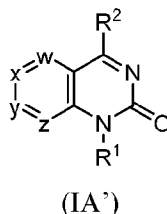


What is Claimed:

1. A compound of Formula (IA'):



where:

w is CR³ or N; x is CR⁴ or N; y is CR⁵ or N; and z is CR⁶ or N, wherein:

R³ is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyloxy, cyano, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkylamino, alkoxyalkyl, alkoxyalkoxy, alkoxyalkylamino, aminoalkyl, aminoalkoxy, aminoalkylamino, heteroaryl, heteroaryloxy, heteroaralkyloxy, heteroarylamino, heterocyclyl, heterocyclyloxy, heterocyclylamino, heterocyclylalkyloxy, heterocyclyloxyalkoxy, or heterocyclyloxyalkylamino, wherein heterocyclyl or heteroaryl, by itself or as part of another group, is unsubstituted or substituted with R^a, R^b, and/or R^c independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, alkoxy carbonyl, hydroxyalkyl, alkoxyalkyl, or aminoalkyl;

R⁵ is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, amino, alkylamino, dialkylamino, alkoxy carbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkylamino, alkoxyalkyl, alkoxyalkoxy, alkoxyalkylamino, aminoalkyl, aminoalkoxy, aminoalkylamino, heteroaryl, heteroaryloxy, heteroarylamino, heterocyclyl, heterocyclyloxy, heterocyclylamino, heterocyclyloxyalkoxy, or heterocyclyloxyalkylamino, wherein heterocyclyl or heteroaryl, by itself or as part of another group, is unsubstituted or substituted with R^a, R^b, and/or R^c independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, hydroxyalkyl, alkoxyalkyl, or aminoalkyl;

R⁴ and R⁶ are independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, or dialkylaminocarbonyl; provided that: (i) no more than two of w, x, y, and z can be N and (ii) at least one of R³, R⁴, R⁵, and R⁶ is other than hydrogen;

R^1 is R^7 wherein R^7 is cycloalkyl, bridged cycloalkyl, fused cycloalkyl, spirocycloalkyl, aryl, heteroaryl, heterocyclyl, bridged heterocyclyl, fused heterocyclyl, or spiroheterocyclyl, wherein aryl, heteroaryl, or heterocyclyl is unsubstituted or substituted with R^d , R^e , and/or R^f ;

R^2 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminocarbonylalkyl, aminosulfonylalkyl, $-O-R^8$, $-NR^9R^{10}$, or $-X^b-R^{11}$ wherein:

R^8 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, cycloalkyl, cycloalkylalkyl, cycloalkoxyalkyl, bridged cycloalkyl, bridged cycloalkylalkyl, fused cycloalkyl, spirocycloalkyl, spirocycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heterocycliloxyalkyl, fused heterocyclyl, fused heterocyclylalkyl, bridged heterocyclyl, bridged heterocyclylalkyl, spiroheterocyclyl, or spiroheterocyclylalkyl, wherein aryl, heteroaryl, or heterocyclyl, by itself or as part of another group, is unsubstituted or substituted with R^g , R^h , and/or R^i ;

R^9 is hydrogen, alkyl, deutoalkyl, or cycloalkyl; and

R^{10} is hydrogen, alkyl, deutoalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, haloalkoxyalkyl, aminoalkyl, aminosulfonylalkyl, thioureidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, cyanoalkyl, alkylcarbonyl, alkoxycarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonylalkyl, cycloalkyl, cycloalkylalkyl, substituted cycloalkyl, substituted cycloalkylalkyl, cycloalkoxyalkyl, bridged cycloalkyl, bridged cycloalkylalkyl, fused cycloalkyl, spirocycloalkyl, spirocycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heteroarylcabonyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocycliloxyalkyl, fused heterocyclyl, fused heterocyclylalkyl, bridged heterocyclyl, bridged heterocyclylalkyl, spiroheterocyclyl, or spiroheterocyclylalkyl, wherein aryl, heteroaryl, or heterocyclyl, by itself or as part of another group, is unsubstituted or substituted with R^j , R^k , and/or R^l ;

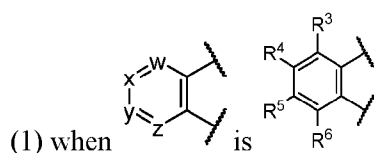
X^b is a bond or alkylene; and

R^{11} is cycloalkyl, bridged cycloalkyl, fused cycloalkyl, spirocycloalkyl, heteroaryl, heterocyclyl, bridged heterocyclyl, fused heterocyclyl, or spiroheterocyclyl, wherein heteroaryl or heterocyclyl is unsubstituted or substituted with R^m , R^n , and/or R^o ; and

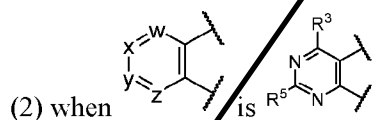
R^d , R^e , R^g , R^h , R^j , R^k , R^m , and R^n are independently selected from alkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, alkylsulfonyl, halo, cyano, carboxy, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, sulfonylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, heterocyclylcarbonyl, and ureido; and

R^f , R^i , R^l , and R^o are independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, amino, alkylamino, cycloalkylsulfonylamino, cyano, cyanoalkyl, alkoxycarbonylalkyl, carboxyalkyl, aminocarbonylalkyl, or $-X^c-R^{12}$ where X^c is bond, alkylene, or heteroalkylene and R^{12} is optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted heterocyclyl; provided that when R^l is heterocyclyl then R^f is not hydroxy; or

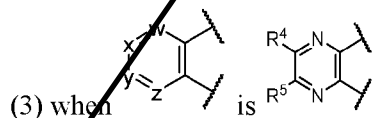
a pharmaceutically acceptable salt thereof; provided that:



where: (a) when R^2 is piperazin-1-yl, 2-methylpiperazin-1-yl, or 1H-benzo[d][1,2,3]triazol-1-yl, R^3 and R^6 are hydrogen, R^4 is chloro and R^5 is bromo or 5-methylindazol-4-yl, then R^1 is not 2-isopropylphenyl; (b) when R^2 and R^6 are methyl and R^3 , R^4 , and R^5 are hydrogen; or R^2 and R^3 are methyl and R^4 , R^5 , and R^6 are hydrogen, then R^1 is not 2,5-, 2,6- or 2,8-dimethylquinolin-4-yl or 2-methyl-5-methoxy-, 2-methyl-6-methoxy- or 2-methyl-8-methoxyquinolin-4-yl; (c) when R^2 is amino or acetylamino, R^4 is dimethylamino, and R^3 , R^5 , and R^6 are hydrogen, then R^1 is not 4-hydroxy-5-hydroxymethyl-tetrahydrofuran-2-yl; (d) when R^5 is fluoro, R^3 , R^4 and R^6 are hydrogen, and R^2 is 4-aminocarbonylmethyl-2-methylphenylamino, then R^1 is not 4-fluoro-2-(2-thiazol-2-ylmethoxy)phenyl, 4-fluoro-2-(2-pyridin-2-ylmethoxy)phenyl, or 4-chloro-2-methoxyphenyl; (e) when R^6 is fluoro, R^3 , R^4 and R^5 are hydrogen, and R^2 is 4-aminocarbonylmethyl-2-methylphenylamino, then R^1 is not 4-fluoro-2-methoxyphenyl; (f) when R^1 is 4-chloro-2-ethoxyphenyl, R^5 is fluoro, and R^3 , R^4 and R^6 are hydrogen, then R^2 is not 3-(2-oxoimidazolidin-1-yl)-2-methylphenylamino;

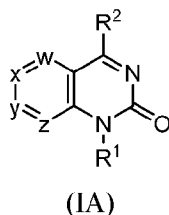


then when R^1 is 4-hydroxy-5-hydroxymethylfuran-1-yl, R^5 is amino, and R^3 is methoxy; then R^2 is not amino; and



then when R^1 is 4-hydroxy-5-hydroxymethylfuran-1-yl, one of R^4 and R^5 is hydrogen, and the other of R^4 and R^5 is methyl or both of R^4 and R^5 are methyl, then R^2 is not amino.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof having a structure of Formula (IA):



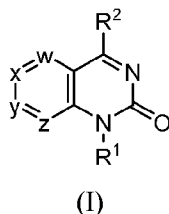
where:

R^4 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, or dialkylaminocarbonyl; provided that: (i) no more than two of w, x, y, and z can be N and (ii) at least one of R^3 , R^4 , R^5 , and R^6 is other than hydrogen;

R^{10} is hydrogen, alkyl, deuterioalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, alkylsulfonyl, alkylsulfonylalkyl, cyanoalkyl, alkylcarbonyl, alkoxycarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonylalkyl, cycloalkyl, cycloalkylalkyl, substituted cycloalkyl, substituted cycloalkylalkyl, cycloalkoxyalkyl, bridged cycloalkyl, bridged cycloalkylalkyl, fused cycloalkyl, spirocycloalkyl, spirocycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heteroarylcarbonyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocycliloxyalkyl, fused heterocyclyl, fused heterocyclylalkyl, bridged heterocyclyl, bridged heterocyclylalkyl, spiroheterocyclyl, or spiroheterocyclylalkyl, wherein aryl, heteroaryl, or heterocyclyl, by itself or as part of another group, is unsubstituted or substituted with R^j , R^k , and/or R^l ; and

R^f , R^i , R^l , and R^o are independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, amino, cycloalkylsulfonylamino, cyano, cyanoalkyl, alkoxycarbonylalkyl, carboxyalkyl, aminocarbonylalkyl, or $-X^c-R^{12}$ where X^c is bond, alkylene, or heteroalkylene and R^{12} is optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted heterocyclyl; provided that when R^1 is heterocyclyl then R^f is not hydroxy;

3. The compound of claim 2 or a pharmaceutically acceptable salt thereof wherein the compound has a structure of Formula (I):



where:

R³ and R⁵ are independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkylamino, alkoxyalkyl, alkoxyalkoxy, alkoxyalkylamino, aminoalkyl, aminoalkoxy, aminoalkylamino, heteroaryl, heteroaryloxy, heteroaryl amino, heterocyclyl, heterocyclyloxy, heterocyclylamino, heterocyclyloxyalkoxy, or heterocyclyloxyalkylamino, wherein heterocyclyl or heteroaryl, by itself or as part of another group, is unsubstituted or substituted with R^a, R^b, and/or R^c independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, hydroxyalkyl, alkoxyalkyl, or aminoalkyl;

R¹ is R⁷ wherein R⁷ is cycloalkyl, bridged cycloalkyl, fused cycloalkyl, spirocycloalkyl, phenyl, heteroaryl, heterocyclyl, bridged heterocyclyl, fused heterocyclyl, or spiroheterocyclyl, wherein phenyl, heteroaryl, or heterocyclyl is unsubstituted or substituted with R^d, R^e, and/or R^f;

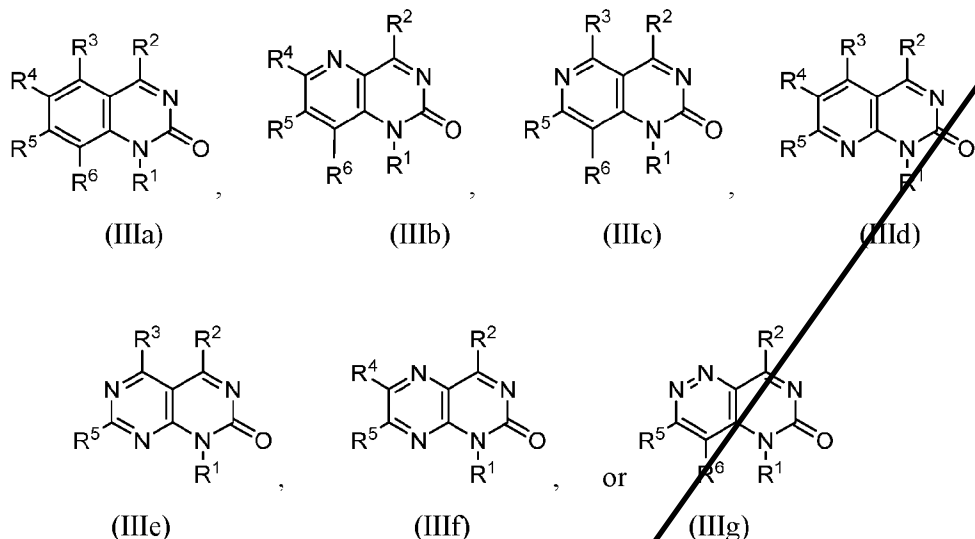
R⁹ is hydrogen, alkyl or cycloalkyl; and

R¹⁰ is hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, alkylcarbonyl, alkoxy carbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkoxyalkyl, bridged cycloalkyl, bridged cycloalkylalkyl, fused cycloalkyl, spirocycloalkyl, spirocycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heteroaryl carbonyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclyloxyalkyl, fused heterocyclyl, fused heterocyclylalkyl, bridged heterocyclyl, bridged heterocyclylalkyl, spiroheterocyclyl, or spiroheterocyclylalkyl, wherein aryl, heteroaryl, or heterocyclyl, by itself or as part of another group, is unsubstituted or substituted with R^j, R^k, and/or R^l;

R^d, R^e, R^g, Rⁿ, R^j, R^k, R^m, and Rⁿ are independently selected from alkyl, haloalkyl, haloalkoxy, alkoxy, alkylsulfonyl, halo, cyano, carboxy, alkoxy carbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, sulfonylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, heterocyclylcarbonyl, and ureido; and

R^f, Rⁱ, R^l, and R^o are independently selected from alkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, or -X^c-R¹² where X^c is bond, alkylene or heteroalkylene and R¹² is optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted heterocyclyl

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof having a structure of formula (IIIa), (IIIb), (IIIc), (IIId), (IIIe), or (IIIg) below:



5. The compound of claim 4, or a pharmaceutically acceptable salt thereof having structure of formula (IIIa).

6. The compound of claim 4, or a pharmaceutically acceptable salt thereof having structure of formula (IIId).

7. The compound of any one of claims 1 to 6 or a pharmaceutically acceptable salt thereof wherein R^2 is $-NR^9R^{10}$.

8. The compound of any one of claims 1 to 6 or a pharmaceutically acceptable salt thereof wherein R^2 is $-OR^8$.

9. The compound of any one of claims 1 to 6 or a pharmaceutically acceptable salt thereof wherein R^2 is R^{11} .

10. The compound of any one of claims 1 to 7 or a pharmaceutically acceptable salt thereof wherein R^9 is deutoalkyl.

11. The compound of any one of claims 1 to 7 or a pharmaceutically acceptable salt thereof wherein R^9 is hydrogen.

12. The compound of any one of claims 1 to 7 or a pharmaceutically acceptable salt thereof wherein R^9 is alkyl.

13. The compound of claim 12 or a pharmaceutically acceptable salt thereof wherein R^9 is methyl or ethyl.

14. The compound of any one of claims 1 to 7 and 11 to 13 or a pharmaceutically acceptable salt thereof wherein R¹⁰ is hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, alkylcarbonyl, alkoxycarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylaminocarbonylalkyl, or dialkylaminocarbonylalkyl.

15. The compound of claim 14 or a pharmaceutically acceptable salt thereof wherein R¹⁰ is hydrogen.

16. The compound of claim 8 or 14 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are alkyl.

17. The compound of claim 16 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are methyl.

18. The compound of 1 to 8 and 11 to 13 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are independently cycloalkyl or cycloalkylalkyl, each ring may independently be unsubstituted or substituted with one or two substituents independently selected from alkyl, halo, or cyano.

19. The compound of claim 18 wherein R⁸ and R¹⁰ are independently cyclopropyl, cyclobutyl, 1-methylcyclopropyl, (cis)-3-hydroxy-3-methylcyclobutyl, (cis)-3-hydroxy-2,2-dimethylcyclobutyl, 1-cyanocyclobutyl, cyclopropylmethyl, 1-hydroxycyclopropmethyl, 1-fluorocyclopropmethyl, (trans)-3-hydroxy-1-methylcyclobutyl, (cis)-3-cyanocyclobutyl, 1-methylcyclobutyl, (cis)-3-hydroxycyclobutyl, (trans)-3-hydroxycyclobutyl, (trans)-3-cyanocyclobutyl, (2S,1R)-2-hydroxycyclobutyl, (1S,2S)-2-hydroxycyclobutyl, (1S,2R)-2-hydroxycyclobutyl, (1R,2R)-2-hydroxycyclobutyl, (1R,2R)-2-fluorocyclopropyl, 1-fluorocyclopropylmethyl, (1S,2R)-2-fluorocyclopropyl, (1R,2S)-2-fluorocyclopropyl, (1S,2S)-2-fluorocyclopropyl, 2,2-difluorocyclopropyl, (R)-1-cyclopropylethyl, or 2,2-difluorocyclopropylmethyl.

20. The compound of claim 18 wherein R⁸ and R¹⁰ are independently cyclopropyl, cyclobutyl, 1-methylcyclopropyl, (cis)-3-hydroxy-3-methylcyclobutyl, (cis)-3-hydroxy-2,2-dimethylcyclobutyl, 1-cyanocyclobutyl, (trans)-3-hydroxy-1-methylcyclobutyl (cis)-3-cyanocyclobutyl, 1-methylcyclobutyl, (cis)-3-hydroxycyclobutyl, (trans)-3-hydroxycyclobutyl, (trans)-3-cyanocyclobutyl, (2S,1R)-2-hydroxycyclobutyl, (1S,2S)-2-hydroxycyclobutyl, (1S,2R)-2-hydroxycyclobutyl, (1R,2R)-2-hydroxycyclobutyl, (1R,2R)-2-fluorocyclopropyl, (1S,2R)-2-fluorocyclopropyl, (1R,2S)-2-fluorocyclopropyl, (1S,2S)-2-fluorocyclopropyl, or 2,2-difluorocyclopropyl.

21. The compound of claim 18 wherein R⁸ and R¹⁰ are independently cyclopropylmethyl, 1-hydroxycyclopropmethyl, 1-fluorocyclopropmethyl, 1-fluorocyclopropylmethyl, (R)-1-cyclopropylethyl, or 2,2-difluorocyclopropylmethyl.

22. The compound of 1 to 8 and 11 to 13 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are independently heteroaryl or heteroaralkyl wherein heteroaryl, by itself or as part heteroaralkyl, is unsubstituted or substituted with R^j, R^k, and/or R^l.

23. The compound of claim 22 wherein R⁸ and R¹⁰ are heteroaryl independently selected from pyrazolyl, oxazolyl, isoxazolyl, imidazolyl, thienyl, pyrrolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinolinyl, isoquinolinyl, indolyl, and indazolyl, each ring is either unsubstituted or substituted with R^j, R^k, and/or R^l.

24. The compound of claim 22 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are heteroaryl independently selected from pyrazolyl, imidazolyl, thienyl, pyrrolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinolinyl, isoquinolinyl, indolyl, and indazolyl, each ring is either unsubstituted or substituted with R^j, R^k, and/or R^l.

25. The compound of claim 22 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are heteroaralkyl independently selected from pyrazolylmethyl, pyrazolylethyl, oxazolylmethyl, isoxazolylmethyl, imidazolylmethyl, imidazolylethyl, thienylmethyl, thienylethyl, pyrrolylmethyl, pyrrolylethyl, pyridinylmethyl, pyridinylethyl, pyrimidinylmethyl, pyrimidinylethyl, pyrazinylmethyl, pyrazinylethyl, pyridazinylmethyl, pyridazinylethyl, quinolinylmethyl, quinolinylethyl, isoquinolinylmethyl, isoquinolinylethyl, indolylmethyl, indolylethyl, indazolylmethyl and indazolylethyl, each ring is either unsubstituted or substituted with R^j, R^k, and/or R^l.

26. The compound of claim 22 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are heteroaralkyl independently selected from pyrazolylmethyl, pyrazolylethyl, imidazolylmethyl, imidazolylethyl, thienylmethyl, thienylethyl, pyrrolylmethyl, pyrrolylethyl, pyridinylmethyl, pyridinylethyl, pyrimidinylmethyl, pyrimidinylethyl, pyrazinylmethyl, pyrazinylethyl, pyridazinylmethyl, pyridazinylethyl, quinolinylmethyl, quinolinylethyl, isoquinolinylmethyl, isoquinolinylethyl, indolylmethyl, indolylethyl, indazolylmethyl and indazolylethyl, each ring is either unsubstituted or substituted with R^j, R^k, and/or R^l.

27. The compound of claim 22 or a pharmaceutically acceptable salt thereof wherein R⁸ and R¹⁰ are 1-methyl-1H-pyrazol-5-yl, isoxazol-4-yl, 3-methyl-1,2,4-oxadiazol-5-yl, 5-methylisoxazol-3-yl, 5-methylisoxazol-4-yl, 3-methoxyisoxazol-5-yl, 3,5-dimethylisoxazol-4-yl, 3-methylisoxazol-4-yl, thiazol-4-yl, thiazol-5-yl, isothiazol-4-yl,

pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, 2-(difluoromethyl)pyridin-4-yl, 2-(difluoromethoxy)pyridin-4-yl, 5-methoxypyridin-3-yl, 6-methylpyridin-3-yl, 6-methoxypyridin-3-yl, 3-cyanopyridin-4-yl, 3-methoxypyridin-4-yl, 3-fluoropyridin-4-yl, 3-chloropyridin-4-yl, 2-(trifluoromethyl)pyridin-4-yl, 2-methylpyridin-4-yl, pyrimidin-5-yl, 1-methyl-1H-imidazol-4-yl, 1-methylpyrazol-3-ylmethyl, 3-methoxyisoxazol-5-ylmethyl, oxazol-2-ylmethyl, oxazol-4-ylmethyl, oxazol-5-ylmethyl, isoxazol-3-ylmethyl, isoxazol-4-ylmethyl, isoxazol-5-ylmethyl, 1-methyl-1H-pyrazol-3-ylmethyl, 1-methyl-1H-pyrazol-4-ylmethyl, 1-methyl-1H-pyrazol-5-ylmethyl, pyridin-4-ylmethyl, pyridin-3-ylmethyl, or pyridin-2-ylmethyl.

28. The compound of any one of claims 1 to 6 or a pharmaceutically acceptable salt thereof wherein R^2 is R^{11} wherein R^{11} is heterocyclyl which is unsubstituted or substituted with R^m , R^n , and/or R^o .

29. The compound of claim 28 or a pharmaceutically acceptable salt thereof wherein R^{11} is oxetanyl, azetidiny, 2-oxoazetidiny, pyrrolidiny, 2-oxopyrrolidiny, piperidiny, piperaziny, or morpholiny, each ring is unsubstituted or substituted with R^m , R^n , and/or R^o .

30. The compound of claim 28 or a pharmaceutically acceptable salt thereof wherein R^{11} is azetidin-1-yl, 4-hydroxyazetidin-1-yl, 4-methylaminocarbonylazetidin-1-yl, 4-dimethylaminocarbonylazetidin-1-yl, 2-hydroxymethylazetidin-1-yl, 2-methylazetidin-1-yl, 2-oxoazetidin-1-yl, pyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 3-methoxypyrrolidin-1-yl, 3-hydroxy-3-methylpyrrolidin-1-yl, piperidin-1-yl, 2-carboxypiperidin-1-yl, 2-aminocarbonylpiperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, or morpholin-4-yl.

31. The compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof wherein R^5 is alkyl, alkoxy, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, aminocarbonyl, heteroaryl, heterocyclyl, wherein heterocyclyl or heteroaryl is unsubstituted or substituted with R^a , R^b , and/or R^c independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, hydroxyalkyl, alkoxyalkyl, or aminoalkyl.

32. The compound of claim 31, or a pharmaceutically acceptable salt thereof wherein R^5 is methyl, ethyl, isopropyl, tert-butyl, methoxy, ethoxy, fluoro, chloro, bromo, trifluoromethyl, difluoromethyl, trifluoromethoxy, difluoromethoxy, cyclopropyl, cyclopentyl, cyano, pyrazolyl, imidazolyl, thienyl, thiazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrimidinyl, oxetan-3-yl, pyrrolidin-1-yl, tetrahydrofuranyl, 2-oxoazetidin-1-yl, or 2-oxopyrrolidin-1-yl, wherein heterocyclyl or heteroaryl rings are unsubstituted or substituted

with R^a, R^b, and/or R^c independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, hydroxyalkyl, alkoxyalkyl, or aminoalkyl.

33. The compound of claim 31, or a pharmaceutically acceptable salt thereof wherein R⁵ is chloro, methyl, ethyl, trifluoromethyl, 1,1-difluoroethyl, or cyclopropyl.

34. The compound of claim 32 wherein R⁵ is chloro, trifluoromethyl, or ethyl.

35. The compound of any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof wherein R⁴ and R⁶ are independently selected from hydrogen, methyl, chloro, fluoro, bromo, methoxy, methylthio, methylsulfonyl, trifluoromethyl, trifluoromethoxy, cyano, amino, methylamino, dimethylamino, methylaminocarbonyl, or dimethylaminocarbonyl.

36. The compound of claim 35, or a pharmaceutically acceptable salt thereof wherein R⁴ is hydrogen, fluoro, bromo, methyl, methoxy, or cyano and R⁶ is hydrogen.

37. The compound of any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof wherein R⁴ and R⁶ are hydrogen.

38. The compound of any one of claims 1 to 37, or a pharmaceutically acceptable salt thereof wherein R³ is hydrogen, alkyl, alkoxy, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, or dialkylaminocarbonyl.

39. The compound of 38 or a pharmaceutically acceptable salt thereof wherein R³ is hydrogen or methoxy.

40. The compound of 38 or a pharmaceutically acceptable salt thereof wherein R³ is hydrogen

41. The compound of 38 or a pharmaceutically acceptable salt thereof wherein R³ is methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, trifluoromethyl, difluoromethyl, trifluoromethoxy, difluoromethoxy, cyclopropyl, cyano, methylsulfonyl, aminocarbonyl, methylamino, or dimethylamino.

42. The compound of any one of claims 1 to 41, or a pharmaceutically acceptable salt thereof wherein R¹ is R⁷ wherein R⁷ is phenyl which is unsubstituted or substituted with R^d, R^e, and/or R^f where R^d and R^e are independently selected from alkyl, haloalkyl, haloalkoxy, alkoxy, alkylsulfonyl, halo, cyano, carboxy, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, sulfonylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, heterocyclylcarbonyl, and ureido; and R^f is selected from alkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, and cyano,

43. The compound of any one of claims 1 to 41, or a pharmaceutically acceptable salt thereof wherein R^1 is R^7 wherein R^7 is phenyl which is unsubstituted or substituted with R^d , R^e , and/or R^f where R^d and R^e are independently selected from methyl, ethyl, fluoro, chloro, bromo, methoxy, ethoxy, cyclopropyl, cyano, methylsulfonyl, methoxymethyl, aminomethyl, 2-hydroxyethyl, or 3-hydroxypropyl and R^f is selected from hydroxy, fluoro, chloro, cyano, and methyl.

44. The compound of any one of claims 1 to 41, or a pharmaceutically acceptable salt thereof wherein R^1 is R^7 wherein R^7 is phenyl which is unsubstituted or substituted with R^f wherein R^f is fluoro, chloro, bromo, or methyl and wherein R^f is attached to carbon atoms on the phenyl ring that is ortho to the carbon atom of the phenyl ring attached to quinazalone nitrogen.

45. The compound of any one of claims 1 to 41, or a pharmaceutically acceptable salt thereof wherein R^1 is R^7 wherein R^7 is heteroaryl which is unsubstituted or substituted with R^d , R^e , and/or R^f where R^d and R^e are independently selected from alkyl, haloalkyl, haloalkoxy, alkoxy, alkylsulfonyl, halo, cyano, carboxy, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, sulfonylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, heterocyclylcarbonyl, and ureido; and R^f is selected from alkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, and cyano,

46. The compound of any one of claims 1 to 41, or a pharmaceutically acceptable salt thereof wherein R^1 is R^7 wherein R^7 is 5 or 6-membered heteroaryl ring such as pyrrolyl, pyrazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyridazinyl, or pyrazinyl, which is unsubstituted or substituted with R^d and/or R^e independently selected from methyl, ethyl, fluoro, chloro, bromo, methoxy, ethoxy, cyclopropyl, cyano, methylsulfonyl, methoxymethyl, aminomethyl, 2-hydroxyethyl, or 3-hydroxypropyl and/or R^f selected from hydroxy, fluoro, chloro, cyano, and methyl.

47. The compound of any one of claims 1 to 41, or a pharmaceutically acceptable salt thereof wherein R^1 pyridinyl which is unsubstituted or substituted with R^f wherein R^f is fluoro, chloro, bromo, or methyl and wherein R^f is attached to carbon atoms on the pyridinyl ring that is ortho to the carbon atom of the pyridinyl ring attached to quinazalone nitrogen.

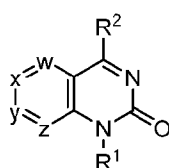
48. The compound of claim 1 wherein the compound is selected from compounds 2-52, 54-83, 85-97, 99-102, 104-106, 109, 112-129, 132-146, 148-151, 153-155, 157, 159-165, 167-190, 192, 195-209, 211, 214, 216-228, 230-252, 255-287, 289-304, 306-310, 312-

339, 341-353, 355, 366-374, 376-387, 389-528, 530-772 in Table 1 or a pharmaceutically acceptable salt thereof.

49. A pharmaceutical composition comprising a compound of any one of claims 1 to 48, or a pharmaceutically acceptable salt thereof at least one pharmaceutically acceptable excipient

50. A method for treating a disease mediated by MAT2A in a patient comprising administering to the patient a therapeutically effective amount of:

(a) a compound of Formula (IIA')



(IIA')

where:

w is CR³ or N; x is CR⁴ or N; y is CR⁵ or N; and z is CR⁶ or N, wherein:

R³ is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyloxy, cyano, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkylamino, alkoxyalkyl, alkoxyalkoxy, alkoxyalkylamino, aminoalkyl, aminoalkoxy, aminoalkylamino, heteroaryl, heteroaryloxy, heteroaralkyloxy, heteroarylamino, heterocyclyl, heterocyclyloxy, heterocyclylamino, heterocyclylalkyloxy, heterocyclyloxyalkoxy, or heterocyclyloxyalkylamino, wherein heterocyclyl or heteroaryl, by itself or as part of another group, is unsubstituted or substituted with R^a, R^b, and/or R^c independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, or aminoalkyl;

R⁵ is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, amino, alkylamino, dialkylamino, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkylamino, alkoxyalkyl, alkoxyalkoxy, alkoxyalkylamino, aminoalkyl, aminoalkoxy, aminoalkylamino, heteroaryl, heteroaryloxy, heteroarylamino, heterocyclyl, heterocyclyloxy, heterocyclylamino, heterocyclyloxyalkoxy, or heterocyclyloxyalkylamino, wherein heterocyclyl or heteroaryl, by itself or as part of another group, is unsubstituted or

substituted with R^a, R^b, and/or R^c independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, cyano, hydroxyalkyl, alkoxyalkyl, or aminoalkyl;

R⁴ and R⁶ are independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfonyl, halo, haloalkyl, haloalkoxy, cycloalkyl, cyano, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, or dialkylaminocarbonyl; provided that: (i) no more than two of w, x, y, and z can be N and (ii) at least one of R³, R⁴, R⁵, and R⁶ is other than hydrogen;

R¹ is R⁷ wherein R⁷ is cycloalkyl, bridged cycloalkyl, fused cycloalkyl, spirocycloalkyl, aryl, heteroaryl, heterocyclyl, bridged heterocyclyl, fused heterocyclyl, or spiroheterocyclyl, wherein aryl, heteroaryl, or heterocyclyl is unsubstituted or substituted with R^d, R^e, and/or R^f;

R² is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminocarbonylalkyl, aminosulfonylalkyl, -O-R⁸, -NR⁹R¹⁰, or -X^b-R¹¹ wherein:

R⁸ is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, cycloalkyl, cycloalkylalkyl, cycloalkoxyalkyl, bridged cycloalkyl, bridged cycloalkylalkyl, fused cycloalkyl, spirocycloalkyl, spirocycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heterocycloxyalkyl, fused heterocyclyl, fused heterocyclylalkyl, bridged heterocyclyl, bridged heterocyclylalkyl, spiroheterocyclyl, or spiroheterocyclylalkyl, wherein aryl, heteroaryl, or heterocyclyl, by itself or as part of another group, is unsubstituted or substituted with R^g, R^h, and/or Rⁱ;

R⁹ is hydrogen, alkyl, deuterioalkyl, or cycloalkyl; and

R¹⁰ is hydrogen, alkyl, deuterioalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, haloalkoxyalkyl, aminoalkyl, aminosulfonylalkyl, thioureidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, cyanoalkyl, alkylcarbonyl, alkoxycarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonylalkyl, cycloalkyl, cycloalkylalkyl, substituted cycloalkyl, substituted cycloalkylalkyl, cycloalkoxyalkyl, bridged cycloalkyl, bridged cycloalkylalkyl, fused cycloalkyl, spirocycloalkyl, spirocycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heteroarylcarbonyl, heterocyclyl, heterocyclylalkyl, heterocycloxyalkyl, heterocycloxyalkyl, fused heterocyclyl, fused heterocyclylalkyl, bridged heterocyclyl, bridged heterocyclylalkyl, spiroheterocyclyl, or spiroheterocyclylalkyl, wherein aryl, heteroaryl, or heterocyclyl, by itself or as part of another group, is unsubstituted or substituted with R^j, R^k, and/or R^l;

X^b is a bond or alkylene; and

R¹¹ is cycloalkyl, bridged cycloalkyl, fused cycloalkyl, spirocycloalkyl, heteroaryl, heterocyclyl, bridged heterocyclyl, fused heterocyclyl, or spiroheterocyclyl, wherein heteroaryl or heterocyclyl is unsubstituted or substituted with R^m, Rⁿ, and/or R^o; and

R^d, R^e, R^g, R^h, R^j, R^k, R^m, and Rⁿ are independently selected from alkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, alkylsulfonyl, halo, cyano, carboxy, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, sulfonylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, heterocyclylcarbonyl, and ureido; and

R^f, Rⁱ, R^l, and R^o are independently selected from alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkoxy, hydroxy, halo, amino, alkylamino, cycloalkylsulfonylamino, cyano, cyanoalkyl, alkoxycarbonylalkyl, carboxyalkyl, aminocarbonylalkyl, or -X^c-R¹² where X^c is bond, alkylene, or heteroalkylene and R¹² is optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted heterocyclyl; provided that when R^l is heterocyclyl then R^f is not hydroxy; or

(b) a compound of any one of claims 2 to 47;

a pharmaceutically acceptable salt thereof.

51. The method of claim 50, wherein the disease is cancer.

52. A method of treating a MTAP null cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound of Formula (IA') as defined in claim 48 or a compound of any one of claims 2 to 48;

a pharmaceutically acceptable salt thereof optionally in a pharmaceutical composition.

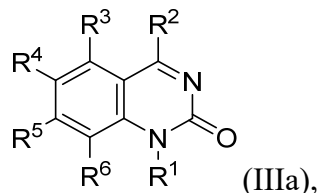
53. A method for treating a cancer in a patient, wherein the cancer is characterized by a reduction or absence of MTAP gene expression, the absence of the MTAP gene, or reduced function of MTAP protein, comprising administering to the subject a therapeutically effective amount of a compound of a compound of Formula (IA') as defined in claim 48 or a compound of any one of claims 2 to 48;

a pharmaceutically acceptable salt thereof optionally in a pharmaceutical composition.

54. The method of any one of claims 51 to 53 wherein the cancer is leukemia, glioma, melanoma, pancreatic, non-small cell lung cancer, bladder cancer, astrocytoma, osteosarcoma, head and neck cancer, myxoid chondrosarcoma, ovarian cancer, endometrial cancer, breast cancer, soft tissue sarcoma, non-Hodgkin lymphoma or mesothelioma.

Claims:

1. A compound of Formula (IIIa):



or a pharmaceutically acceptable salt thereof, wherein

R³ is hydrogen;

R⁵ is C₁₋₆ haloalkyl or halo;

R⁴ is hydrogen;

R⁶ is hydrogen;

R¹ is R⁷ wherein R⁷ is phenyl or 5- to 6- membered heteroaryl, wherein phenyl or heteroaryl, is unsubstituted or substituted with R^d, R^e, and/or R^f;

R² is -NR⁹R¹⁰;

R⁹ is hydrogen;

R¹⁰ is hydrogen, C₁₋₆ alkyl, or C₃₋₆ cycloalkyl, wherein C₃₋₆ cycloalkyl is unsubstituted or substituted with halo; and

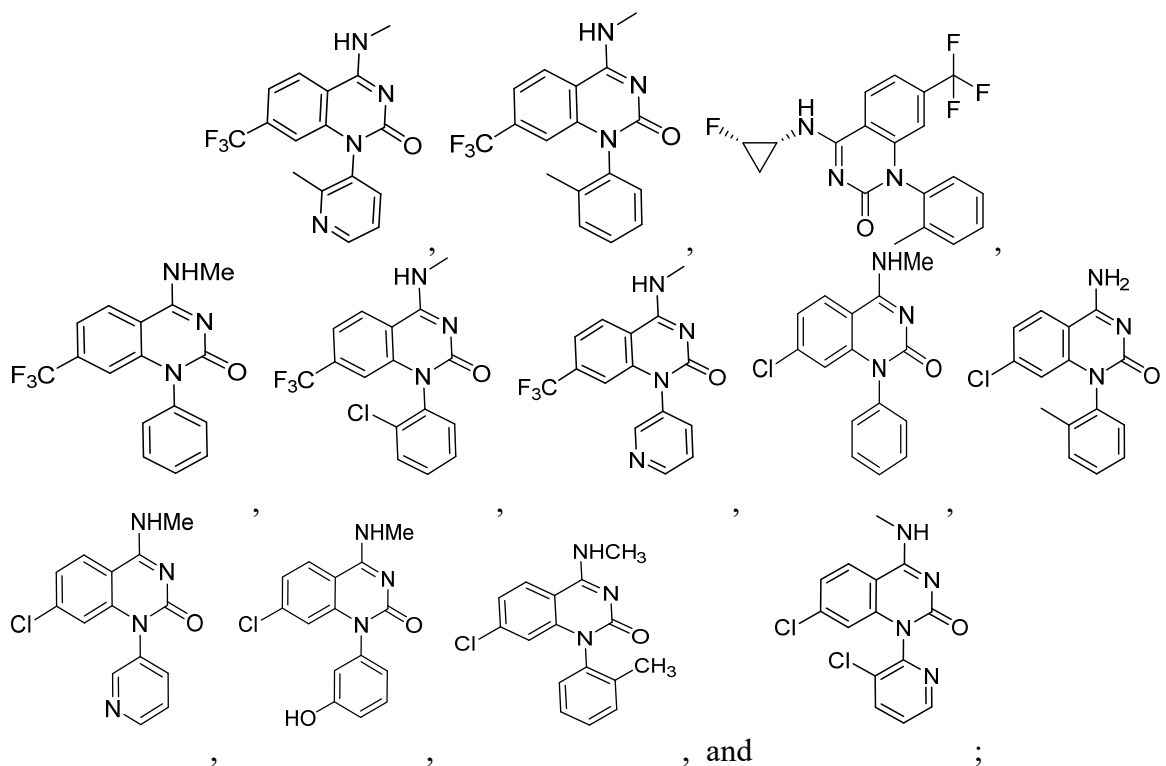
R^d and R^e are independently selected from C₁₋₆ alkyl, halo, and hydroxy; and

R^f is selected from C₁₋₆ alkyl, halo, and hydroxy.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁷ is phenyl, wherein phenyl is unsubstituted or substituted with R^d, R^e, and/or R^f, wherein R^d, and R^e are independently selected from C₁₋₆ alkyl, halo, and hydroxy, and R^f is selected from C₁₋₆ alkyl, halo, and hydroxy.

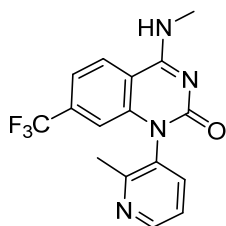
3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁷ is pyridinyl, wherein the pyridinyl is unsubstituted or substituted with R^d, R^e, and/or R^f, wherein R^d and R^e are independently selected from C₁₋₆ alkyl and halo, and R^f is selected from C₁₋₆ alkyl and halo.

4. A compound that is selected from:

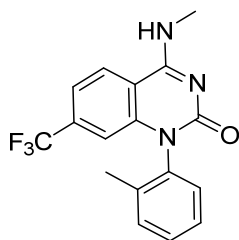


or a pharmaceutically acceptable salt thereof.

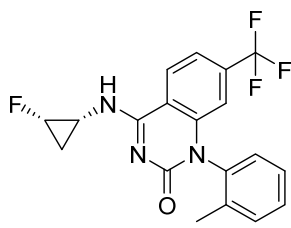
5. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



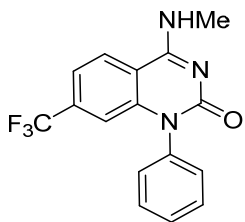
6. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



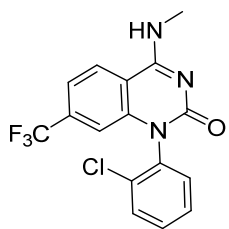
7. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



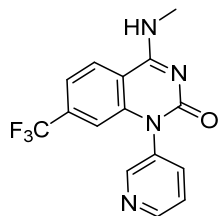
8. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



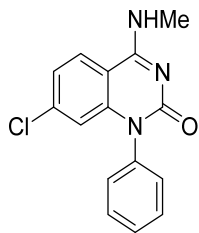
9. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



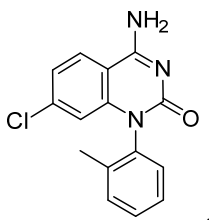
10. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



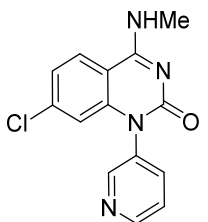
11. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



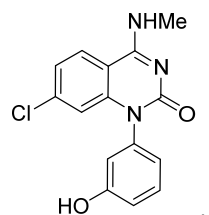
12. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



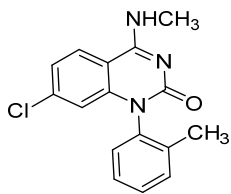
13. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



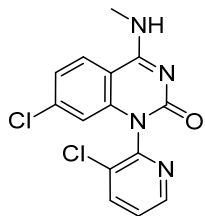
14. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



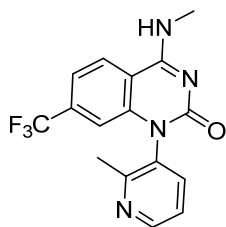
15. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



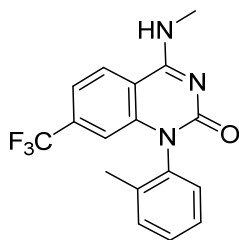
16. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein the compound is:



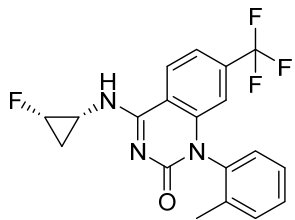
17. The compound according to claim 4, wherein the compound is:



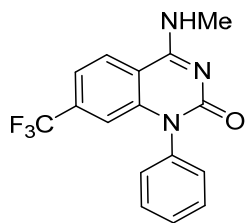
18. The compound according to claim 4, wherein the compound is:



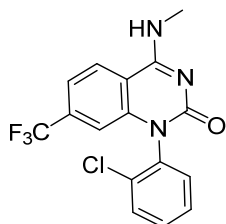
19. The compound according to claim 4, wherein the compound is:



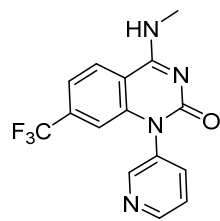
20. The compound according to claim 4, wherein the compound is:



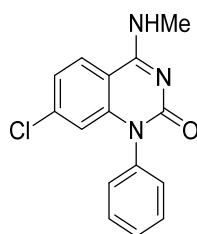
21. The compound according to claim 4, wherein the compound is:



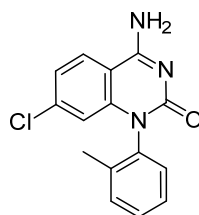
22. The compound according to claim 4, wherein the compound is:



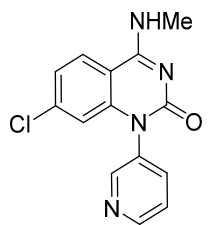
23. The compound according to claim 4, wherein the compound is:



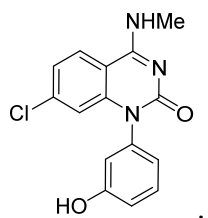
24. The compound according to claim 4, wherein the compound is:



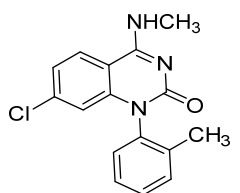
25. The compound according to claim 4 wherein the compound is:



26. The compound according to claim 4, wherein the compound is:



27. The compound according to claim 4, wherein the compound is:



28. The compound according to claim 4, wherein the compound is:

