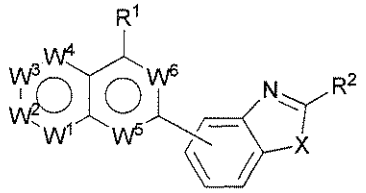
SUMMARY OF THE ~~INVENTION~~DISCLOSURE

[0012] In one embodiment, the ~~invention~~disclosure provides a compound of Formula I:



Formula I

or its pharmaceutically acceptable salts thereof, wherein

X is O or S or N;

W^1 is N, NR^3, CR^3, or C=O, W^2 is N, NR^4, CR^4, or C=O, W^3 is N, NR^5 or CR^5, W^4 is N, C=O or CR^6, wherein no more than two N atoms and no more than two C=O groups are adjacent;

W^5 is N or CR^7;

W^6 is N or CR^8;

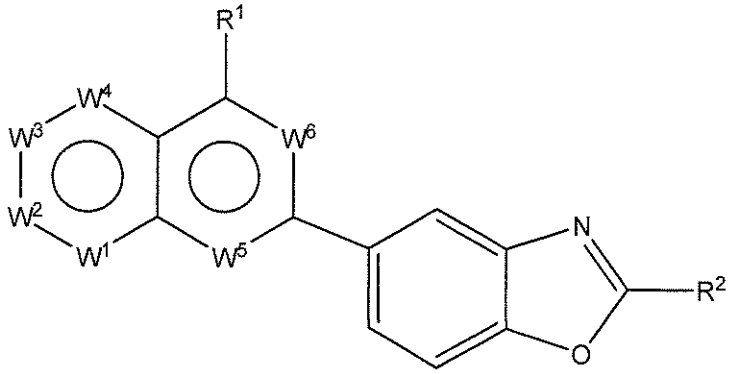
R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^3 and R^4 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

or R^3 and R^4 taken together form a cyclic moiety; and

R^5, R^6 , R^7 and R^8 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0013] In some embodiments, the compound has the formula:

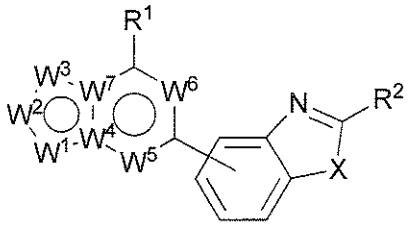


[0014] In still other embodiments of compounds of Formula I, W^1 is CR^3, W^2 is CR^4, W^3 is CR^5, W^4 is N, W^5 is CR^7, and W^6 is CR^8; W^1 is N, W^2 is CR^4, W^3 is CR^5, W^4 is N, W^5 is CR^7, and W^6 is CR^8; or W^1 is CR^3, W^2 is N, W^3 is CR^5, W^4 is N, W^5 is CR^7, and W^6 is CR^8. In some embodiments, W^5 and W^6 are CH. In other embodiments, R^2 is amino. In yet other embodiments, R^1 is H.

[0015] In some embodiments of compounds of Formula I, W^1 is CR^3 and R^3 is alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety. In some embodiments, R^3 is aryl, heteroaryl, heterocycloalkyl, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety. In other embodiments, W^1 is CR^3 and W^2 is CR^4; and R^3 and R^4 taken together form a cyclic moiety. In one embodiment, R^3 and R^4 taken together form a 5-membered heterocyclic ring. In some embodiments, W^4 is N. In other embodiments, X is O.

[0016] Compounds of Formula I are also provided wherein the cyclic moiety is further substituted with alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0017] In another aspect, the ~~invention~~disclosure provides a compound of Formula II:



Formula II

or its pharmaceutically acceptable salts thereof, wherein

X is O or S or N;

W^1 is S, N, NR^3 or CR^3, W^2 is N or CR^4, W^3 is S, N or CR^5, W^4 is N or C, and W^7 is N or C, wherein no more than two N atoms and no more than two C=O groups are adjacent;

W^5 is N or CR^7;

W^6 is N or CR^8;

R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl,

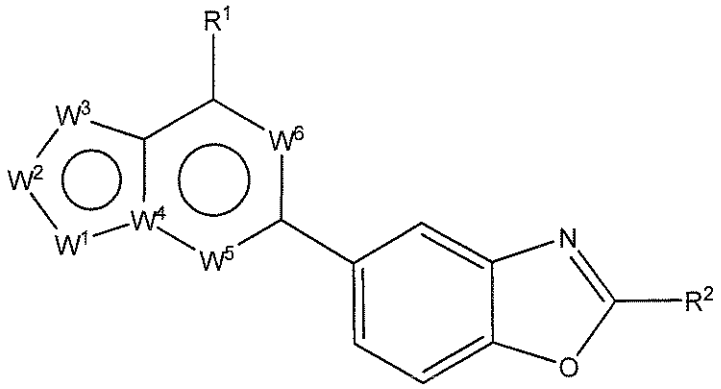
acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^3 and R^4 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

or R^3 and R^4 taken together form a cyclic moiety; and

R^5, R^7 and R^8 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0018] In one embodiment, the compound of the present ~~invention~~disclosure has the formula:



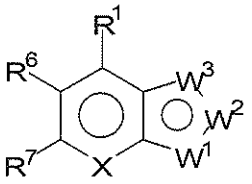
[0019] In other embodiments, W^1 is CR^3, W^2 is CR^4, W^3 is N, W^4 is N, W^5 is CR^7, and W^6 is CR^8; W^1 is CR^3, W^2 is CR^4, W^3 is N, W^4 is N, W^5 is CR^7, and W^6 is CR^8; W^1 is CR^3, W^2 is CR^4, W^3 is N, W^4 is N, W^5 is N, and W^6 is CR^8; W^1 is NR^3, W^2 is CR^4, W^3 is N, W^4 is C, W^5 is CR^7, and W^6 is CR^8; W^1 is S, W^2 is CR^4, W^3 is N, W^4 is C, W^5 is CR^7, and W^6 is CR^8; or W^1 is CR^3, W^2 is CR^4, W^3 is S, W^4 is C, W^5 is N, and W^6 is N. In some embodiments, W^5 and W^6 are CH. In other embodiments, R^2 is amino. In still other embodiments, R^1 is H.

[0020] In some embodiments, W^1 is CR^3 and R^3 is alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety. In other embodiments, R^3 is aryl, heteroaryl, heterocycloalkyl, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety. In some embodiments, W^1 is CR^3 and W^2 is CR^4, and R^3 and R^4 taken together form a cyclic moiety. In other embodiments, R^3 and R^4 taken together form a 5-membered heterocyclic ring.

[0021] In some embodiments, W^4 is N. In other embodiments, the cyclic moiety is further substituted with alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety. In still other embodiments, R^1 is alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken

together with nitrogen to form a cyclic moiety. In some embodiments of the compound of Formula II, X is O. In other embodiments of compounds of Formula II, W^7 is C.

[0022] The ~~invention~~disclosure further provides a compound of Formula III:



or its pharmaceutically acceptable salts thereof, wherein

W^1 is CR^3, W^2 is C-benzoxazolyl substituted with R^2 and W^3 is S;

W^1 is CR^3, W^2 is C-benzoxazolyl substituted with R^2 and W^3 is CR^5;

W^1 is N or NR^3, W^2 is CR^4, and W^3 is C-benzoxazolyl substituted with R^2;

W^1 is CR^3, W^2 is CR^4, and W^3 is C-benzoxazolyl substituted with R^2; or

W^1 is N or NR^3, W^2 is NR^4, and W^3 is C-benzoxazolyl substituted with R^2;

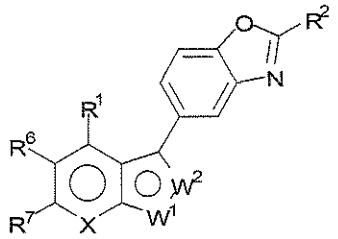
X is N;

R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^3 and R^4 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

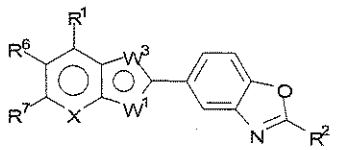
R^5, R^6 , R^7 and R^8 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0023] In some embodiments of the compound of Formula III, the compound is:



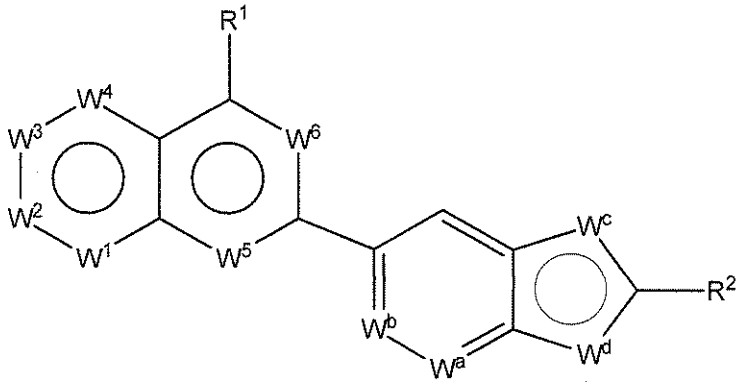
wherein W^1 is CR^3 or NR^3 and W^2 is CR^4.

[0024] In one embodiment, the compound is:



wherein W^1 is CR^3 or NR^3 and W^3 is CR^5.

[0025] In another aspect, the ~~inventiondisclosure~~ provides a compound of Formula IV:



Formula IV

or its pharmaceutically acceptable salts thereof, wherein:

W^1 is N, NR^3, CR^3, or C=O; W^2 is N, NR^4, CR^4, or C=O; W^3 is N, NR^5 or CR^5; W^4 is N, C=O or CR^6, wherein no more than two N atoms and no more than two C=O groups are adjacent;

W^5 is N or CR^7;

W^6 is N or CR^8;

W^a and W^b are independently N or CR^9;

one of W^c and W^d is N, and the other is O, NR^{10}, or S;

R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^3 and R^4 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

or R^3 and R^4 taken together form a cyclic moiety;

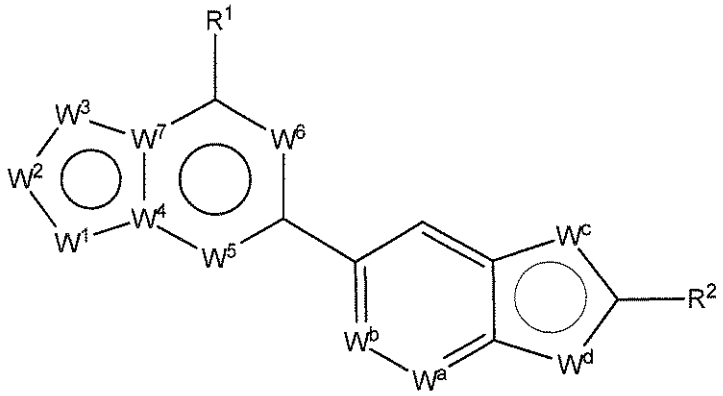
R^5, R^6 , R^7 and R^8 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^9 is alkyl or halo; and

R^{10} is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0026] In some embodiments of the compound of Formula IV, W^1 is CR^3, W^2 is CR^4, W^3 is CR^5, W^4 is N, W^5 is CR^7, and W^6 is CR^8; W^1 is N, W^2 is CR^4, W^3 is CR^5, W^4 is N, W^5 is CR^7, and W^6 is CR^8; or W^1 is CR^3, W^2 is N, W^3 is CR^5, W^4 is N, W^5 is CR^7, and W^6 is CR^8. In some embodiments of the compound of Formula IV, W^b is N. In other embodiments, W^a is CR^9 and R^9 is alkyl.

[0027] The ~~invention~~disclosure also provides a compound of Formula V:



Formula V

or its pharmaceutically acceptable salts thereof, wherein

W^1 is S, N, NR^3 or CR^3, W^2 is N or CR^4, W^3 is S, N or CR^5, W^4 is N or C, and W^7 is N or C, wherein no more than two N atoms and no more than two C=O groups are adjacent;

W^5 is N or CR^7;

W^6 is N or CR^8;

W^a and W^b are independently N or CR^9;

one of W^c and W^d is N, and the other is O, NR^{10}, or S;

R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^3 and R^4 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

or R^3 and R^4 taken together form a cyclic moiety;

R^5, R^7 and R^8 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^9 is alkyl or halo; and

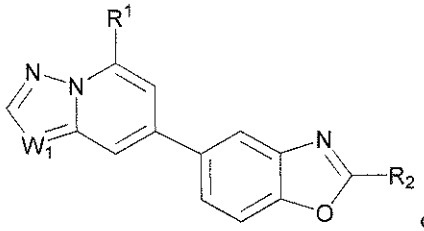
R^{10} is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0028] In some embodiments of the compound of Formula V, W^1 is CR^3, W^2 is CR^4, W^3 is N, W^4 is N, W^5 is CR^7, and W^6 is CR^8. In other embodiments, W^1 is CR^3, W^2 is CR^4, W^3 is N, W^4 is N, W^5 is CR^7, and W^6 is CR^8. In other embodiments, W^1 is CR^3, W^2 is CR^4, W^3 is N, W^4 is N, W^5 is N, and W^6 is CR^8. In still other embodiments, W^1 is NR^3, W^2 is CR^4, W^3 is N, W^4 is C, W^5 is CR^7, and W^6 is CR^8. In other embodiments, W^1 is S, W^2 is CR^4,

W^3 is N, W^4 is C, W^5 is CR^7, and W^6 is CR^8. In other embodiments, W^1 is CR^3, W^2 is CR^4, W^3 is S, W^4 is C, W^5 is N, and W^6 is N.

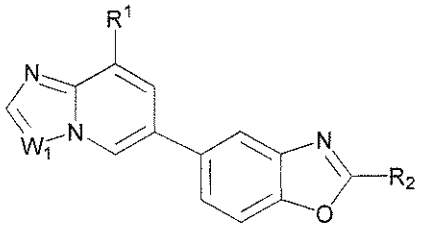
[0029] In some embodiments of the compound of Formula V, W^b is N. In other embodiments, W^a is CR^9 and R^9 is alkyl.

[0030] The ~~invention~~disclosure further provides compounds of Formula V-A and V-B:



Formula V-A

or



Formula V-B

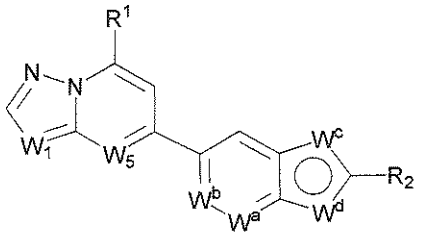
or its pharmaceutically acceptable salts thereof, wherein

W^1 is CR^3;

R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

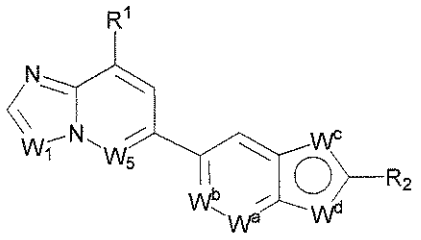
and R^3 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0031] Also provided herein are compounds of Formula V-C and V-D:



Formula V-C

or



Formula V-D

or its pharmaceutically acceptable salts thereof, wherein

W^1 is CR^3;

W^5 is N or CR^7;

W^a and W^b are independently N or CR^9;

one of W^c and W^d is N, and the other is O, NR^{10}, or S;

R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^3 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl,

sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

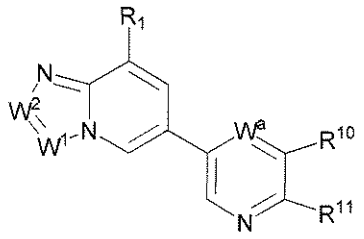
R^7 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^9 is alkyl or halo; and

R^{10} is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0032] In some embodiments of the compound of Formula V-C or V-D, W^b is N. In other embodiments, W^a is CR^9 and R^9 is alkyl.

[0033] Also provided herein is a compound of Formula VI:



or its pharmaceutically acceptable salts thereof, wherein

W^1 is CR^3; W_2 is CR^4;

W^a is CH or N;

R^1 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

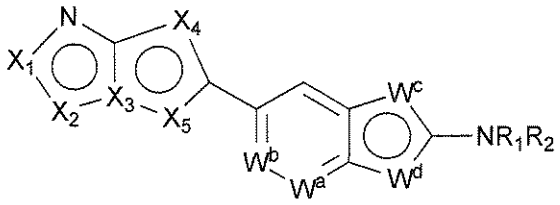
R^3 is alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^4 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

or R^3 and R^4 taken together form a cyclic moiety; and

R^{10} and R^{11} are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0034] The ~~invention~~disclosure further provides a compound of Formula VII:



or a pharmaceutically acceptable salt thereof, wherein

X_1 is CR^3, NR^3, or S;

X_2 is CR^4, NR^4, CR^4 ----- CR^5, or CR^4 ----- NR^5;

X_3 and X_4 are independently C or N;

X_5 is CR^6, NR^6, or S;

X_4 is CR^7, NR^7, CR^7 ----- CR^8, or CR^7 ----- NR^8;

W^a and W^b are independently N or CR^9;

one of W^c and W^d is N, and the other is O, NR^{10}, or S;

R^1 and R^2 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^3 and R^4 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

or R^3 and R^4 taken together form a cyclic moiety;

R^5, R^6 , R^7, and R^8 are independently hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety;

R^9 is alkyl or halo; and

R^{10} is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, heterocycloalkyloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, carbonate, or NR′R″ wherein R′ and R″ are taken together with nitrogen to form a cyclic moiety.

[0035] In some embodiments of the compound of Formula VII, W^b is N. In other embodiments, W^a is CR^9 and R^9 is alkyl.

[0036] In yet another embodiment, the present ~~invention~~disclosure provides a composition comprising a pharmaceutically acceptable excipient and one or more compound disclosed herein. In some embodiments, the composition is a liquid, solid, semi-solid, gel, or an aerosol form.

[0036a] In one embodiment, there is provided a compound or pharmaceutically acceptable salt as defined above, for use in treating a condition mediated by a phosphatidyl inositol-3 kinase (PI3 kinase).

[0037] In still yet another embodiment, the present ~~invention~~disclosure provides a method for inhibiting a phosphatidyl inositol-3 kinase (PI3 kinase), comprising: contacting the PI3 kinase with an effective amount of a compound disclosed herein. In some embodiments, the PI3 kinase is PI3 kinase alpha. The step of contacting may further

comprise contacting a cell that expresses one or more type I PI3 kinases, including PI3 kinease alpha. In some embodiments, the method further comprises administering a second therapeutic agent to the cell.

[0038] The present ~~invention~~disclosure also provides a method for treating a condition associated with PI3 kinase, comprising administering to a subject in need thereof an effective amount of the compound disclosed herein. In some embodiments, the condition associated with PI3 kinase is selected from the group consisting of asthma, emphysema, bronchitis, psoriasis, allergy, anaphylaxis, rheumatoid arthritis, graft versus host disease, lupus erythematosus, psoriasis, restenosis, benign prostatic hypertrophy, diabetes, pancreatitis, proliferative glomerulonephritis, diabetes- induced renal disease, inflammatory bowel disease, atherosclerosis, eczema, scleroderma, diabetes, diabetic retinopathy, retinopathy of prematurity, age-related macular degeneration, hemangioma, glioma, melanoma, Kaposi's sarcoma and ovarian, breast, lung, pancreatic, prostate, colon and epidermoid cancer.

INCORPORATION BY REFERENCE

[0039] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0040] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0041] Figure 1 illustrates the selectivity and potency of inhibition of an exemplary compound of the invention (e.g., compound 54) with respect to a number of kinases.

[0042] Figure 2 shows that an exemplary compound of the invention (e.g., compound 54) inhibits the PI3K pathway and the proliferation of tumor cells with a PI3Kα mutation.

[0043] Figure 3 shows the inhibition of angiogenesis by a compound of the invention, and comparison to the activity of a non-specific inhibitor of PI3Ks (Pan-PI3K Inh).

[0044] Figure 4 shows the *in vivo* efficacy of a compound of the invention by comparison to a Pan-PI3K inhibitor, as measured by tumor weight and downstream markers of kinase activity, as well as a comparison of the effect on blood glucose.

[0045] Figure 5 shows impact of a compound of the invention on tumor size, and that localization and viability of spleen-derived marginal zone B cells is not affected by the compound, in contrast to a Pan-PI3K inhibitor.

[0046] Figure 6 shows the *in vivo* efficacy of a compound of the invention against a tumor lacking a PI3Kα mutation, compared to a kinase inhibitor with specificity for mTor.

[0047] Figure 7 shows the synergistic effect of combining a compound of the invention with a MEK inhibitor.