein the one or more point mutations in an *EGFR* gene results in the translation of an EGFR protein having one or more amino acid

substitutions at one or more of the following amino acid positions exemplified in **Table 1a** and **1b**.

487. The method of claim 486, wherein the one or more point mutations is selected from the mutations in **Table 1a** and **1b** (e.g., L858R, G719S, G719C, G719A, L861Q, a deletion in exon 19 and/or an insertion in exon 20).

488. The method of claim 485, wherein the one or more point mutations is an EGFR inhibitor resistance mutation (e.g., L718Q, L747S, D761Y, T790M, C797S, T854A).

489. The method of claim 485, wherein the one or more point mutations in an *EGFR* gene include a deletion in exon 19 of a human *EGFR* gene.

490. The method of claim 485, wherein the one or more point mutations is an EGFR insertion in exon 20 of a human *EGFR* gene.

491. The method of claim 490, wherein the insertion in exon 20 of a human *EGFR* gene is selected from: A767_V769insX, V769_D770insX, D770_N771insX, N771_P772insX, P772_H773insX, and H773_V774insX.

492. The method of claim 491, wherein the insertion in exon 20 of a human *EGFR* gene is selected from: A767_V769dupASV, V769_D770insASV, D770_N771insNPG, D770_N771insNPY, D770_N771insSVD, D770_N771insGL, N771_H773dupNPH, N771_P772insN, N771_P772insH, N771_P772insV, P772_H773insDNP, P772_H773insPNP, H773_V774insNPH, H773_V774insH, H773_V774insPH, H773_V774insAH, and P772_H773insPNP.

493. A method for treating cancer in a subject in need thereof, the method comprising (a) determining that the cancer is associated with a dysregulation of a *HER2* gene, a HER2 kinase, or expression or activity or level of any of the same; and (b)

administering to the subject a therapeutically effective amount of a compound of any one of claims 1-412, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

494. A method of treating a HER2-associated cancer in a subject, the method comprising administering to a subject identified or diagnosed as having a HER2-associated cancer a therapeutically effective amount of a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

495. A method of treating a HER2-associated cancer in a subject, the method comprising:

(a) determining that the cancer in the subject is a HER2-associated cancer; and

(b) administering to the subject a therapeutically effective amount of a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

496. A method of treating a subject, the method comprising administering a therapeutically effective amount of a compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413, to a subject having a clinical record that indicates that the subject has a dysregulation of a *HER2* gene, a HER2 kinase, or expression or activity or level of any of the same.

497. The method of any one of claims 493 and 495, wherein the step of determining that the cancer in the subject is a HER2-associated cancer includes performing an assay to detect dysregulation in a *HER2* gene, a HER2 kinase protein, or expression or activity or level of any of the same in a sample from the subject.

498. The method of claim 497, further comprising obtaining a sample from the subject.

499. The method of claim 498, wherein the sample is a biopsy sample.

500. The method of any one of claims 493-499, wherein the assay is selected from the group consisting of sequencing, immunohistochemistry, enzyme-linked immunosorbent assay, and fluorescence in situ hybridization (FISH).

501. The method of claim 500, wherein the FISH is break apart FISH analysis.

502. The method of claim 500, wherein the sequencing is pyrosequencing or next generation sequencing.

503. The method of any one of claims 493, 496, and 497, wherein the dysregulation in a *HER2* gene, a HER2 kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *HER2* gene.

504. The method of claim 503, wherein the one or more point mutations in a *HER2* gene results in the translation of a HER2 protein having one or more amino acid substitutions at one or more of the following amino acid positions exemplified in **Table 3**.

505. The method of claim 503, wherein the one or more point mutations is selected from the mutations in **Table 3** (e.g., S310F, S310Y, R678Q, R678W, R678P, I767M, V773M, V777L, and V842I).

506. The method of any one of claims 492, 495, and 496, wherein the dysregulation in a *HER2* gene, a HER2 kinase protein, or expression or activity or level of any of the same is an insertion in exon 20 of the human *HER2* gene.

507. The method of claim 506, wherein the insertion in exon 20 of the human *HER2* gene is deletions at an amino acid position selected from: 774, 775, 776, 777, 778, and 780.

508. The method of claim 507, wherein the insertion in exon 20 of a human *HER2* gene is selected from: M774AYVM, M774del insWLV, A775_G776insYVMA, A775_G776insAVMA, A775_G776insSVMA, A775_G776insVAG, A775insV G776C, A775_G776insI, G776del insVC2, G776del insVV, G776del insLC, G776C V777insC, G776C V777insV, V777_G778insCG, G778_S779insCPG, and P780_Y781insGSP.

509. The method of any one of claims 494, 495, and 497, wherein the HER2-associated cancer is selected from the group consisting of: colon cancer, lung cancer, or breast cancer.

510. The method of claim 509, wherein the lung cancer is non-small cell lung cancer.

511. The method of any one of claims 496-510, further comprising administering an additional therapy or therapeutic agent to the subject.

512. The method of claim 511, wherein the additional therapy or therapeutic agent is selected from radiotherapy, cytotoxic chemotherapeutics, kinase targeted therapeutics, apoptosis modulators, signal transduction inhibitors, immune targeted therapies and angiogenesis-targeted therapies.

513. The method of claim 511, wherein said additional therapeutic agent is a second compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413.

514. The method of claim 511, wherein said additional therapeutic agent is selected from one or more kinase targeted therapeutics.

515. The method of claim 511, wherein said additional therapeutic agent is a tyrosine kinase inhibitor.

~~**516.** The method of claim 511, wherein said additional therapeutic agent is an EGFR inhibitor.~~

~~**517.** The method of claim 511, wherein said additional therapeutic agent is selected from osimertinib, gefitinib, erlotinib, afatinib, lapatinib, neratinib, AZD-9291, CL-387785, CO-1686, WZ4002, and combinations thereof.~~

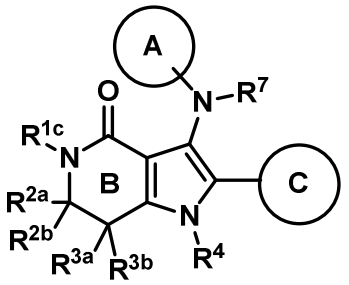
~~**518.** The method of claim 511, wherein said additional therapeutic agent is a HER2 inhibitor.~~

~~**519.** The method of claim 518, wherein the HER2 inhibitor is selected from trastuzumab, pertuzumab, trastuzumab emtansine, lapatinib, KU004, neratinib, dacomitinib, afatinib, tucatinib, erlotinib, pyrotinib, poziotinib, CP-724714, CUDC-101, sapitinib (AZD8931), tanespimycin (17-AAG), IPI-504, PF299, pelitinib, S- 22261-1, and AEE-788.~~

~~**520.** The method of any one of claims 514-519, wherein the compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413, and the additional therapeutic agent are administered simultaneously as separate dosages.~~

~~**521.** The method of any one of claims 514-519, wherein the compound of any one of claims 1-412 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 413, and the additional therapeutic agent are administered as separate dosages sequentially in any order.~~

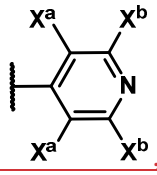
1. A compound of Formula (**I**):



Formula (**I**)

or a pharmaceutically acceptable salt thereof, wherein:

Ring C is selected from the group consisting of:

- 

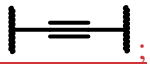
, wherein:
  - each $\mathbf{X^b}$ is independently $\mathbf{X^1}$, $\mathbf{R^c}$, or H; and
  - each $\mathbf{X^a}$ is independently selected from the group consisting of: H, halo; cyano; $C_{1\text{-}10}$ alkyl which is optionally substituted with from 1-6 independently selected $\mathbf{R^a}$; $C_{2\text{-}6}$ alkenyl; $-S(O)_{1\text{-}2}(C_{1\text{-}4}$ alkyl); $-S(O)(=NH)(C_{1\text{-}4}$ alkyl); $-N\mathbf{R^eR^f}$; –OH; $-S(O)_{1\text{-}2}N\mathbf{R'R''}$; $-C_{1\text{-}4}$ thioalkoxy; $-NO_2$; $-C(=O)(C_{1\text{-}10}$ alkyl); $-C(=O)O(C_{1\text{-}4}$ alkyl); -C(=O)OH; $-C(=O)N\mathbf{R'R''}$; and $–SF_5$;
- 2-pyridyl or 3-pyridyl, each optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 $\mathbf{R^c}$;
- 2-pyridonyl or 4-pyridonyl, each optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 $\mathbf{R^c}$, wherein the ring nitrogen atom is optionally substituted with $\mathbf{R^d}$;
- heteroaryl including 6 ring atoms, wherein from 2-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N($\mathbf{R^d}$), and wherein the heteroaryl is optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 $\mathbf{R^c}$;
- heteroaryl including 5 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0\text{-}2}$, and

wherein the heteroaryl is optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 $\mathbf{R^c}$;

- bicyclic heteroaryl including 7-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$;
- C_{3-10} cycloalkyl or C_{3-10} cycloalkenyl, each of which is optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$;
- heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$; and
- C_{6-10} aryl optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 $\mathbf{R^c}$;

$\mathbf{X^1}$ is $-(\mathbf{X^2})_{\mathbf{m}}\text{-}\mathbf{L^1}\text{-}\mathbf{R^5}$, wherein: **m** is 0 or 1;

$\mathbf{X^2}$ is selected from the group consisting of:

- -O-, -N($\mathbf{R^N}$)-, or $-S(O)_{0-2}$;
-  ;
- $-C_{2-6}$ alkenylene optionally substituted with from 1-3 $\mathbf{R^a}$;
- -C(=O)O-*, -C(=O)N($\mathbf{R^N}$)-*, or $-S(O)_{1-2}N(\mathbf{R^N})$-*;
- -OC(=O)-*, -N($\mathbf{R^N}$)C(=O)-*, or $-N(\mathbf{R^N})S(O)_{1-2}$-*; and
- -OC(=O)N($\mathbf{R^N}$)-*, -N($\mathbf{R^N}$)C(=O)O-*, -N($\mathbf{R^N}$)C(=O)N($\mathbf{R^N}$)-*, or $-N(\mathbf{R^N})S(O)_{1-2}N(\mathbf{R^N})$-*,

wherein the asterisk represents point of attachment to $\mathbf{L^1}$;

$\mathbf{L^1}$ is selected from the group consisting of: a bond and $C_{1\text{-}10}$ alkylene optionally substituted with from 1-6 $\mathbf{R^a}$;

$\mathbf{R^5}$ is selected from the group consisting of:

- H;
- halo;
- -OH;
- $-N\mathbf{R^e}\mathbf{R^f}$;
- $-C_{1\text{-}6}$ alkoxy or $-S(O)_{0\text{-}2}(C_{1\text{-}6}$ alkyl), each optionally substituted with from 1-6 $\mathbf{R^a}$;
- $-\mathbf{R^g}$;
- $-\mathbf{L^5}\text{-}\mathbf{R^g}$;
- $-\mathbf{R^{g2}}\text{-}\mathbf{R^W}$ or $-\mathbf{R^{g2}}\text{-}\mathbf{R^Y}$; and
- $-\mathbf{L^5}\text{-}\mathbf{R^{g2}}\text{-}\mathbf{R^W}$ or $-\mathbf{L^5}\text{-}\mathbf{R^{g2}}\text{-}\mathbf{R^Y}$;

provided that:

when $\mathbf{L^1}$ is a bond, then $\mathbf{R^5}$ is selected from the group consisting of: H, $-\mathbf{R^g}$, $-\mathbf{R^{g2}}\text{-}\mathbf{R^W}$, and $-\mathbf{R^{g2}}\text{-}\mathbf{R^Y}$; and

$\mathbf{X^1}$ is other than H, -OH, or NH_2;

$\mathbf{L^5}$ is selected from the group consisting of: –O-, $-S(O)_{0\text{-}2}$, -NH-, and $-N(\mathbf{R^d})$-;

$\mathbf{R^W}$ is $-\mathbf{L^W}\text{-}\mathbf{W}$,

wherein $\mathbf{L^W}$ is $C(=O)$, $S(O)_{1\text{-}2}$, $OC(=O)$*, $NHC(=O)$*, $N\mathbf{R^d}C(=O)$*, $NHS(O)_{1\text{-}2}$*, or $N\mathbf{R^d}S(O)_{1\text{-}2}$*, wherein the asterisk represents point of attachment to $\mathbf{W}$, and

$\mathbf{W}$ is selected from the group consisting of:

- $C_{2\text{-}6}$ alkenyl; $C_{2\text{-}6}$ alkynyl; or $C_{3\text{-}10}$ allenyl, each of which is optionally substituted with from 1-3 $\mathbf{R^a}$ and further optionally substituted with $\mathbf{R^g}$, wherein $\mathbf{W}$ is attached to $\mathbf{L^W}$ via an sp^2 or sp hybridized carbon atom, thereby providing an α, β-unsaturated system; and
- bicyclo[$\mathbf{x}$.$\mathbf{y}$.0]cycloalkyl optionally substituted with from 1-2 $\mathbf{R^c}$, wherein $\mathbf{x}$ is 1 or 2; and $\mathbf{y}$ is an integer from 1 to 6;

$\mathbf{R^Y}$ is selected from the group consisting of: -$\mathbf{R^g}$ and -$(\mathbf{L^g})_g$-$\mathbf{R^g}$;

each of $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$ is independently selected from the group consisting of: H; halo; -OH; -C(O)OH or –C(O)NH_2; -CN; -$\mathbf{R^b}$; -$\mathbf{L^b}$-$\mathbf{R^b}$; -N$\mathbf{R^e R^f}$; -$\mathbf{R^g}$; -$(\mathbf{L^g})_g$-$\mathbf{R^g}$; -$(\mathbf{L^g})_g$-$\mathbf{R^W}$; -$(\mathbf{L^g})_g$-$\mathbf{R^{g2}}$-$\mathbf{R^W}$; and -$C_{1\text{-}6}$ alkoxy or -$C_{1\text{-}6}$ thioalkoxy, each optionally substituted with from 1-6 $\mathbf{R^a}$; provided that $\mathbf{R^{1c}}$ is other than halo, –CN, or –C(O)OH; or

two of variables $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$, together with the **Ring B** ring atoms to which each is attached, form a fused saturated or unsaturated ring of 3-12 ring atoms;

- wherein from 0-2 of the ring atoms are each an independently selected heteroatom (in addition to –N($\mathbf{R^{1c}}$)- when –N($\mathbf{R^{1c}}$)- forms part of the fused saturated or unsaturated ring), wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N($\mathbf{R^d}$), O, and $S(O)_{0\text{-}2}$; and
- wherein the fused saturated or unsaturated ring of 3-12 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo, $\mathbf{R^c}$, and $\mathbf{R^W}$; or

one of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ and one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ combine to form a double bond between the **Ring B** atoms to which each is attached;

Ring A is $\mathbf{R^g}$;

$\mathbf{R^4}$ and $\mathbf{R^7}$ are independently H or $\mathbf{R^d}$;

each occurrence of $\mathbf{R^a}$ is independently selected from the group consisting of: –OH; -halo; –N$\mathbf{R^e R^f}$; $C_{1\text{-}4}$ alkoxy; $C_{1\text{-}4}$ haloalkoxy; -C(=O)O($C_{1\text{-}4}$ alkyl); -C(=O)($C_{1\text{-}4}$ alkyl); -C(=O)OH; -CON**R'R''**; -$S(O)_{1\text{-}2}$N**R'R''**; -$S(O)_{1\text{-}2}$($C_{1\text{-}4}$ alkyl); and cyano;

each occurrence of $\mathbf{R^b}$ is independently $C_{1\text{-}6}$ alkyl, $C_{2\text{-}6}$ alkenyl, or $C_{2\text{-}6}$ alkynyl, each of which is optionally substituted with from 1-6 $\mathbf{R^a}$;

each occurrence of $\mathbf{L^b}$ is independently C(=O); C(=O)O; $S(O)_{1\text{-}2}$; C(=O)NH*; C(=O)N$\mathbf{R^d}$*; $S(O)_{1\text{-}2}$NH*; or $S(O)_{1\text{-}2}$N($\mathbf{R^d}$)*, wherein the asterisk represents point of attachment to $\mathbf{R^b}$;

each occurrence of $\mathbf{R^c}$ is independently selected from the group consisting of: halo; cyano; C_{1-10} alkyl which is optionally substituted with from 1-6 independently selected $\mathbf{R^a}$; C_{2-6} alkenyl; C_{2-6} alkynyl; C_{1-4} alkoxy optionally substituted with C_{1-4} alkoxy or C_{1-4} haloalkoxy; C_{1-4} haloalkoxy; $-S(O)_{1-2}(C_{1-4}$ alkyl); $-S(O)(=NH)(C_{1-4}$ alkyl); $-N\mathbf{R^eR^f}$; –OH; $-S(O)_{1-2}N\mathbf{R'R''}$; $-C_{1-4}$ thioalkoxy; $-NO_2$; $-C(=O)(C_{1-10}$ alkyl); $-C(=O)O(C_{1-4}$ alkyl); -C(=O)OH; $-C(=O)N\mathbf{R'R''}$; and $-SF_5$;

each occurrence of $\mathbf{R^d}$ is independently selected from the group consisting of: C_{1-6} alkyl optionally substituted with from 1-3 independently selected $\mathbf{R^a}$; $-C(O)(C_{1-4}$ alkyl); $-C(O)O(C_{1-4}$ alkyl); $-CON\mathbf{R'R''}$; $-S(O)_{1-2}N\mathbf{R'R''}$; $-S(O)_{1-2}(C_{1-4}$ alkyl); -OH; and C_{1-4} alkoxy;

each occurrence of $\mathbf{R^e}$ and $\mathbf{R^f}$ is independently selected from the group consisting of: H; C_{1-6} alkyl optionally substituted with from 1-3 substituents each independently selected from the group consisting of $N\mathbf{R'R''}$, -OH, C_{1-6} alkoxy, C_{1-6} haloalkoxy, and halo; $-C(O)(C_{1-4}$ alkyl); $-C(O)O(C_{1-4}$ alkyl); $-CON\mathbf{R'R''}$; $-S(O)_{1-2}N\mathbf{R'R''}$; $-S(O)_{1-2}(C_{1-4}$ alkyl); -OH; and C_{1-4} alkoxy;

each occurrence of $\mathbf{R^g}$ is independently selected from the group consisting of:

- C_{3-10} cycloalkyl or C_{3-10} cycloalkenyl, each of which is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$;
- heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$;
- heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 $\mathbf{R^c}$; and
- C_{6-10} aryl optionally substituted with from 1-4 $\mathbf{R^c}$;

each occurrence of $\mathbf{L^g}$ is independently selected from the group consisting of: -O-, -NH-, $-N\mathbf{R^d}$-, $-S(O)_{0-2}$, C(O), and C_{1-3} alkylene optionally substituted with from 1-3 $\mathbf{R^a}$;

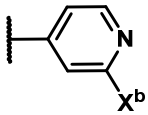
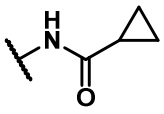
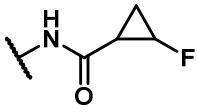
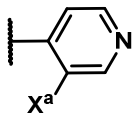
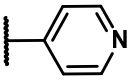
each **g** is independently 1, 2, or 3;

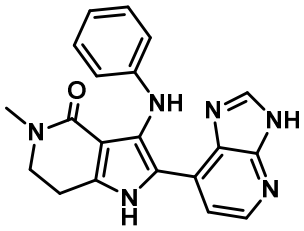
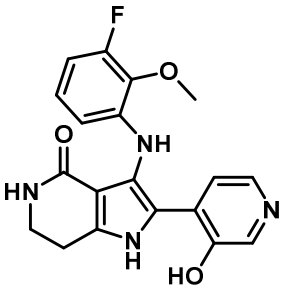
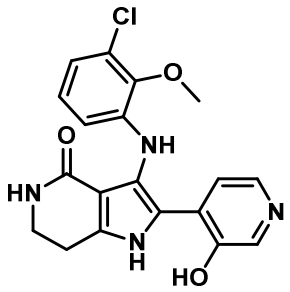
each $\mathbf{R^{g2}}$ is a divalent $\mathbf{R^{g}}$ group;

each occurrence of **R'** and **R''** is independently selected from the group consisting of: H; -OH; and C_{1-4} alkyl; and

each occurrence of $\mathbf{R^{N}}$ is independently H, C_{1-3} alkyl, or C_{3-6} cycloalkyl,

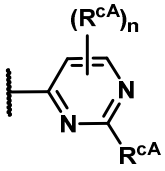
provided that one or more of the following applies:

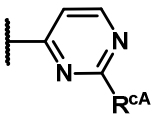
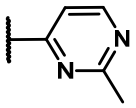
- when $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ are H or methyl; $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are H; **Ring C** is  ; and $\mathbf{X^{b}}$ is H, methyl, NH_2, NHC(=O)Me, NHC(=O)iPr, NHC(=O)NHEt,  ,  , then **Ring A** is other than unsubstituted phenyl;
- when $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$ are each H; **Ring C** is  ; and $\mathbf{X^{a}}$ is methyl or F, then **Ring A** is other than unsubstituted phenyl;
- when $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$ are each H; **Ring C** is  , then **Ring A** is other than 4-fluorophenyl; and

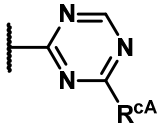
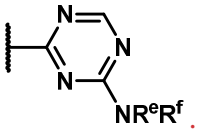
- the compound is other than:  ,  , or  .

2. The compound of claim 1, wherein **Ring C** is heteroaryl including 6 ring atoms, wherein from 2-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N($\mathbf{R^d}$), and wherein the heteroaryl is optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^c}$.

3. The compound of claim 1, wherein **Ring C** is pyrimidyl optionally substituted with from 1-3 $\mathbf{R^{cA}}$, optionally wherein **Ring C** is pyrimidyl substituted with from 1-2 $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^c}$.

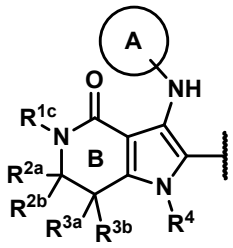
4. The compound of claim 1, wherein **Ring C** is  , wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^c}$; and **n** is 0, 1, or 2.

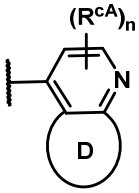
5. The compound of claim 1, wherein **Ring C** is  , wherein $\mathbf{R^{cA}}$ is $C_{1\text{-}3}$ alkyl optionally substituted with from 1-3 independently selected halo; optionally wherein, **Ring C** is  .

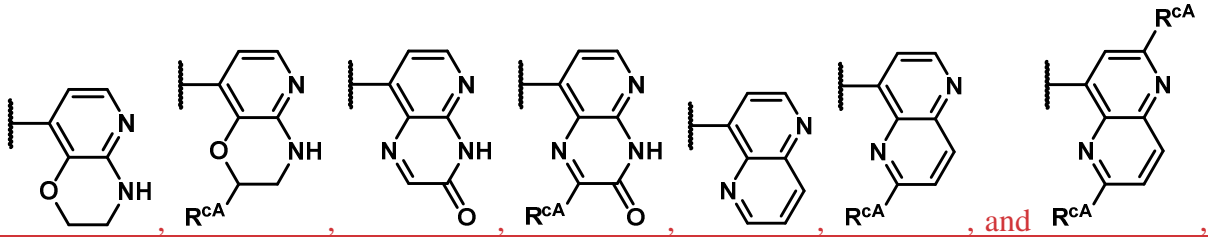
6. The compound of claim 1, wherein **Ring C** is triazinyl optionally substituted with from 1-2 $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$, such as wherein **Ring C** is  , optionally wherein **Ring C** is  .

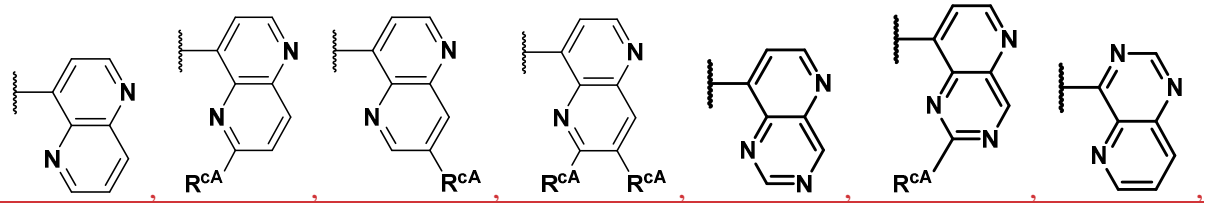
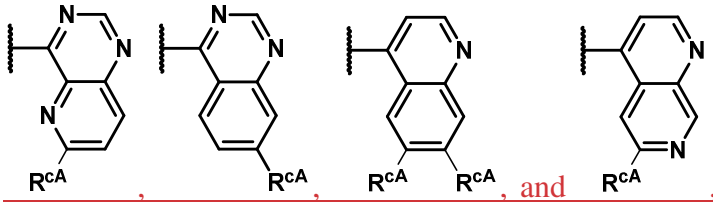
7. The compound of claims 1, wherein **Ring C** is heteroaryl including 6 ring atoms, wherein from 2-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N($\mathbf{R^{d}}$), and wherein the heteroaryl is substituted with $\mathbf{X^{1}}$ and further optionally substituted with from 1-2 $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

8. The compound of claim 1, wherein **Ring C** is bicyclic heteroaryl including 7-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with $\mathbf{X^{1}}$ and further optionally substituted with from 1-4 $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

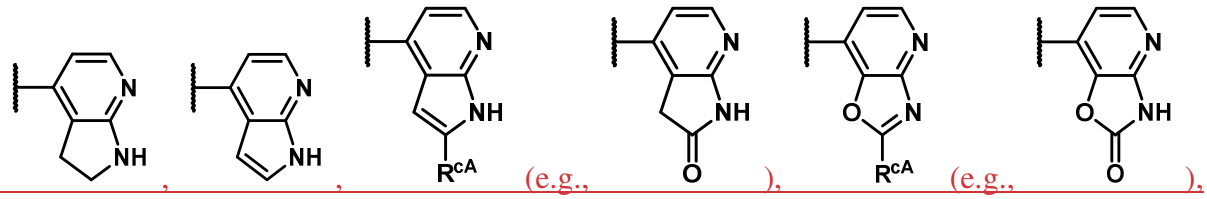
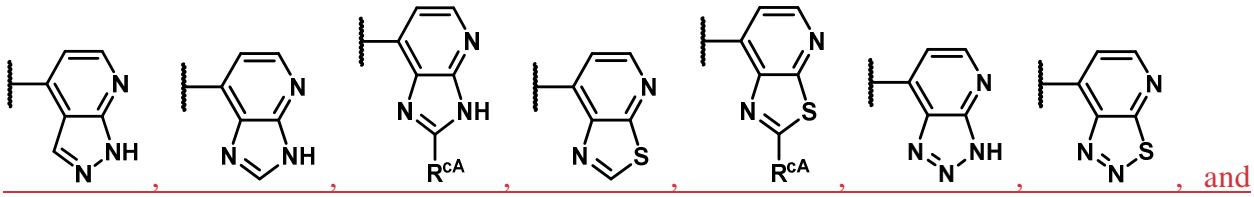
9. The compound of claims 16, wherein **Ring C** is connected to  via a 6-membered ring.

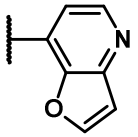
10. The compound of claim 1, wherein **Ring C** is  ; **Ring D** is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R^{cA}}$; **n** is 0, 1, or 2; and each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

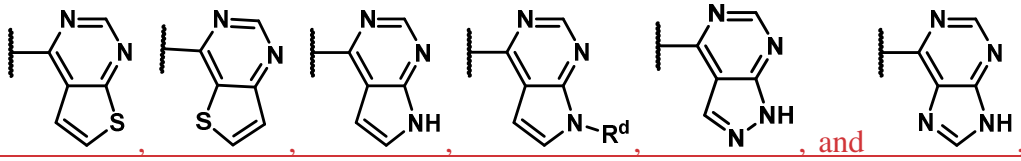
11. The compound of claim 1, wherein **Ring C** is selected from the group consisting of:  , and , each further optionally substituted with $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

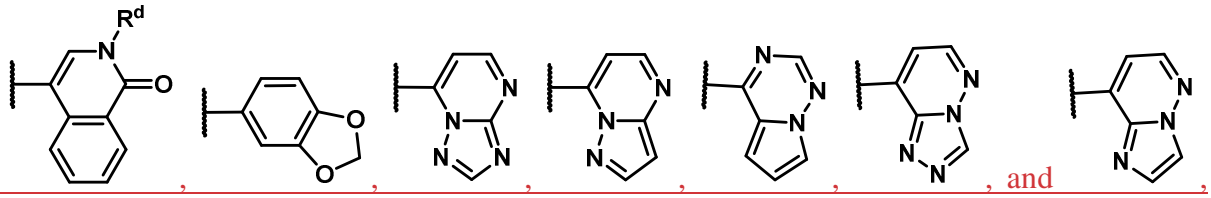
12. The compound of claim 1, wherein **Ring C** is selected from the group consisting of:  ,  , and  , each further optionally substituted with $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

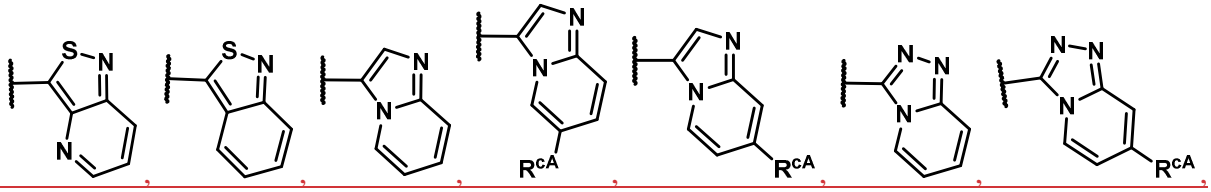
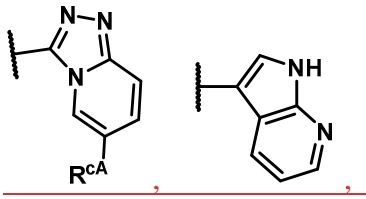
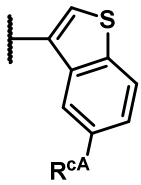
13. The compound of claim 10, wherein **Ring D** is a partially unsaturated or aromatic ring including 5 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R^{cA}}$.

14. The compound of claim 1, wherein **Ring C** is selected from the group consisting of:  , and  ,


, each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

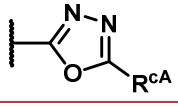
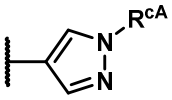
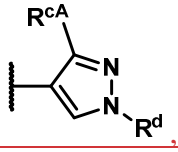
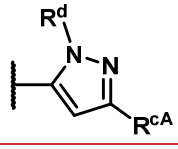
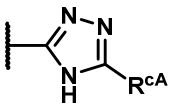
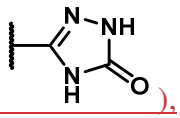
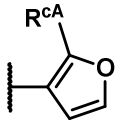
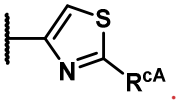
15. The compound of claim 1, wherein **Ring C** is selected from the group consisting of:  , and , each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

16. The compound of claim 1, wherein **Ring C** is selected from the group consisting of:  , and , each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

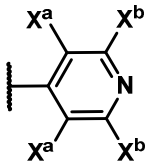
17. The compound of claim 1, wherein **Ring C** is selected from the group consisting of:  ,  , and  , each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

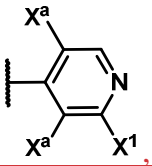
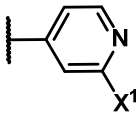
18. The compound of claim 1, wherein **Ring C** is heteroaryl including 5 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R}^{d}$), O, and S(O)$_{0\text{-}2}$, and wherein the heteroaryl is optionally substituted with $\mathbf{X}^{1}$ and further optionally substituted with from 1-4 $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

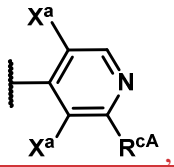
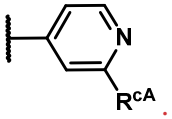
19. The compound of claim 1, wherein **Ring C** is selected from the group consisting of: pyrazolyl, imidazolyl, thiazolyl, oxazolyl, triazolyl, furanyl, thiophenyl, oxadiazolyl, and thiadiazolyl, each optionally substituted with from 1-2 $\mathbf{R^{cA}}$, wherein a ring nitrogen atom is optionally substituted with $\mathbf{R^{d}}$, and each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

20. The compound of claim 1, wherein **Ring C** is selected from the group consisting of:  ,  ,  ,  ,  (e.g., ),  , and  .

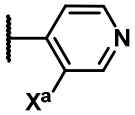
21. The compound of claim 1, wherein **Ring C** is 2-pyridonyl or 4-pyridonyl, each optionally substituted with $\mathbf{X^{1}}$ and further optionally substituted with from 1-4 $\mathbf{R^{cA}}$, wherein the ring nitrogen atom is optionally substituted with $\mathbf{R^{d}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

22. The compound of claim 1, wherein **Ring C** is  .

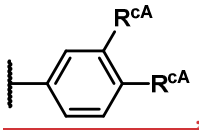
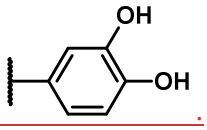
23. The compound of claim 1, wherein **Ring C** is  , optionally wherein **Ring C** is  .

24. The compound of claim 1, wherein **Ring C** is  , wherein $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$, optionally wherein **Ring C** is  .

25. The compound of claim 1, wherein each $\mathbf{X^{a}}$ is selected from the group consisting of: H; halo; and $C_{1\text{-}6}$ alkyl optionally substituted with from 1-6 $\mathbf{R^{a}}$.

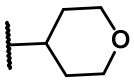
26. The compound of claim 1, wherein **Ring C** is  ; wherein $\mathbf{X^{a}}$ is selected from the group consisting of: -F; -Cl; -H; and $C_{1\text{-}3}$ alkyl optionally substituted with from 1-3 independently selected halo.

27. The compound of claim 1, wherein **Ring C** is $C_{6\text{-}10}$ aryl optionally substituted with $\mathbf{X^{1}}$ and further optionally substituted with from 1-4 $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

28. The compound of claim 1, wherein **Ring C** is phenyl optionally substituted with from 1-4 $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$, optionally wherein **Ring C** is  , such as  .

29. The compound of claim 1, wherein **Ring C** is heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0\text{-}2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with $\mathbf{X^{1}}$ and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

30. The compound of claim 1, wherein **Ring C** is heterocyclyl including from 4-8, such as 5-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from

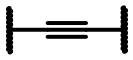
the group consisting of N, N(H), N($\mathbf{R^d}$), O, and S(O)$_{0-2}$, and wherein the heterocyclyl is optionally substituted with $\mathbf{X^1}$ and further optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^{cA}}$, wherein each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^c}$, optionally wherein **Ring C** is  .

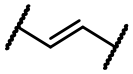
31. The compound of claim 1, wherein **m** is 1.

32. The compound of claim 1, wherein $\mathbf{X^2}$ is selected from the group consisting of: -O-, -N($\mathbf{R^N}$)-, and –S(O)$_{0-2}$.

33. The compound of claim 1, wherein $\mathbf{X^2}$ is selected from the group consisting of: -OC(=O)-*, -N($\mathbf{R^N}$)C(=O)-*, and –N($\mathbf{R^N}$)S(O)$_{1-2}$-*.

34. The compound of claim 1, wherein $\mathbf{X^2}$ is selected from the group consisting of: -OC(=O)N($\mathbf{R^N}$)-*, -N($\mathbf{R^N}$)C(=O)O-*, -N($\mathbf{R^N}$)C(=O)N($\mathbf{R^N}$)-*, and –N($\mathbf{R^N}$)S(O)$_{1-2}$N($\mathbf{R^N}$)-*.

35. The compound of claim 1, wherein $\mathbf{X^2}$ is  .

36. The compound of claim 1, wherein $\mathbf{X^2}$ is  .

37. The compound of claim 1, wherein **m** is 0.

38. The compound of claim 1, wherein $\mathbf{L^1}$ is a bond.

39. The compound of claim 1, wherein $\mathbf{L^1}$ is C$_{1-10}$ alkylene optionally substituted with from 1-6 $\mathbf{R^a}$.

40. The compound of claim 1, wherein $\mathbf{R^5}$ is -C$_{1-6}$ alkoxy or -S(O)$_{0-2}$(C$_{1-6}$ alkyl), each optionally substituted with from 1-6 $\mathbf{R^a}$.

41. The compound of claim 1, wherein $\mathbf{R^5}$ is H or halo, optionally wherein $\mathbf{R^5}$ is H or -F.

42. The compound of claim 1, wherein $\mathbf{R^5}$ is –OH or -N$\mathbf{R^eR^f}$.

43. The compound of claim 1, wherein $\mathbf{R^5}$ is -$\mathbf{R^g}$.

44. The compound of claim 1, wherein $\mathbf{R^5}$ is selected from the group consisting of:

- heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 $\mathbf{R^c}$; and
- C_{6-10} aryl optionally substituted with from 1-4 $\mathbf{R^c}$.

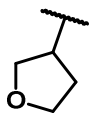
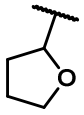
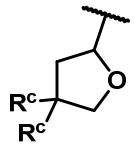
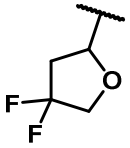
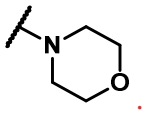
45. The compound of claim 1, wherein $\mathbf{R^5}$ is phenyl optionally substituted with from 1-4 $\mathbf{R^c}$.

46. The compound of claim 1, wherein $\mathbf{R^5}$ is heteroaryl including from 5-6 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 $\mathbf{R^c}$.

47. The compound of claim 1, wherein $\mathbf{R^5}$ is selected from the group consisting of:

- C_{3-10} cycloalkyl or C_{3-10} cycloalkenyl, each of which is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$; and
- heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$.

48. The compound of claim 1, wherein $\mathbf{R^5}$ is C_{3-10} cycloalkyl, optionally C_{3-6} cycloalkyl, optionally substituted with from 1-4 $\mathbf{R^c}$, optionallywherein $\mathbf{R^5}$ is cyclopropyl.

49. The compound of claim 1, wherein $\mathbf{R^5}$ is heterocyclyl including from 4-8, optionally 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$, optionally wherein $\mathbf{R^5}$ is  ,  ,  ,  , or  .

50. The compound of claim 1, wherein $\mathbf{R^5}$ is selected from the group consisting of: -$\mathbf{R^{g2}}$-$\mathbf{R^W}$ and –$\mathbf{R^{g2}}$-$\mathbf{R^Y}$.

51. The compound of claim 50, wherein the **–R^{g2}** group present in **R^5** is $C_{6\text{-}10}$ arylene optionally substituted with from 1-4 **R^c**.

52. The compound of claim 50, wherein the **R^Y** group present in **R^5** is **–R^g**; optionally wherein the **R^Y** group present in **R^5** is heterocyclyl or heterocycloalkenyl including from 3-10 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N(**R^d**), O, and $S(O)_{0\text{-}2}$, and wherein the heterocyclyl or heterocycloalkenyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and **R^c**.

53. The compound of claim 1, wherein **R^5** is **–L^5-R^g**, optionally wherein **R^5** is –O-**R^g**.

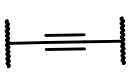
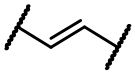
54. The compound of claim 1, wherein **X^1** is **–$(X^2)_m$-L^1-R^5**, wherein:

- **m** is 0 or 1;
- **X^2** is –N(**R^N**)- or -O-;
- **L^1** is a bond or $C_{1\text{-}6}$ alkylene optionally substituted with from 1-3 **R^a**; and
- **R^5** is –**R^g**.

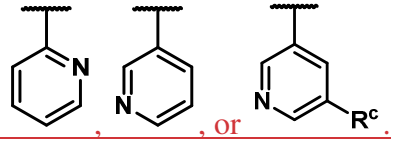
55. The compound of claim 1, wherein **X^1** is **–X^2-L^1-R^5**, wherein:

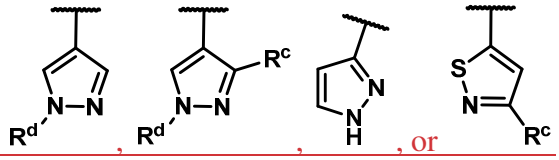
- **X^2** is -N(**R^N**)C(=O)-*, -N(**R^N**)$S(O)_2$-*, -N(**R^N**)C(=O)O-*, or N(**R^N**)C(=O)N(**R^N**)*;
- **L^1** is a bond or $C_{1\text{-}6}$ alkylene optionally substituted with from 1-3 **R^a**; and
- **R^5** is –**R^g**.

56. The compound of claim 1, wherein **X^1** is **–X^2-L^1-R^5**, wherein:

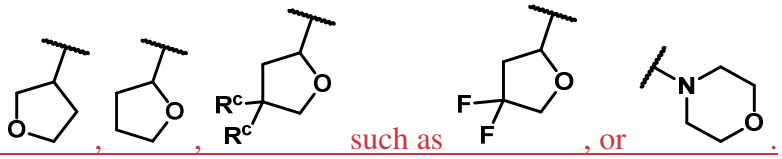
- **X^2** is  or  ;
- **L^1** is a bond or $C_{1\text{-}6}$ alkylene optionally substituted with from 1-3 **R^a**; and
- **R^5** is –**R^g**.

57. The compound of claim 54, wherein **R^5** is phenyl optionally substituted with from 1-4 **R^c**, optionally wherein **R^5** is phenyl optionally substituted with from 1-2 independently selected halo, such as –F.

58. The compound of claim 54, wherein $\mathbf{R^5}$ is heteroaryl including 6 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), and N($\mathbf{R^d}$), and wherein the heteroaryl is optionally substituted with from 1-4 $\mathbf{R^c}$, optionally wherein $\mathbf{R^5}$ is  .

59. The compound of claim 54, wherein $\mathbf{R^5}$ is heteroaryl including 5 ring atoms, wherein from 1-4, such as 2-4, ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 $\mathbf{R^c}$, optionally wherein $\mathbf{R^5}$ is  .

60. The compound of claim 54, wherein $\mathbf{R^5}$ is C_{3-10} cycloalkyl, such as C_{3-6} cycloalkyl, optionally substituted with from 1-4 $\mathbf{R^c}$, optionally wherein $\mathbf{R^5}$ is cyclopropyl.

61. The compound of claim 54, wherein $\mathbf{R^5}$ is heterocyclyl including from 4-8, such as 4-6, ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$, optionally wherein $\mathbf{R^5}$ is  .

62. The compound of claim 1, wherein $\mathbf{X^1}$ is $-(\mathbf{X^2})_{\mathbf{m}}\text{-}\mathbf{L^1}\text{-}\mathbf{R^5}$, wherein:

- **m** is 0 or 1;
- $\mathbf{X^2}$ is -N($\mathbf{R^N}$)- or –O-;
- $\mathbf{L^1}$ is a bond or C_{1-6} alkylene optionally substituted with from 1-3 $\mathbf{R^a}$; and
- $\mathbf{R^5}$ is $-\mathbf{R^{g2}}\text{-}\mathbf{R^Y}$.

63. The compound of claims 1, wherein $\mathbf{X^1}$ is $\mathbf{-X^2\text{-}L^1\text{-}R^5}$, wherein:

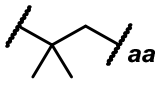
- $\mathbf{X^2}$ is -N($\mathbf{R^N}$)-, –O-, -N($\mathbf{R^N}$)C(=O)-*, -N($\mathbf{R^N}$)S(O)$_2$-, -N($\mathbf{R^N}$)C(=O)O-*, or -N($\mathbf{R^N}$)C(=O)N($\mathbf{R^N}$)-*;
- $\mathbf{L^1}$ is $C_{1\text{-}6}$ alkylene optionally substituted with from 1-3 $\mathbf{R^a}$; and
- $\mathbf{R^5}$ is H, halo, $C_{1\text{-}6}$ alkoxy optionally substituted with from 1-3 $\mathbf{R^a}$, or –OH.

64. The compound of claim 54, wherein **m** is 0.

65. The compound of claim 54, wherein **m** is 1.

66. The compound of claim 54, wherein $\mathbf{L^1}$ is a bond.

67. The compound of claim 54, wherein $\mathbf{L^1}$ is $C_{1\text{-}3}$ alkylene, optionally –CH_2-, -CH_2CH_2-, or –CH(Me)-.

68. The compound of claim 54, wherein $\mathbf{L^1}$ is branched $C_{3\text{-}6}$ alkylene, optionally  or 

, wherein ***aa*** is the point of attachment to $\mathbf{R^5}$.

69. The compound of claim 1, wherein $\mathbf{X^1}$ is $\mathbf{-L^1\text{-}R^5}$, wherein $\mathbf{L^1}$ is $C_{1\text{-}6}$ alkylene optionally substituted with from 1-3 $\mathbf{R^a}$; and $\mathbf{R^5}$ is $\mathbf{-L^5\text{-}R^g}$; optionally wherein $\mathbf{R^5}$ is –O-$\mathbf{R^g}$; optionally wherein $\mathbf{R^5}$ is –O-(phenyl), wherein the phenyl is optionally substituted with from 1-2 $\mathbf{R^c}$.

70. The compound of claim 69, wherein $\mathbf{L^1}$ is $C_{1\text{-}3}$ alkylene, optionally –CH_2-, -CH_2CH_2-, or –CH(Me)-.

71. The compound of claim 2, wherein each occurrence of $\mathbf{R^{cA}}$ is independently selected from the group consisting of: halo; cyano; $C_{1\text{-}10}$ alkyl which is optionally substituted with from 1-6 independently selected $\mathbf{R^a}$; $C_{1\text{-}4}$ alkoxy optionally substituted with $C_{1\text{-}4}$ alkoxy or $C_{1\text{-}4}$ haloalkoxy; $C_{1\text{-}4}$ haloalkoxy; -S(O)$_{1\text{-}2}$($C_{1\text{-}4}$ alkyl); -N$\mathbf{R^eR^f}$; –OH; -S(O)$_{1\text{-}2}$N**R'R''**; -$C_{1\text{-}4}$ thioalkoxy; -C(=O)($C_{1\text{-}10}$ alkyl); -C(=O)O($C_{1\text{-}4}$ alkyl); -C(=O)OH; and -C(=O)N**R'R''**.

72. The compound of claim 1, wherein $\mathbf{R^{1c}}$ is H.

73. The compound of claim 1, wherein $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ are both H.

74. The compound of claim 1, wherein from 1-2 of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ is an independently selected substituent that is other than H.

75. The compound of claim 1, wherein one of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$, optionally $\mathbf{R^{2a}}$, is a substituent that is other than H; optionally wherein one of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$, optionally $\mathbf{R^{2a}}$, is $\mathbf{R^{b}}$; optionally wherein one of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$, optionally $\mathbf{R^{2a}}$, is $C_{1\text{-}6}$ alkyl, which is optionally substituted with from 1-6 $\mathbf{R^{a}}$.

76. The compound of claim 1, wherein $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are both H.

77. The compound of claim 1, wherein from 1-2 of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ is an independently selected substituent that is other than H.

78. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is a substituent that is other than H.

79. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $\mathbf{R^{b}}$.

80. The compound of claim1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $C_{1\text{-}6}$ alkyl which is optionally substituted with from 1-6 $\mathbf{R^{a}}$.

81. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $C_{1\text{-}3}$ alkyl, optionally methyl or ethyl.

82. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $C_{1\text{-}3}$ alkyl substituted with from 1-3 independently selected halo; optionally wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $–CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CHF_2$, or $-CH_2CH_2F$.

83. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $C_{1\text{-}3}$ alkyl substituted with $C_{1\text{-}4}$ alkoxy, $C_{1\text{-}4}$ haloalkoxy, or $\mathbf{NR^eR^f}$.

84. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $–CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, $-CH_2CH(Me)OMe$, $-CH_2OEt$, $-CH_2CH_2OCHF_2$ $-CH_2N\mathbf{R^eR^f}$ (e.g., $-CH_2N(CF_3)Me$), or $–CH_2CH_2N\mathbf{R^eR^f}$ (e.g., $-CH_2CH_2NMe_2$).

85. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $C_{1\text{-}3}$ alkyl substituted with $C_{1\text{-}4}$ alkoxy; .

86. The compound of claim 1 wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $-CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, $-CH_2CH(Me)OMe$, or $-CH_2OEt$, such as $-CH_2OMe$; such as $-CH_2CH_2OMe$; optionally the other one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3b}}$ is H.

87. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $\mathbf{R^g}$ or $-(\mathbf{L^g})_g\text{-}\mathbf{R^g}$.

88. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is selected from the group consisting of:

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0\text{-}2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$; and

$C_{3\text{-}6}$ cycloalkyl optionally substituted with from 1-4 $\mathbf{R^c}$.

89. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $-(C_{1\text{-}3}$ alkylene)-$\mathbf{R^g}$ or $-(C_{1\text{-}3}$ alkylene)-O-$\mathbf{R^g}$, and optionally the $\mathbf{R^g}$ group of $\mathbf{R^{3a}}$ or $\mathbf{R^{3b}}$ is:

$C_{3\text{-}6}$ cycloalkyl optionally substituted with from 1-4 $\mathbf{R^c}$, or

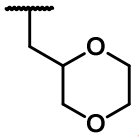
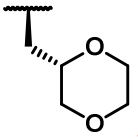
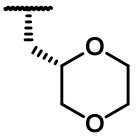
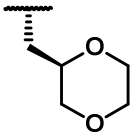
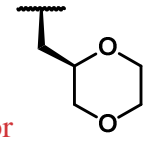
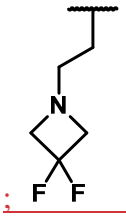
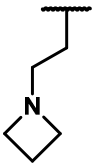
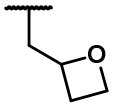
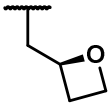
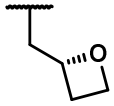
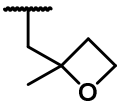
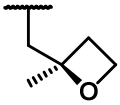
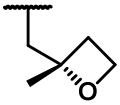
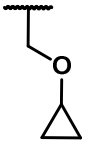
heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0\text{-}2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^c}$.

90. The compound of claim 1, wherein one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $-CH_2\text{-}\mathbf{R^g}$, $-CH_2CH_2\mathbf{R^g}$, or $-CH_2\text{-O-}\mathbf{R^g}$, wherein the $\mathbf{R^g}$ group of $\mathbf{R^{3a}}$ or $\mathbf{R^{3b}}$ is:

$C_{3\text{-}6}$ cycloalkyl optionally substituted with from 1-4 $\mathbf{R^c}$, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0\text{-}2}$, and

wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and **R**^{c}.

91. The compound of claim 1, wherein one of **R**^{3a} and **R**^{3b}, optionally **R**^{3a}, is selected from the group consisting of:  , such as  ,  ,  , or  ;  ;  ;  , such as  or  ;  , such as  or  ;  , such as  or  ;  ; and  .

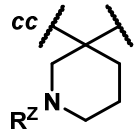
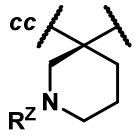
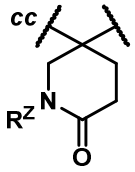
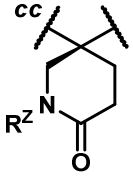
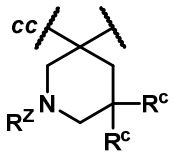
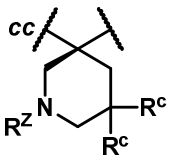
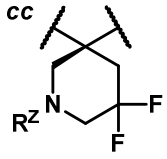
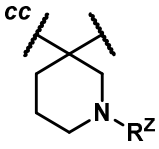
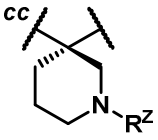
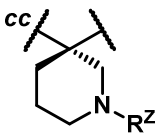
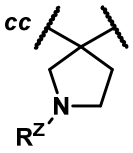
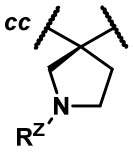
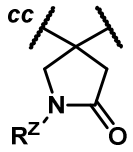
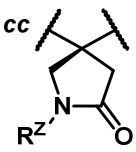
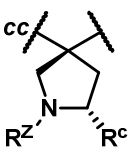
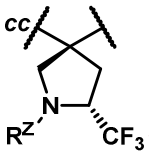
92. The compound of claim 1 wherein one of **R**^{3a} and **R**^{3b}, optionally **R**^{3a}, is-(**L**^{g})$_{g}$-**R**^{W}.

93. The compound of claim 1 wherein the other of **R**^{3a} and **R**^{3b} is –H.

94. The compound of claim 1, wherein the other of **R**^{3a} and **R**^{3b} is C_{1-3} alkyl, such as methyl; or wherein the other of **R**^{3a} and **R**^{3b} is halo, such as -F.

95. The compound of claim 1, wherein **R**^{3a} and **R**^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused saturated or unsaturated ring of 3-12 ring atoms;

- wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(**R**^{d}), O, and $S(O)_{0-2}$; and
- wherein the fused saturated or unsaturated ring of 3-12 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo, **R**^{c}, and **R**^{W}.

96. The compound of claim 1, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused ring selected from the group consisting of:  such as  ;  such as  ;  such as  (e.g., );  such as  or  ;  such as  ;  such as  ; and  such as  (e.g., ), wherein R^{Z} is H, R^{d}, C(=O)-**W**, or $S(O)_2$**W**; and ***cc*** represents the point of attachment to $C(R^{2a}R^{2b})$.

97. The compound of claim 1, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) taken together with the **Ring B** ring atoms to which each is attached, form a fused saturated or unsaturated ring of 3-12 ring atoms;

wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, $N(R^{d})$, O, and $S(O)_{0-2}$; and

wherein the fused saturated or unsaturated ring of 3-12 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and R^{c}.

98. The compound of claim 1, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) taken together with the **Ring B** ring atoms to which each is attached, form a fused C_{3-6} cycloalkyl which is optionally substituted with from 1-2 R^{c}.

99. The compound of claim 1, wherein one of R^{2a} and R^{2b} (such as R^{2a}) and one of R^{3a} and R^{3b} (such as R^{3a}) combine to form a double bond between the **Ring B** atoms to which each is attached.

100. The compound of claim 99, wherein the other of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ and the other of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are each H.

101. The compound of claim 1, wherein the other one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ is $\mathbf{R^{g}}$ or $\mathbf{-(L^{g})_{g}-R^{g}}$.

102. The compound of claim 1, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $C_{1\text{-}3}$ alkyl optionally substituted with from 1-3 $\mathbf{R^{a}}$; and the other of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ is H, optionally each $\mathbf{R^{a}}$ substituent present in $\mathbf{R^{3a}}$ or $\mathbf{R^{3b}}$ is independently selected from the group consisting of: halo, $C_{1\text{-}4}$ alkoxy, and $C_{1\text{-}4}$ haloalkoxy.

103. The compound of claim 1, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is $C_{1\text{-}3}$ alkyl optionally substituted with from $C_{1\text{-}4}$ alkoxy; optionally one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, such as $\mathbf{R^{3a}}$, is -CH_2CH_2-OMe; and the other of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ is H.

104. The compound of claim 1, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; and $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are independently selected $C_{1\text{-}3}$ alkyl.

105. The compound of claim 1, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$, optionally $\mathbf{R^{3a}}$, is $\mathbf{-R^{g}}$, $\mathbf{-(}C_{1\text{-}3}$ alkylene)-$\mathbf{R^{g}}$, or $\mathbf{-(}C_{1\text{-}3}$ alkylene)-O-$\mathbf{R^{g}}$,

optionally wherein the $\mathbf{R^{g}}$ group of $\mathbf{R^{3a}}$ or $\mathbf{R^{3b}}$ is:

$C_{3\text{-}6}$ cycloalkyl optionally substituted with from 1-4 $\mathbf{R^{c}}$, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0\text{-}2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^{c}}$; and

the other of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ is H.

106. The compound of claim 1, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; and $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ taken together with the **Ring B** ring carbon atom to which each is attached form a fused $C_{3\text{-}6}$ (optionally C_3 or C_4) cycloalkyl, wherein the fused cycloalkyl ring is optionally substituted with from 1-2 $\mathbf{R^{c}}$.

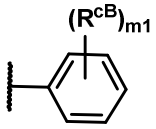
107. The compound of claim 1, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; and $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-6 ring atoms;

- wherein from 1-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$; and
- wherein the fused saturated ring of 4-6 ring atoms is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and $\mathbf{R^{c}}$.

108. The compound of claim 1, wherein $\mathbf{R^{1c}}$ is H; one of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ (optionally $\mathbf{R^{2a}}$) and one of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ (optionally $\mathbf{R^{3a}}$) taken together with the **Ring B** ring atoms to which each is attached, form a fused C_{3-6} (such as C_3 or C_4) cycloalkyl which is optionally substituted with from 1-2 $\mathbf{R^{c}}$; and the other of $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ and the other of $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are each H.

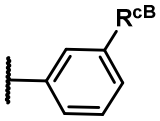
109. The compound of claim 1, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$ are each H.

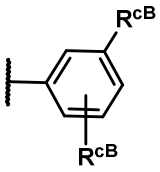
110. The compound of claim 1, wherein $\mathbf{R^{4}}$ is H; and $\mathbf{R^{7}}$ is H.

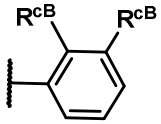
111. The compound of claim 1, wherein **Ring A** is 

, wherein each $\mathbf{R^{cB}}$ is an independently selected $\mathbf{R^{c}}$; and **m1** is 0, 1, 2, 3, or 4.

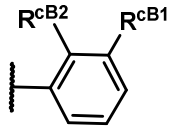
112. The compound of claim 111, wherein **m1** is 1 or 2, optionally wherein **m1** is 2.

113. The compound of claim 1, wherein **Ring A** is 

or 

(e.g., 

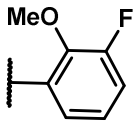
), wherein each $\mathbf{R^{cB}}$ is an independently selected $\mathbf{R^{c}}$.

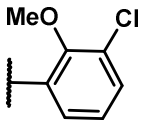
114. The compound of claim 1, wherein **Ring A** is 

, wherein $\mathbf{R^{cB1}}$ is $\mathbf{R^c}$; and $\mathbf{R^{cB2}}$ is H or $\mathbf{R^c}$, optionally wherein $\mathbf{R^{cB1}}$ and $\mathbf{R^{cB2}}$ are each independently selected from the group consisting of: -halo, optionally wherein the halo is -Cl or -F; -CN; C_{1-4} alkoxy; C_{1-4} haloalkoxy; C_{1-3} alkyl; and C_{1-3} alkyl substituted with from 1-6 independently selected halo.

115. The compound of claim 114, wherein $\mathbf{R^{cB1}}$ is halo, optionally wherein $\mathbf{R^{cB1}}$ is –F or $\mathbf{R^{cB1}}$ is –Cl.

116. The compound of claim 114, wherein $\mathbf{R^{cB2}}$ is C_{1-4} alkoxy or C_{1-4} haloalkoxy.

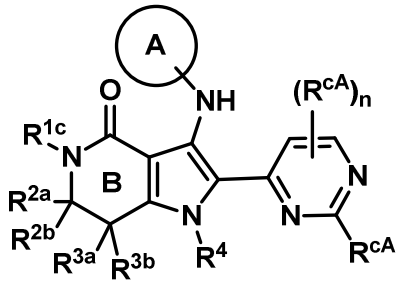
117. The compound of claim 1, wherein **Ring A** is 

or 

.

118. The compound of claim 1, wherein **Ring A** is heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 $\mathbf{R^c}$.

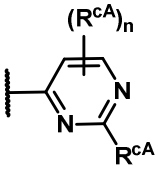
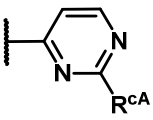
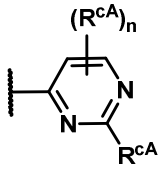
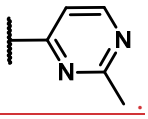
119. The compound of claim 1, wherein the compound is a compound of Formula (**I-a**):



Formula (**I-a**)

or a pharmaceutically acceptable salt thereof,

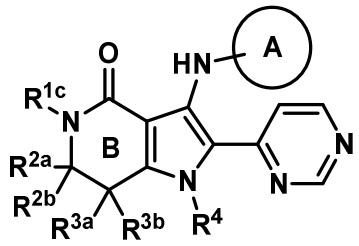
wherein: each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^c}$; and **n** is 0, 1, or 2.

120. The compound of claim 119, wherein  is  , wherein R^{cA} is C_{1-3} alkyl optionally substituted with from 1-3 independently selected halo; optionally wherein  is  .

121. The compound of claim 119, wherein one of R^{3a} and R^{3b}, optionally R^{3a}, is C_{1-3} alkyl substituted with C_{1-4} alkoxy; optionally wherein the other one of of R^{3a} and R^{3b}, such as R^{3b} is H.

122. The compound of claim 120 wherein one of R^{3a} and R^{3b}, optionally R^{3a}, is $-CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, $-CH_2CH(Me)OMe$, or $-CH_2OEt$; optionally wherein one of R^{3a} and R^{3b}, such as R^{3a} is $-CH_2CH_2OMe$.

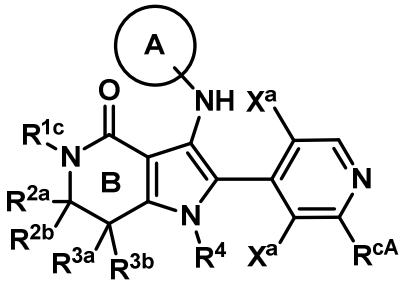
123. The compound of claim 1, wherein the compound is a compound of Formula (**I-b**):



Formula (**I-b**)

or a pharmaceutically acceptable salt thereof.

124. The compound of claim 1, wherein the compound is a compound of Formula (**I-c**):

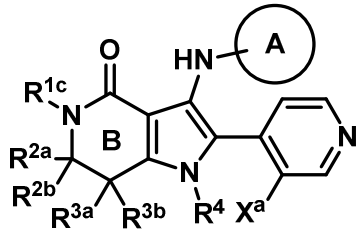


Formula (**I-c**)

or a pharmaceutically acceptable salt thereof,

wherein: $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$.

125. The compound of claim 1, wherein the compound is a compound of Formula (**I-d**):

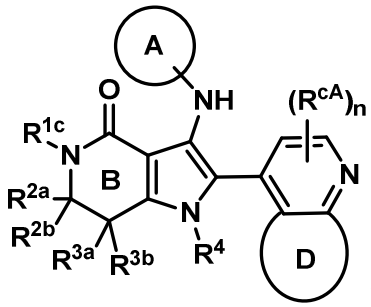


Formula (**I-d**)

or a pharmaceutically acceptable salt thereof, wherein:

$\mathbf{X^{a}}$ is selected from the group consisting of: H; -F; -Cl; $C_{1\text{-}6}$ alkyl; and $C_{1\text{-}3}$ alkyl substituted with from 1-3 independently selected halo.

126. The compound of claim 1, wherein the compound is a compound of Formula (**I-e**):



Formula (**I-e**)

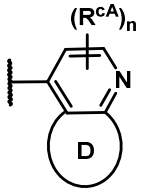
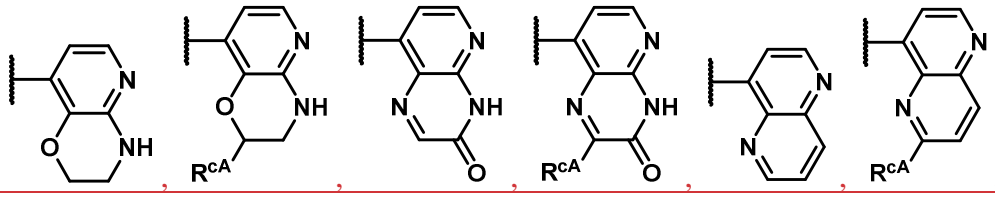
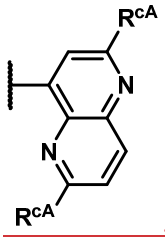
or a pharmaceutically acceptable salt thereof,

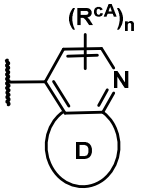
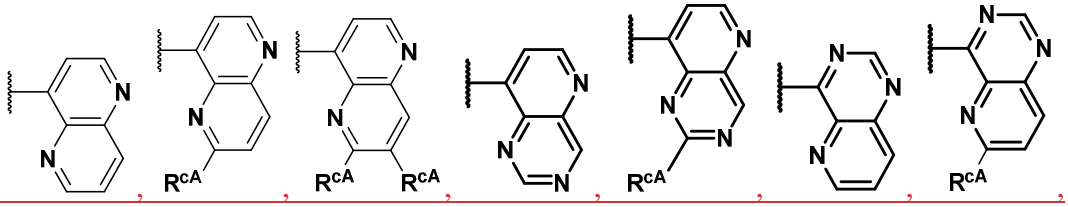
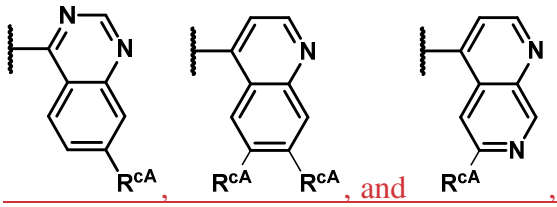
wherein:

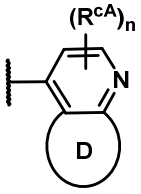
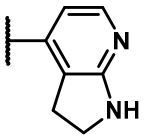
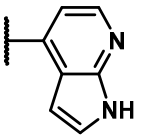
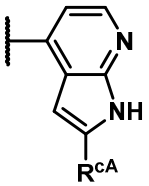
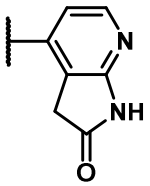
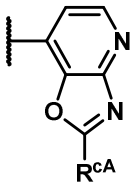
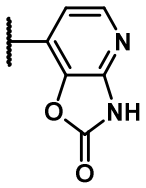
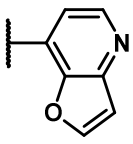
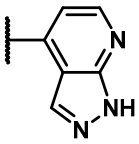
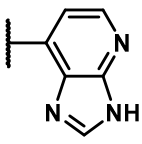
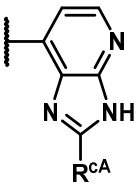
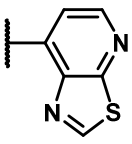
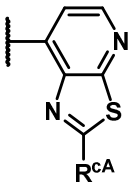
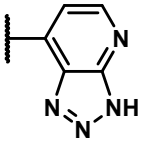
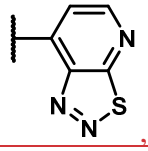
each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$;

n is 0, 1, or 2; and

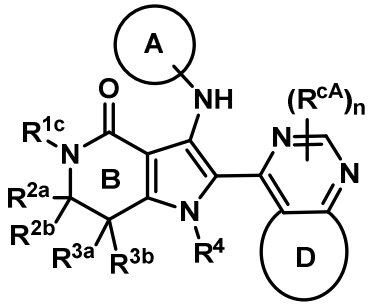
Ring D is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0\text{-}2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R^{cA}}$.

127. The compound of claim 126, wherein  is selected from the group consisting of:  , and  , each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

128. The compound of claim 126, wherein  is selected from the group consisting of:  ,  , and , each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

129. The compound of claim 126, wherein  is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and , each further optionally substituted with $\mathbf{R}^{cA}$, wherein each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$.

130. The compound of claim 1, wherein the compound is a compound of Formula **(I-f)**:



Formula **(I-f)**

or a pharmaceutically acceptable salt thereof,

wherein:

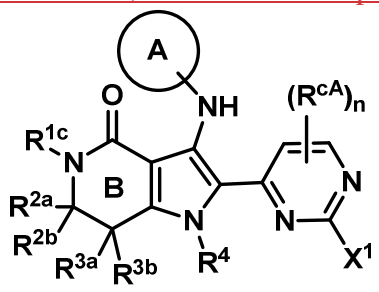
each $\mathbf{R}^{cA}$ is an independently selected $\mathbf{R}^{c}$;

n is 0 or 1; and

Ring D is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R}^{d}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R}^{cA}$.

131. The compound of claim 130, wherein **Ring D** is a partially unsaturated or aromatic ring including 6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N(**R**^{d}), O, and S(O)$_{0\text{-}2}$, wherein **Ring D** is optionally substituted with from 1-2 **R**^{cA}.

132. The compound of claim 1, wherein the compound is a compound of Formula (**I-g**):

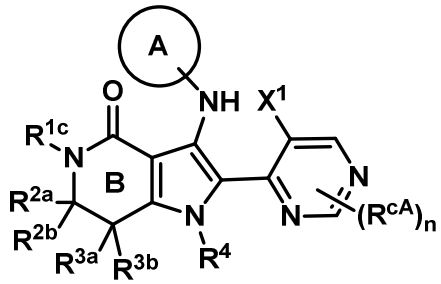


Formula (**I-g**)

or a pharmaceutically acceptable salt thereof,

wherein: each **R**^{cA} is an independently selected **R**^{c}; and **n** is 0, 1, or 2.

133. The compound of claim 1, wherein the compound is a compound of Formula (**I-h**):

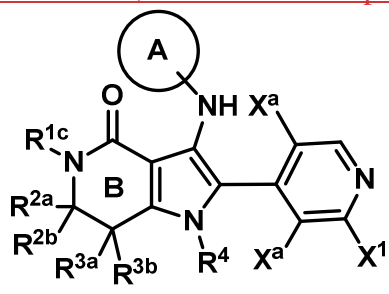


Formula (**I-h**)

or a pharmaceutically acceptable salt thereof,

wherein: each **R**^{cA} is an independently selected **R**^{c}; and **n** is 0, 1, or 2.

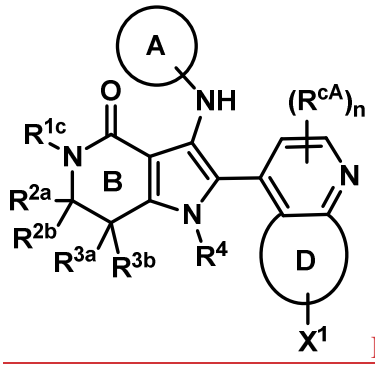
134. The compound of claim 1, wherein the compound is a compound of Formula (**I-i**):



Formula (**I-i**)

or a pharmaceutically acceptable salt thereof.

135. The compound of claim 1, wherein the compound is a compound of Formula (**I-j**):



Formula (**I-j**)

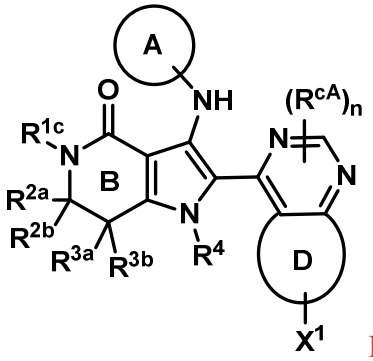
or a pharmaceutically acceptable salt thereof;

wherein **n** is 0, 1, or 2;

each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$; and

Ring D is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R^{cA}}$.

136. The compound of claim 1, wherein the compound is a compound of Formula (**I-k**):



Formula (**I-k**)

or a pharmaceutically acceptable salt thereof;

wherein **n** is 0 or 1;

each $\mathbf{R^{cA}}$ is an independently selected $\mathbf{R^{c}}$; and

Ring D is a partially unsaturated or aromatic ring including from 5-6 ring atoms, wherein from 0-2 of the ring atoms are heteroatoms each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$, wherein **Ring D** is optionally substituted with from 1-2 $\mathbf{R^{cA}}$.

137. The compound of claim 119, wherein each occurrence of $\mathbf{R^{cA}}$ is independently selected from the group consisting of: halo; cyano; C_{1-10} alkyl which is optionally substituted with from 1-6 independently selected $\mathbf{R^{a}}$; C_{1-4} alkoxy optionally substituted with C_{1-4} alkoxy or C_{1-4} haloalkoxy; C_{1-4} haloalkoxy; $-S(O)_{1-2}(C_{1-4}$ alkyl); $-N\mathbf{R^{e}R^{f}}$; –OH; $-S(O)_{1-2}N\mathbf{R'R''}$; $-C_{1-4}$ thioalkoxy; $-C(=O)(C_{1-10}$ alkyl); $-C(=O)O(C_{1-4}$ alkyl); -C(=O)OH; and $-C(=O)N\mathbf{R'R''}$.

138. The compound of claim 119, wherein $\mathbf{R^{1c}}$ is H.

139. The compound of claim 119, wherein $\mathbf{R^{2a}}$ and $\mathbf{R^{2b}}$ are both H.

140. The compound of claim 119, wherein $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are both H.

141. The compound of claim 119, wherein $\mathbf{R^{3a}}$ is a substituent that is other than H.

142. The compound of claim 119, wherein $\mathbf{R^{3a}}$ is C_{1-6} alkyl which is optionally substituted with from 1-6 $\mathbf{R^{a}}$, such as wherein $\mathbf{R^{3a}}$ is C_{1-3} alkyl, such as methyl or ethyl.

143. The compound of claim 119, wherein $\mathbf{R^{3a}}$ is C_{1-3} alkyl substituted with C_{1-4} alkoxy, C_{1-4} haloalkoxy, or $N\mathbf{R^{e}R^{f}}$, such as wherein $\mathbf{R^{3a}}$ is $–CH_2OMe$, $-CH_2CH_2OMe$, $-CH(Me)CH_2OMe$, $-CH_2CH(Me)OMe$, $-CH_2OEt$, $-CH_2N\mathbf{R^{e}R^{f}}$ (e.g., $-CH_2N(CF_3)Me$), or $–CH_2CH_2N\mathbf{R^{e}R^{f}}$ (e.g., $-CH_2CH_2NMe_2$).

144. The compound of claim 119, wherein $\mathbf{R^{3a}}$ is selected from the group consisting of:

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^{c}}$; and

C_{3-6} cycloalkyl optionally substituted with from 1-4 $\mathbf{R^{c}}$.

145. The compound of claim 119, wherein $\mathbf{R^{3a}}$ is $–(C_{1-3}$ alkylene)-$\mathbf{R^{g}}$ or $-(C_{1-3}$ alkylene)-O-$\mathbf{R^{g}}$, and optionally the $\mathbf{R^{g}}$ group of $\mathbf{R^{3a}}$ is:

C_{3-6} cycloalkyl optionally substituted with from 1-4 $\mathbf{R^{c}}$, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0-2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^{c}}$.

146. The compound of claim 119, wherein $\mathbf{R^{3a}}$ is $–CH_2$-$\mathbf{R^{g}}$, or $–CH_2CH_2\mathbf{R^{g}}$, wherein $\mathbf{R^{g}}$ is 1,4-dioxanyl.

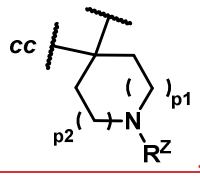
147. The compound of claim 119, wherein R^{3a} is-$(L^g)_g$-R^W.

148. The compound of claim 119, wherein R^{3a} is -$(L^g)_g$-R^{g2}-R^W.

149. The compound of claim 119, wherein R^{3b} is H.

150. The compound of claim 119, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-8 ring atoms;

- wherein from 0-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N(R^d), O, and $S(O)_{0-2}$; and
- wherein the fused saturated ring of 4-8 ring atoms is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo, R^c, and R^W.

151. The compound of claim 119, wherein R^{3a} and R^{3b}, together with the **Ring B** ring atom to which each is attached, form: 

, which is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and R^c, wherein:

p1 and **p2** are independently 0, 1, or 2;

R^Z is H, R^d, C(=O)-**W**, or $S(O)_2$**W**; and

cc represents the point of attachment to C($R^{2a}R^{2b}$).

152. The compound of claim 119, wherein R^{3a} and R^{3b} together with the **Ring B** ring atom to which each is attached form a fused C_{3-6} cycloalkyl, wherein the fused C_{3-6} cycloalkyl is optionally substituted with from 1-2 R^c.

153. The compound of claim 119, wherein R^{2a} and R^{3a} taken together with the **Ring B** ring atoms to which each is attached, form a fused C_{3-6} (e.g., C_3 or C_4) cycloalkyl which is optionally substituted with from 1-2 R^c.

154. The compound of claim 119, wherein R^{2b} and R^{3b} are each H.

155. The compound of claim 119, wherein R^{1c}, R^{2a}, and R^{2b} are each H; R^{3a} is C_{1-3} alkyl optionally substituted with from 1-3 R^a; and R^{3b} is H, optionally each R^a substituent present in R^{3a} is independently selected from the group consisting of: halo, C_{1-4} alkoxy, and C_{1-4} haloalkoxy.

156. The compound of claim 119, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; and $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ are independently selected $C_{1\text{-}3}$ alkyl.

157. The compound of claim 119, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; $\mathbf{R^{3a}}$, is $-\mathbf{R^{g}}$, $-(C_{1\text{-}3}$ alkylene)-$\mathbf{R^{g}}$, or $-(C_{1\text{-}3}$ alkylene)-O-$\mathbf{R^{g}}$,

optionally wherein the $\mathbf{R^{g}}$ group of $\mathbf{R^{3a}}$ is:

$C_{3\text{-}6}$ cycloalkyl optionally substituted with from 1-4 $\mathbf{R^{c}}$, or

heterocyclyl including from 4-6 ring atoms, wherein from 1-3 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^{d}}$), O, and $S(O)_{0\text{-}2}$, and wherein the heterocyclyl is optionally substituted with from 1-4 substituents independently selected from the group consisting of oxo and $\mathbf{R^{c}}$; and

$\mathbf{R^{3b}}$ is H.

158. The compound of claim 119, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; and $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ taken together with the **Ring B** ring carbon atom to which each is attached form a fused $C_{3\text{-}6}$ (such as C_3 or C_4) cycloalkyl, wherein the fused cycloalkyl ring is optionally substituted with from 1-2 $\mathbf{R^{c}}$.

159. The compound of claim 119, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, and $\mathbf{R^{2b}}$ are each H; and $\mathbf{R^{3a}}$ and $\mathbf{R^{3b}}$ together with the **Ring B** ring atom to which each is attached, form a fused saturated ring of 4-6 ring atoms;

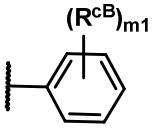
- wherein from 1-2 of the ring atoms are each an independently selected heteroatom, wherein each of the independently selected heteroatoms is selected from the group consisting of N, NH, N($\mathbf{R^{d}}$), O, and $S(O)_{0\text{-}2}$; and
- wherein the fused saturated ring of 4-6 ring atoms is optionally substituted with from 1-2 substituents independently selected from the group consisting of oxo and $\mathbf{R^{c}}$.

160. The compound of claim 119, wherein $\mathbf{R^{1c}}$ is H; $\mathbf{R^{2a}}$ and $\mathbf{R^{3a}}$ taken together with the **Ring B** ring atoms to which each is attached, form a fused $C_{3\text{-}6}$ (e.g., C_3 or C_4) cycloalkyl which is optionally substituted with from 1-2 $\mathbf{R^{c}}$; and $\mathbf{R^{2b}}$ and $\mathbf{R^{3b}}$ are each H.

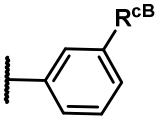
161. The compound of claim 119, wherein $\mathbf{R^{1c}}$ is H; $\mathbf{R^{2a}}$ and $\mathbf{R^{3a}}$ combine to form a double bond between the **Ring B** atoms to which each is attached; and $\mathbf{R^{2b}}$ is H; and $\mathbf{R^{3b}}$ is $-(\mathbf{L^g})_{g}-\mathbf{R^g}$.

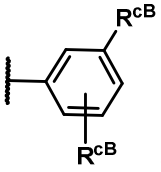
162. The compound of claim 119, wherein $\mathbf{R^{1c}}$, $\mathbf{R^{2a}}$, $\mathbf{R^{2b}}$, $\mathbf{R^{3a}}$, and $\mathbf{R^{3b}}$ are each H.

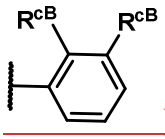
163. The compound of claim 119, wherein $\mathbf{R^4}$ is H.

164. The compound of claim 119, wherein **Ring A** is 

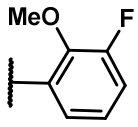
, wherein each $\mathbf{R^{cB}}$ is an independently selected $\mathbf{R^c}$; and **m1** is 0, 1, 2, 3, or 4.

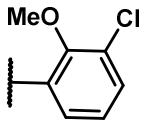
165. The compound of claim 119, wherein **Ring A** is 

or 

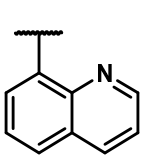
(e.g., 

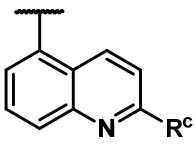
), wherein each $\mathbf{R^{cB}}$ is an independently selected $\mathbf{R^c}$.

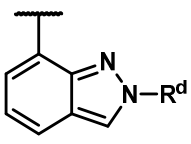
166. The compound of claim 119, wherein **Ring A** is 

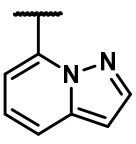
or 

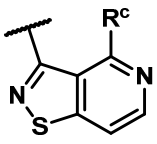
.

167. The compound of claim 119, wherein **Ring A** is bicyclic heteroaryl including from 9-10 ring atoms, wherein from 1-4 ring atoms are heteroatoms, each independently selected from the group consisting of N, N(H), N($\mathbf{R^d}$), O, and $S(O)_{0-2}$, and wherein the heteroaryl is optionally substituted with from 1-4 $\mathbf{R^c}$, optionally wherein: **Ring A** is selected from the group consisting of: 

, 

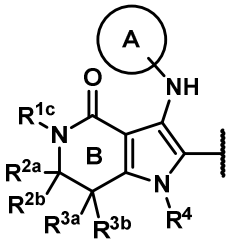
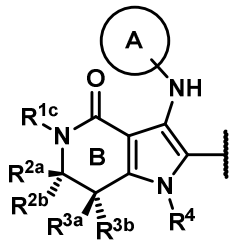
, 

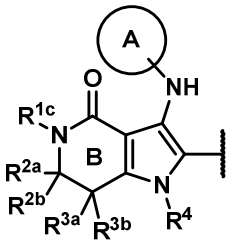
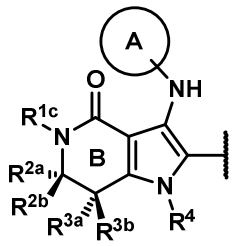
, 

, 

, and 

, each of which is further optionally substituted with $\mathbf{R^c}$.

168. The compound of claim 1, wherein the  moiety is  .

169. The compound of claim 1, wherein the  moiety is  .

170. The compound of claim 1, wherein the compound is selected from the group consisting of the compounds delineated in **Table C1**, or a pharmaceutically acceptable salt thereof.

171. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and pharmaceutically acceptable diluent or carrier.

172. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

173. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer, wherein the cancer is associated with a

dysregulation of an *EGFR* gene, an EGFR kinase, or expression or activity or level of any of the same.

174. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an EGFR-associated cancer.

175. The use of claim 173, wherein the dysregulation in an *EGFR* gene, an EGFR kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *EGFR* gene.

176. The use of claim 175, wherein the one or more point mutations in an *EGFR* gene results in the translation of an EGFR protein having one or more amino acid substitutions at one or more of the following amino acid positions exemplified in **Table 1a** and **1b**.

177. The use of claim 176, wherein the one or more point mutations is selected from the mutations in **Table 1a** and **1b** (e.g., L858R, G719S, G719C, G719A, L861Q, a deletion in exon 19 and/or an insertion in exon 20).

178. The use of claim 177, wherein the one or more point mutations is an EGFR inhibitor resistance mutation (e.g., L718Q, L747S, D761Y, T790M, C797S, T854A).

179. The use of claim 176, wherein the one or more point mutations in an *EGFR* gene include a deletion in exon 19 of a human *EGFR* gene.

180. The use of claim 176, wherein the one or more mutations is an EGFR insertion in exon 20 of a human *EGFR* gene.

181. The use of claim 178, wherein the insertion in exon 20 of a human EGFR gene is selected from: V769_D770insX, D770_N771insX, N771_P772insX, P772_H773insX, and H773_V774insX.

182. The use of claim 178, wherein the insertion in exon 20 of a human *EGFR* gene is selected from: Y772_A775dup, A775_G776insYVMA, G776delinsVC, G776delinsVV, V777_G778insGSP, and P780_Y781insGSP.

183. The use of claim 174, wherein the EGFR-associated cancer is selected from the group consisting of: oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer, a hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytomaLi-Fraumeni tumor, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer and skin cancer.

184. The use of any one of claim 174, wherein the EGFR-associated cancer is selected from the group consisting of: lung cancer, pancreatic cancer, head and neck cancer, melanoma, colon cancer, renal cancer, leukemia, glioblastoma, or breast cancer.

185. The use of claim 183, wherein the lung cancer is non-small cell lung cancer.

186. The use of claim 172, wherein the cancer is a HER2-associated cancer.

187. The use of claim 186, wherein the HER2-associated cancer is associated with a dysregulation of a *HER2* gene, a HER2 kinase, or expression or activity or level of any of the same.

188. The use of claim 187, wherein the dysregulation in a *HER2* gene, a HER2 kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *HER2* gene.

189. The use of claim 188, wherein the one or more point mutations in a *HER2* gene

results in the translation of a HER2 protein having one or more amino acid substitutions at one or more of the following amino acid positions exemplified in **Table 3**.

190. The use of claim 189, wherein the one or more point mutations is selected from the mutations in **Table 3** (e.g., S310F, S310Y, R678Q, R678W, R678P, I767M, V773M, V777L, and V842I).

191. The use of claim 172, wherein the cancer is selected from the group consisting of: non-small cell lung cancer, pancreatic cancer, and colorectal cancer.

192. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an EGFR-associated cancer that has one or more EGFR inhibitor resistance mutations.

193. A method for modulating EGFR in a mammalian cell, the method comprising contacting the mammalian cell with an effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof.

194. The method of claim 193, wherein the contacting occurs in vitro.

195. The method of claim 193, wherein the mammalian cell is a mammalian cancer cell.

196. The method of claim 195, wherein the mammalian cancer cell is a mammalian EGFR-associated cancer cell.

197. The method of claim 193, wherein the cell has a dysregulation of an *EGFR* gene, an EGFR kinase protein, or expression or activity or level of any of the same.

198. The method of claim 197, wherein the dysregulation in an *EGFR* gene, an EGFR kinase protein, or expression or activity or level of any of the same is one or more point mutations in the *EGFR* gene.

199. The method of claim 198, wherein the one or more point mutations in an *EGFR* gene results in the translation of an EGFR protein having one or more amino acid substitutions at one or more of the following amino acid positions exemplified in **Table 1a** and **1b**.

200. The method of claim 199, wherein the one or more point mutations is selected from the mutations in **Table 1a** and **1b** (e.g., L858R, G719S, G719C, G719A, L861Q, a deletion in exon 19 and/or an insertion in exon 20).

201. The method of claim 198, wherein the one or more point mutations is an EGFR inhibitor resistance mutation (e.g., L718Q, L747S, D761Y, T790M, C797S, T854A).

202. The method of claim 198, wherein the one or more point mutations in an *EGFR* gene include a deletion in exon 19 of a human *EGFR* gene.

203. The method of claim 198, wherein the one or more point mutations is an EGFR insertion in exon 20 of a human *EGFR* gene.

204. The method of claim 203, wherein the insertion in exon 20 of a human *EGFR* gene is selected from: A767_V769insX, V769_D770insX, D770_N771insX, N771_P772insX, P772_H773insX, and H773_V774insX.

205. The method of claim 204, wherein the insertion in exon 20 of a human *EGFR* gene is selected from: A767_V769dupASV, V769_D770insASV, D770_N771insNPG, D770_N771insNPY, D770_N771insSVD, D770_N771insGL, N771_H773dupNPH, N771_P772insN, N771_P772insH, N771_P772insV, P772_H773insDNP, P772_H773insPNP, H773_V774insNPH, H773_V774insH, H773_V774insPH, H773_V774insAH, and P772_H773insPNP.

206. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer associated with a dysregulation of a *HER2* gene,

a HER2 kinase, or expression or activity or level of any of the same.

207. A compound of claim 1, or a pharmaceutically acceptable salt thereof, for use in therapy.