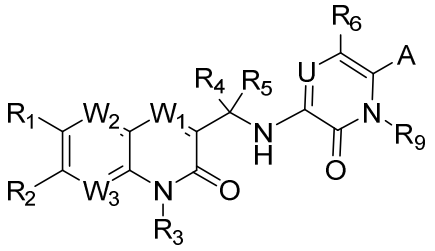
CLAIMS:

1. A compound of Formula I:



(I)

or pharmaceutical salt, enantiomer, hydrate, solvate, or tautomer thereof,

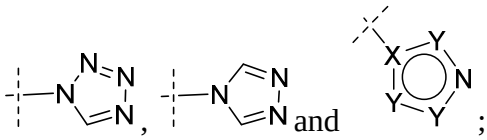
wherein:

each W_1 and W_2 is independently CH, CF or N;

W_3 is independently CR_2 or N;

U is N or CR_6;

A is selected from the group consisting of H, D, halogen, CN, -CHO, -COOH, -COOR, $-C(O)NH_2$, -C(O)NHR, $R'S(O)_2$-, $-O(CH_2)_nC(O)R'$, R'S(O)-, heteroaryl, -SOMe, $–SO_2Me$,



wherein X and Y are independently in each occurrence C , N, NR', S, and O, provided that the ring containing X and Y cannot have more than 4 N or NH atoms or more than one S or O atoms, and wherein the S and O are not contiguous;

R and R' at each occurrence are independently selected from the group consisting of H, OH, CN, $-CH_2CN$, halogen, $-NR_7R_8$, $CHCF_2$, CF_3, C_1-C_6 alkyl, $R_7S(O)_2$-, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, 3- to 8-membered heterocyclyl, aryl, and heteroaryl, wherein each R is optionally substituted with one or more substituents

selected from the group consisting of OH, halogen, C_1-C_6 alkoxy, NH_2, $R_7S(O)_2$-, CN, C_3-C_8 cycloalkyl , 3- to 8-membered heterocyclyl, aryl, heteroaryl, and $R_7S(O)$-;

R_1 is independently OH, CN, halogen, $CHCF_2$, CF_3, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkenyl, C_3-C_8 cycloalkyl, 3- to 8-membered heterocyclyl, aryl, or heteroaryl, wherein each C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 3- to 8-membered heterocyclyl, aryl, or heteroaryl is optionally substituted one or more times with substituents selected from the group consisting of halogen, OH, NH_2, CN, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

each R_2 is independently H, OH, CN, halogen, CF_3, CHF_2, benzyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, NH_2, $-O(CH_2)_nR'$, $-O(CH_2)_nC(O)NHR'$, $-O(CH_2)_nC(O)R'$, NHR_7, $-N(R_7)(R_8)$, $NHC(O)R_7$, $NHS(O)R_7$, $NHS(O)_2R_7$, $NHC(O)OR_7$, $NHC(O)NHR_7$, $-S(O)_2NHR_7$, $NHC(O)N(R_8)R_7$, OCH_2R_7, CHRR' or $OCHR'R_7$, wherein C_1-C_6 alkyl, C_1-C_6 alkoxy is optionally substituted with one or more substituents selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkyl substituted with one or more halogen, 3- to 8-membered heterocyclyl, aryl, -heteroaryl-$C(O)NH_2$, and heteroaryl;

or R_1 and R_2 can combine to form a C_4-C_6 cycloalkyl or a 3- to 8- membered heterocyclyl containing at least one atom selected from the group consisting of N, O, and S;

R_3 is H, C_1-C_6 alkyl, or -OH;

R_4 and R_5 are independently H, halogen, CH_2OH, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted with halogen, or R_4 and R_5 when combined can form a C_3-C_6 cycloalkyl or C_3-C_6 heterocyclyl;

each R_6 is H, halogen, C_1-C_6 alkyl, C_1-C_6 alkyl substituted with halogen, C_1-C_6 alkoxy, C_1-C_6 alkoxy substituted with one or more halogen, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 3- to 8-membered heterocyclyl, aryl, or heteroaryl;

R_7 and R_8 are independently H, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 3- to 8-membered heterocyclyl, aryl, and heteroaryl; or when combined R_7 and R_8 can form a 3- to 8-membered heterocyclyl or heteroaryl ring;

R_9 is independently H, D, CD_3, CF_3, C_1-C_6 alkyl, $C_{2\text{-}6}$ alkenyl, $C_{3\text{-}6}$ alkynyl, C_3-C_8 cycloalkyl, wherein the alkyl, alkenyl, alkynyl, and cycloalkyl is optionally substituted with amino, OH, halo, or alkoxy;

n is 0, 1, or 2; and

r is 0, 1, or 2;

with the proviso that when A is H, then R_1 is not C_1-C_6 alkyl or C_1-C_6 alkoxy and R_1 and R_2 cannot combine to form a 3- to 8- membered heterocyclyl.

2. The compound of claim 1, wherein A is CN, H or F.

3. The compound of claim 2, wherein A is CN and U is N.

4. The compound of claim 1, wherein A is CN and R_9 is H, C_1-C_6 alkyl or C_3-C_6 cycloalkyl.

5. The compound of claim 4, wherein R_9 is methyl.

6. The compound of claim 1, wherein R_3 is H, methyl or ethyl.

7. The compound of claim 1, wherein:

a) R_4 and R_5 are H; or

b) R_4 is H and R_5 is methyl; or

c) R_4 and R_5 are halogen; or

d) R_4 is F and R_5 is methyl; or

e) R_4 and R_5 can combine to form a C_3-C_5 cycloalkyl.

8. The compound of claim 1, wherein R_4 is H and R_5 is (*S*)-methyl.

9. The compound of claim 1, wherein W_1, W_2, and W_3 are CH, or CF.

10. The compound of claim 1, wherein W_1 or W_3 is N.

11. The compound of claim 1, wherein R_1 is halogen.

12. The compound of claim 11, wherein R_1 is chloro.

13. The compound of claim 1, wherein:

a) R_2 is H, halogen, or C_1-C_6 alkoxy; or

b) R_2 is C_1-C_6 alkoxy substituted with heteroaryl or 3- to 8-membered heterocyclyl.

14. The compound of claim 1 selected from the group consisting of:

5-{[(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)methyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

6-chloro-3-{[(1-ethyl-2-oxo-1,2-dihydropyridin-3-yl)amino]methyl}-1,2-dihydroquinolin-2-one;

6-chloro-3-{[(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)amino]methyl}-1,2-dihydroquinolin-2-one;

5-{[(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)methyl]amino}-6-oxo-1,6-dihydropyridine-2-carbonitrile;

6-chloro-3-{[(1-cyclopropyl-2-oxo-1,2-dihydropyridin-3-yl)amino]methyl}-1,2-dihydroquinolin-2-one;

3-{[(6-bromo-2-oxo-1,2-dihydropyridin-3-yl)amino]methyl}-6-chloro-1,2-dihydroquinolin-2-one;

6-chloro-7-methoxy-3-{[(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)amino]methyl}-1,2-dihydroquinolin-2-one;

6-chloro-3-{[(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)amino]methyl}-7-(pyridin-2-ylmethoxy)-1,2-dihydroquinolin-2-one;

5-{[(1S)-1-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1R)-1-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(6-chloro-7-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyrazine-2-carbonitrile;

5-{[(1R)-1-(6-chloro-7-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[1-(6-chloro-7-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(6-chloro-7-methoxy-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1R)-1-(6-chloro-7-methoxy-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[1-(6-chloro-7-methoxy-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-[6-chloro-2-oxo-7-(pyridin-2-ylmethoxy)-1,2-dihydroquinolin-3-yl]ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1R)-1-[6-chloro-2-oxo-7-(pyridin-2-ylmethoxy)-1,2-dihydroquinolin-3-yl]ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-({1-[6-chloro-2-oxo-7-(pyridin-2-ylmethoxy)-1,2-dihydroquinolin-3-yl]ethyl}amino)-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-{6-chloro-2-oxo-7-[(1R)-1-(pyridin-2-yl)ethoxy]-1,2-dihydroquinolin-3-yl}ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-[6-chloro-7-(cyclopropylmethoxy)-2-oxo-1,2-dihydroquinolin-3-yl]ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-[6-chloro-2-oxo-7-(propan-2-yloxy)-1,2-dihydroquinolin-3-yl]ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(6-chloro-8-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(6-chloro-2-oxo-1,2-dihydro-1,8-naphthyridin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1R)-1-(7-chloro-3-oxo-3,4-dihydroquinoxalin-2-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(7-chloro-3-oxo-3,4-dihydroquinoxalin-2-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-6-oxo-1-(trifluoromethyl)-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-[7-(azetidin-1-yl)-6-chloro-2-oxo-1,2-dihydro-1,8-naphthyridin-3-yl]ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

5-{[(1S)-1-[7-(azetidin-1-yl)-6-chloro-2-oxo-1,2-dihydroquinolin-3-yl]ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile;

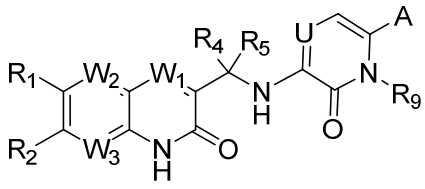
6-chloro-3-[(1S)-1-{[1-methyl-2-oxo-6-(1H-1,2,3,4-tetrazol-1-yl)-1,2-dihydropyridin-3-yl]amino}ethyl]-1,2-dihydroquinolin-2-one; and

5-{[(1S)-1-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carboxamide.

15. The compound of claim 1, wherein the compound is 5-{[(1S)-1-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)ethyl]amino}-1-methyl-6-oxo-1,6-dihydropyridine-2-carbonitrile.

16. The compound of claim 1 having:

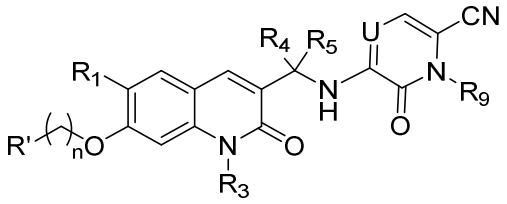
a) the Formula Ia:



(Ia);

or

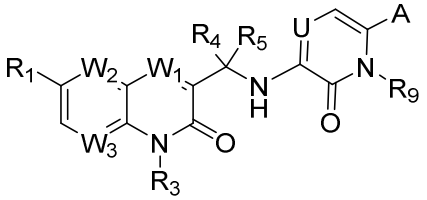
b) the Formula Ia-2:



(Ia-2);

or

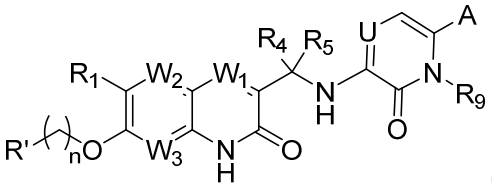
c) the Formula Ib:



(Ib).

17. The compound of claim 16 having:

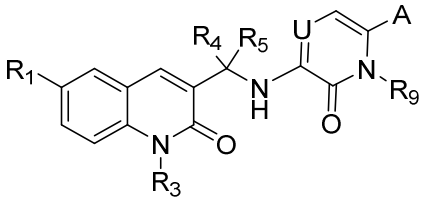
a) the Formula Ia-1:



(Ia-1);

or

b) the Formula Ib-1:



(Ib-1).

18. A pharmaceutical composition comprising the compound according to any one of claims 1-17 and pharmaceutically acceptable carrier.