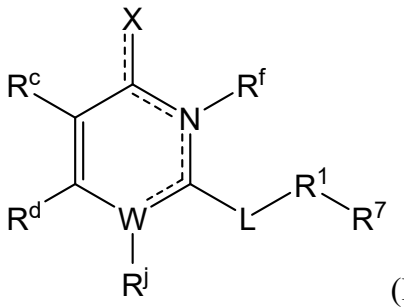
Claims:

1. A compound represented by Formula (II):



(II)

or a pharmaceutically acceptable salt or tautomer thereof, wherein:

X is H, S, SR^2, NR^2, $NR^2R^{2'}$, O, OH, OR^h, F, or Br;

W is N or C;

(i) when W is N, then: L is $–(C(R^5)_2)_mCH=CH(C(R^5)_2)_p–$, ,
$–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$, $–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$cyclopropyl–, $–(C(R^5)_2)_mY^1CH=CH-$,
$–(C(R^5)_2)_mNR^3C=(O)(C(R^5)_2)_p–$, $–(C(R^5)_2)_m$phenyl$(C(R^5)_2)_p–$,
$–(C(R^5)_2)_m$pyridinyl$(C(R^5)_2)_p–$, or $–(C(R^5)_2)_m$thiophenyl$(C(R^5)_2)_p–$;

(ii) when W is C, then: L is $–(C(R^5)_2)_mCH=CH(C(R^5)_2)_p–$, $–(C(R^5)_2)_o–$,
$–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$, , $–(C(R^5)_2)_m Y^1CH=CH–$, $–(C(R^5)_2)_mC=(O)(CH_2)_p–$,
$–(C(R^5)_2)_mC=(O)O(C(R^5)_2)_p–$, $–(C(R^5)_2)_mC=(O)NR^3(C(R^5)_2)_p–$,
$–(C(R^5)_2)_mNR^3C=(O)(C(R^5)_2)_p–$, $–(C(R^5)_2)_m$phenyl$(C(R^5)_2)_p–$,
$–(C(R^5)_2)_m$pyridinyl$(C(R^5)_2)_p–$, or $–(C(R^5)_2)_m$thiophenyl$(C(R^5)_2)_p–$;

Y^1 is O, NR^4, or $S(O)_q$;

each Y^2 is independently O, NH or S;

R^1 is absent, C_6-C_{10} arylene, heteroarylene, or C_3-C_8cycloalkylene, wherein the heteroarylene comprises one or two 5- to 7-membered rings and 1-4 heteroatoms selected from N, O and S, and wherein the C_6-C_{10} arylene, heteroarylene, and C_3-C_8cycloalkylene are optionally substituted with one to two R^e;

R^2 is H or C_1-C_4 alkyl;

$R^{2'}$ is C_1-C_4 alkyl, or C_3-C_7 cycloalkyl; or

R^2 and $R^{2'}$ together with the nitrogen atom to which they are attached form a 3- to 7-membered heterocycloalkyl ring comprising 1-3 additional heteroatoms selected from N, O and S;

R^3 is H or C_1-C_4 alkyl;

R^4 is H or C_1-C_4 alkyl;

each R^5 is independently at each occurrence H or C_1-C_4 alkyl;

each R^6 is independently at each occurrence H or C_1-C_4 alkyl;

R^7 is A, B, or C;

A is $-(C(R^6)_2)_rCO_2R^x$, $-Y^2(C(R^6)_2)_rCO_2R^x$, $-(C(R^6)_2)_r$tetrazole, $-(C(R^6)_2)_r$oxadiazolone, $-(C(R^6)_2)_r$tetrazolone, $-(C(R^6)_2)_r$thiadiazolol, $-(C(R^6)_2)_r$ isoxazol-3-ol, $-(C(R^6)_2)_rP(O)(OH)OR^x$, $-(C(R^6)_2)_rS(O)_2OH$, $-(C(R^6)_2)_rC(O)NHCN$, or $-(C(R^6)_2)_rC(O)NHS(O)_2$alkyl, wherein $-(C(R^6)_2)_r$tetrazole, $-(C(R^6)_2)_r$oxadiazolone, $-(C(R^6)_2)_r$tetrazolone, $-(C(R^6)_2)_r$thiadiazolol, $-(C(R^6)_2)_r$ isoxazol-3-ol are optionally substituted with C_1-C_6 alkyl,

B is $-(C(R^6)_2)_rS(O)_2OC_1$-C_4 alkyl, $-O(C(R^6)_2)_rS(O)_2OC_1$-C_4 alkyl, $-Y^2(C(R^6)_2)_rC(O)NR^gR^{g'}$, $-Y^2(C(R^6)_2)_rS(O)_2NR^gR^{g'}$, $-(C(R^6)_2)_rC(O)NHR^{g'}$, $-(C(R^6)_2)_rS(O)_2NR^gR^{g'}$, $-(C(R^6)_2)_rC(O)NHS(O)_2NR^gR^{g'}$, $-(C(R^6)_2)_rCO_2R^i$, $-(C(R^6)_2)_rNHCO_2R^x$, $-(C(R^6)_2)_rP(O)(OR^x)_2$, $-O(C(R^6)_2)_rP(O)(OR^x)_2$, $-(C(R^6)_2)_rS(O)_2OH$, $-O(C(R^6)_2)_rS(O)_2OH$, $-(C(R^6)_2)_rP(O)_2OR^x$, or $-O(C(R^6)_2)_rP(O)_2OR^x$,

C is $-(CH_2)_rCN$, $-(CH_2)_sOH$, chloro, bromo, $-(C(R^6)_2)_rC_6$-C_{10} aryl, $-(C(R^6)_2)_rS$-C_6-C_{10} aryl, $-(C(R^6)_2)_r$heteroaryl, $-O(C(R^6)_2)_r$heteroaryl, $-O(C(R^6)_2)_r$heterocycloalkyl, $-O(C(R^6)_2)_rOH$, $-OR^y$, $-(C(R^6)_2)_rC(O)NHCN$, $-CH=CHCO_2R^x$, or $-(C(R^6)_2)_rC(O)NHS(O)_2C_1$-$C_4$ alkyl, wherein the aryl and heteroaryl are substituted with one to three substituents each independently selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, chloro, bromo and OH, and wherein the heterocycloalkyl is substituted with one to two =O or =S;

R^c is C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, $-CN$, $-OR^x$, or $-CO_2R^x$;

R^d is methyl, CF_3, CR^fF_2, $-CH_2$-C_6-C_{10} aryl, $-CH_2$-CH_2-C_6-C_{10} aryl, $-(C(R^6)_2)_t$-5- or 6-membered heteroaryl, $-(C(R^6)_2)_t$-5- or 6-membered cycloalkyl, optionally substituted 5- or 6-membered heteroaryl, or optionally substituted 5- or 6-membered cycloalkyl;

each R^e is independently at each occurrence C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, chloro, bromo, C_1-C_6 haloalkyl, -NHR^z, -OH, or -CN;

R^f is absent, H, or methyl;

R^g is H, C_1-C_6 alkyl, OH, -$S(O)_2$(C_1-C_6 alkyl), or $S(O)_2N$(C_1-C_6 alkyl)$_2$;

$R^{g'}$ is H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, 4- to 7-membered heterocycloalkyl ring comprising 1-3 heteroatoms selected from N, O and S, C_6-C_{10} aryl, or 5- to 7-membered heteroaryl comprising 1-3 heteroatoms selected from N, O and S, wherein the alkyl is optionally substituted with one or more substituents independently selected from halogen and -OH, and wherein the cycloalkyl, heterocycloalkyl, aryl and heteroaryl are optionally substituted with one or more substituents independently selected from C_1-C_6 alkyl, halogen, and -OH;

R^h is H, C_1-C_4 alkyl, or 3- to 7- membered heterocycloalkyl ring comprising 1-3 heteroatoms selected from N, O and S, wherein the alkyl is optionally substituted with one or more substituents each independently selected from NH_2, C_1-C_4 alkylamino, C_1-C_4 dialkylamino, and $C(O)NH_2$; and wherein the heterocycloalkyl is optionally substituted with one or more substituents each independently selected from C_1-C_6 alkyl and C_1-C_6 haloalkyl;

R^i is (i) –$(CH_2)_s$OC(O)C_1-C_6 alkyl, wherein the alkyl is substituted with one or more NH_2; (ii) $(CH_2CH_2O)_nCH_2CH_2OH$; or (iii) C_1-C_6 alkyl substituted with one or more substituents each independently selected from OH and 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from O, N, or S;

R^j is absent, H, C_1-C_6 alkyl, or -CN;

each R^x is independently at each occurrence H, C_1-C_6 alkyl, or C_6-C_{10} aryl;

each R^y and R^z is independently H, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

each m, p, q, r, and t is independently 0, 1 or 2;

n is 0, 1, 2, or 3;

s is 1 or 2;

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

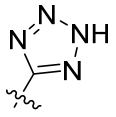
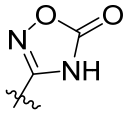
≡ represents a single bond or a double bond; and

provided that

when X is O; R^f is H; W is C; R^j is –CN; L is $–SCH_2$-; R^1 is phenylene or pyridine; then R^7 is not -COOH;

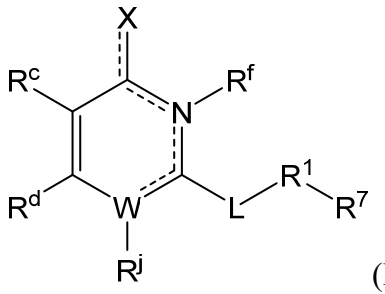
when X is O; R^f is H; W is C; R^j is –CN; L is $–SCH_2$-; R^1 is phenylene or pyridine; and R^7 is tetrazole; then R^c is not H;

when X is O; R^f is H; W is C; R^j is –CN; L is -S-$C(R^5)_2$ or $–SCH_2CH_2$-; R^1 is absent; then R^7 is not COOH or tetrazole;

when X is O, R^f is H; W is N; R^j is absent; R^d is methyl, optionally substituted 5- to 10-membered aryl, optionally substituted 5- or 6-membered heteroaryl, or optionally substituted 5- or 6-membered cycloalkyl; L is $–SCH_2–$ or $-OCH_2$-; and R^1 is phenylene; then R^7 is not –COOH, $-CH_2COOH$, , or ; and

when X is O, R^f is H, W is N, R^j is absent, L is $–NHCH_2–$, $–CH_2NH–$, or –NH-C(O)-, and R^1 is phenylene, then R^d is not phenyl.

2. A compound represented by Formula (I):



(I)

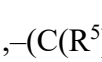
or a pharmaceutically acceptable salt or tautomer thereof,

wherein:

X is H, S, SR^2, NR^2, $NR^2R^{2'}$, O, OH, OR^h, F, or Br;

W is N or C;

(i) when W is N, then:

L is $–(C(R^5)_2)_mCH=CH(C(R^5)_2)_p–$, ,$–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$, $–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$cyclopropyl–, $–(C(R^5)_2)_mY^1CH=CH–$, $–(C(R^5)_2)_mNR^3C=(O)(C(R^5)_2)_p–$, $–(C(R^5)_2)_m$phenyl$(C(R^5)_2)_p–$, $–(C(R^5)_2)_m$pyridinyl$(C(R^5)_2)_p–$, or $–(C(R^5)_2)_m$thiophenyl$(C(R^5)_2)_p–$;

(ii) when W is C, then:

L is $–(C(R^5)_2)_mCH=CH(C(R^5)_2)_p–$, $–(C(R^5)_2)_o–$, $–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$,

, $–(C(R^5)_2)_m Y^1CH=CH–$, $–(C(R^5)_2)_mC=(O)(CH_2)_p–$,

$–(C(R^5)_2)_mC=(O)O(C(R^5)_2)_p–$, $–(C(R^5)_2)_mC=(O)NR^3(C(R^5)_2)_p–$,

$–(C(R^5)_2)_mNR^3C=(O)(C(R^5)_2)_p–$, $–(C(R^5)_2)_m$phenyl$(C(R^5)_2)_p–$,

$–(C(R^5)_2)_m$pyridinyl$(C(R^5)_2)_p–$, or $–(C(R^5)_2)_m$thiophenyl$(C(R^5)_2)_p–$;

Y^1 is O, NR^4, or $S(O)_q$;

each Y^2 is independently O, NH or S;

R^1 is absent or C_6-C_{10} arylene or heteroarylene, wherein the heteroarylene comprises one or two 5- to 7-membered rings and 1-4 heteroatoms selected from N, O and S, and wherein the C_6-C_{10} arylene or heteroarylene are optionally substituted with one to two R^e;

R^2 is H or C_1-C_4 alkyl;

$R^{2'}$ is C_1-C_4 alkyl, or C_3-C_7 cycloalkyl; or

R^2 and $R^{2'}$ together with the nitrogen atom to which they are attached form a 3- to 7-membered heterocycloalkyl ring comprising 1-3 additional heteroatoms selected from N, O and S;

R^3 is H or C_1-C_4 alkyl;

R^4 is H or C_1-C_4 alkyl;

each R^5 is independently at each occurrence H or C_1-C_4 alkyl;

each R^6 is independently at each occurrence H or C_1-C_4 alkyl;

R^7 is A, B, or C;

A is $-(C(R^6)_2)_rCO_2R^x$, $-Y^2(C(R^6)_2)_rCO_2R^x$, $-(CH_2)_r$tetrazole, $-(CH_2)_r$oxadiazolone, $-(CH_2)_r$tetrazolone, $-(CH_2)_r$thiadiazolol, $-(CH_2)_r$ isoxazol-3-ol, $-(CH_2)_rP(O)(OH)OR^x$, $-(CH_2)_rS(O)_2OH$, $-(CH_2)_rC(O)NHCN$, or $-(CH_2)_rC(O)NHS(O)_2$alkyl, wherein $-(CH_2)_r$tetrazole, $-(CH_2)_r$oxadiazolone, $-(CH_2)_r$tetrazolone, $-(CH_2)_r$thiadiazolol, $-(CH_2)_r$ isoxazol-3-ol are optionally substituted with C_1-C_6 alkyl,

B is $-(C(R^6)_2)_rS(O)_2OC_1$-C_4 alkyl, $-O(C(R^6)_2)_rS(O)_2OC_1$-C_4 alkyl, $-Y^2(C(R^6)_2)_rC(O)NR^gR^{g'}$, $-Y^2(C(R^6)_2)_rS(O)_2NR^gR^{g'}$, $-(CH_2)_rC(O)NR^gR^{g'}$, $-(CH_2)_rS(O)_2NR^gR^{g'}$,

$-(CH_2)_rC(O)NHS(O)_2NR^gR^{g'}$, $-(C(R^6)_2)_rCO_2R^i$, $-(C(R^6)_2)_rNHCO_2R^x$, $-(C(R^6)_2)_rP(O)(OR^x)_2$, $-O(C(R^6)_2)_rP(O)(OR^x)_2$, $-(C(R^6)_2)_rS(O)_2OH$, $-O(C(R^6)_2)_rS(O)_2OH$, $-(C(R^6)_2)_rP(O)_2OR^x$, or $-O(C(R^6)_2)_rP(O)_2OR^x$,

C is $-(CH_2)_rCN$, $-(CH_2)_sOH$, chloro, bromo, $-(C(R^6)_2)_rC_6$-C_{10} aryl, $-(C(R^6)_2)_rS$-C_6-C_{10} aryl, $-(C(R^6)_2)_r$heteroaryl, $-O(C(R^6)_2)_r$heteroaryl, $-O(C(R^6)_2)_r$heterocycloalkyl, $-O(C(R^6)_2)_rOH$, $-OR^y$, $-(C(R^6)_2)_rC(O)NHCN$, $-CH=CHCO_2R^x$, or $-(C(R^6)_2)_rC(O)NHS(O)_2C_1$-$C_4$ alkyl, wherein the aryl and heteroaryl are substituted with one to three substituents each independently selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, chloro, bromo, and OH, and wherein the heterocycloalkyl is substituted with one to two =O or =S;

R^c is C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, $-CN$, $-OR^x$, or $-CO_2R^x$;

R^d is methyl, CF_3, CR^fF_2, $-CH_2$-C_6-C_{10} aryl, $-CH_2$-CH_2-C_6-C_{10} aryl, $-(C(R^6)_2)_t$-5- or 6-membered heteroaryl, $-(C(R^6)_2)_t$-5- or 6-membered cycloalkyl, optionally substituted 5- or 6-membered heteroaryl, or optionally substituted 5- or 6-membered cycloalkyl;

each R^e is independently at each occurrence C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, chloro, bromo, C_1-C_6 haloalkyl, $-NHR^z$, -OH, or -CN;

R^f is absent, H, or methyl;

R^g is H, C_1-C_6 alkyl, OH, $-S(O)_2(C_1$-C_6 alkyl), or $S(O)_2N(C_1$-C_6 alkyl$)_2$;

$R^{g'}$ is H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, 4- to 7-membered heterocycloalkyl ring comprising 1-3 heteroatoms selected from N, O and S, C_6-C_{10} aryl, or 5- to 7-membered heteroaryl comprising 1-3 heteroatoms selected from N, O and S, wherein the alkyl is optionally substituted with one or more substituents independently selected from halogen and -OH, and wherein the cycloalkyl, heterocycloalkyl, aryl and heteroaryl are optionally substituted with one or more substituents independently selected from C_1-C_6 alkyl, halogen, and -OH;

R^h is H, C_1-C_4 alkyl, or 3- to 7- membered heterocycloalkyl ring comprising 1-3 heteroatoms selected from N, O and S, wherein the alkyl is optionally substituted with one or more substituents each independently selected from NH_2, C_1-C_4 alkylamino, C_1-C_4 dialkylamino, and $C(O)NH_2$; and wherein the heterocycloalkyl is optionally substituted with one or more substituents each independently selected from C_1-C_6 alkyl and C_1-C_6 haloalkyl;

R^i is (i) $-(CH_2)_sOC(O)C_1$-C_6 alkyl, wherein the alkyl is substituted with one or more NH_2; (ii) $(CH_2CH_2O)_nCH_2CH_2OH$; or (iii) C_1-C_6 alkyl substituted with one or more

substituents each independently selected from OH and 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from O, N, or S;

R^j is absent, H, C_1-C_6 alkyl, or -CN;

each R^x is independently at each occurrence H, C_1-C_6 alkyl, or C_6-C_{10} aryl;

each R^y and R^z is independently H, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

each m, p, q, r, and t is independently 0, 1 or 2;

n is 0, 1, 2, or 3;

s is 1 or 2;

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

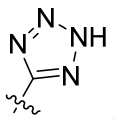
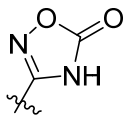
$\equiv$ represents a single bond or a double bond; and

provided that

when X is O; R^f is H; W is C; R^j is –CN; L is $–SCH_2$-; R^1 is phenylene or pyridine; then R^7 is not -COOH;

when X is O; R^f is H; W is C; R^j is –CN; L is $–SCH_2$-; R^1 is phenylene or pyridine; and R^7 is tetrazole; then R^c is not H;

when X is O; R^f is H; W is C; R^j is –CN; L is -S-C$(R^5)_2$ or $–SCH_2CH_2$-; R^1 is absent; then R^7 is not COOH or tetrazole;

when X is O, R^f is H; W is N; R^j is absent; R^d is methyl, optionally substituted 5- to 10-membered aryl, optionally substituted 5- or 6-membered heteroaryl, or optionally substituted 5- or 6-membered cycloalkyl; L is $–SCH_2–$ or $-OCH_2$-; and R^1 is phenylene; then R^7 is not –COOH, $-CH_2COOH$, , or ; and

when X is O, R^f is H, W is N, R^j is absent, L is $–NHCH_2–$, $–CH_2NH–$, or –NH-C(O)-, and R^1 is phenylene, then R^d is not phenyl.

3. The compound of claim 1 or 2, wherein X is O, OH, OR^h, F, Br, or Cl.

4. The compound of claim 1 or 2, wherein X is H, S, SR^2, NR^2, or $NR^2R^{2'}$.

5. The compound of any one of claims 1-4, wherein R^f is absent.

6. The compound of any one of claims 1-4, wherein R^f is H or methyl.

7. The compound of any one of claims 1-6, wherein W is N.

8. The compound of claim 7, wherein R^j is absent.

9. The compound of any one of claims 1-6, wherein W is C.

10. The compound of claim 9, wherein R^j is H, C_1-C_6 alkyl, or –CN.

11. The compound of claim 9 or 10, wherein R^j is –CN.

12. The compound of any one of claims 1-11, wherein R^c is C_1-C_6 alkyl, –CN, or halogen.

13. The compound of any one of claims 1-12, wherein R^c is –CN or halogen.

14. The compound of any one of claims 1-12, wherein R^c is –CN.

15. The compound of any one of claims 1-14, wherein R^d is methyl.

16. The compound of any one of claims 1-14, wherein R^d is optionally substituted 5- or 6-membered heteroaryl.

17. The compound of any one of claims 1-14, wherein R^d is optionally substituted 5- or 6-membered cycloalkyl.

18. The compound of any one of claims 1-14, wherein R^d is methyl, cyclohexyl, pyridinyl, thiazolyl, or thienyl.

19. The compound of any one of claims 1-14, wherein R^d is methyl, cyclohexyl, pyridinyl, thiazolyl, or thienyl.

20. The compound of any one of claims 1-14, wherein R^d is methyl.

21. The compound of any one of claims 1-14, wherein R^d is $–CF_3$.

22. The compound of any one of claims 1-14, wherein R^d is CR^fF_2.

23. The compound of any one of claims 1-14, wherein R^d is $-CH_2$-C_6-C_{10} aryl, $-CH_2$-CH_2-C_6-C_{10} aryl, $-(C(R^6)_2)_r$-5- or 6-membered heteroaryl, $-(C(R^6)_2)_r$-5- or 6-membered cycloalkyl.

24. The compound of any one of claims 1-14, wherein R^d is $-CH_2$-C_6-C_{10} aryl or $-CH_2$-CH_2-C_6-C_{10} aryl.

25. The compound of any one of claims 1-24, wherein L is $–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$.

26. The compound of claim 25, wherein Y^1 is S.

27. The compound of any one of claims 1-24, wherein L is $–(C(R^5)_2)_mNR^3C=(O)(C(R^5)_2)_p–$ or $–(C(R^5)_2)_mY^1(C(R^5)_2)_p–$cyclopropyl–.

28. The compound of any one of claims 1-27, wherein R^1 is C_6-C_{10} arylene.

29. The compound of any one of claims 1-27, wherein R^1 is heteroarylene.

30. The compound of any one of claims 1-27, wherein R^1 is absent.

31. The compound of any one of claims 1-30, wherein R^7 is A.

32. The compound of claim 31, wherein A is $-(C(R^6)_2)_rCO_2R^x$ or $-(CH_2)_r$tetrazole, wherein the $-(CH_2)_r$tetrazole is optionally substituted with C_1-C_6 alkyl.

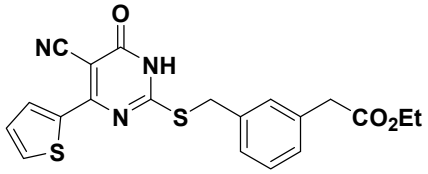
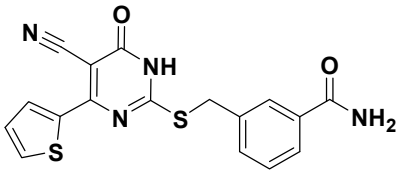
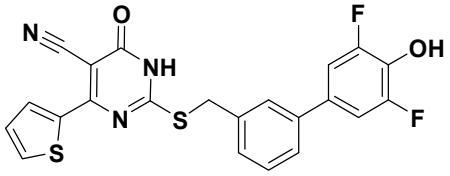
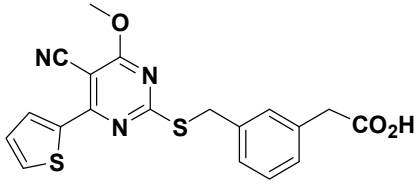
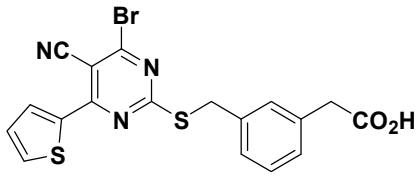
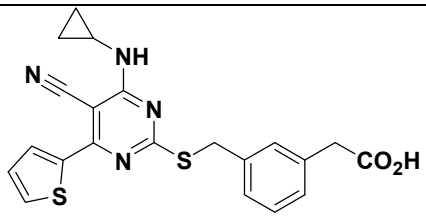
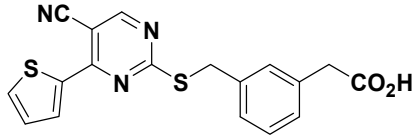
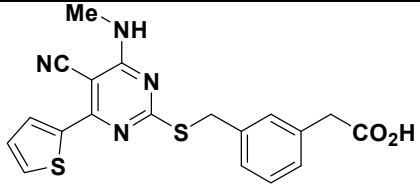
33. The compound of any one of claims 1-30, wherein R^7 is B.

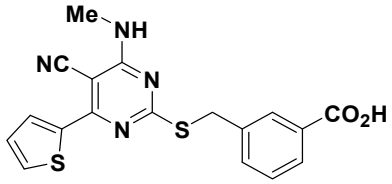
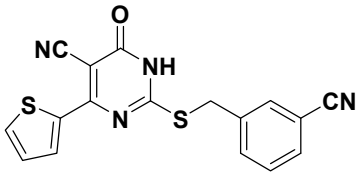
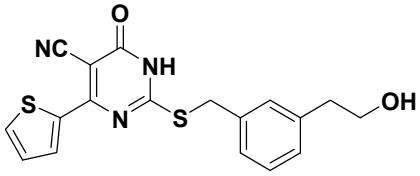
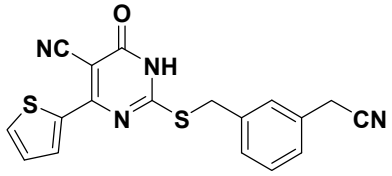
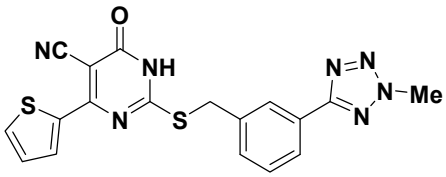
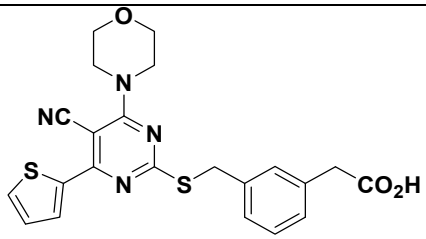
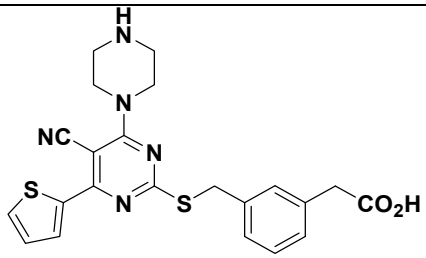
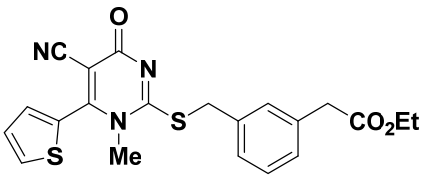
34. The compound of claim 33, wherein B is $-(CH_2)_rC(O)NR^gR^{g'}$, or $-(CH_2)_rS(O)_2NR^gR^{g'}$,

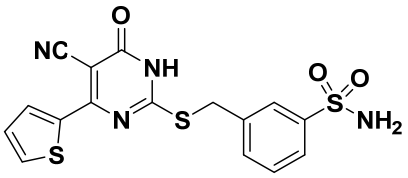
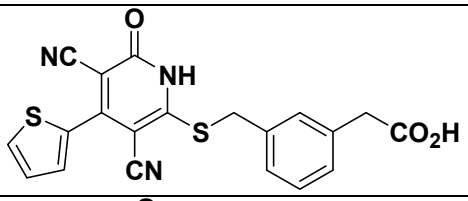
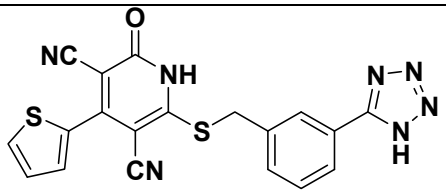
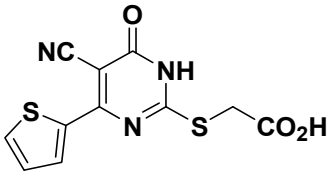
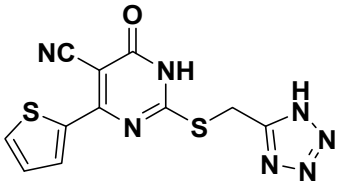
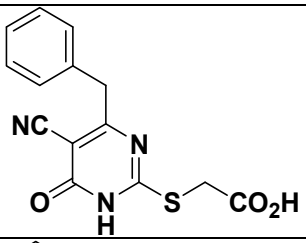
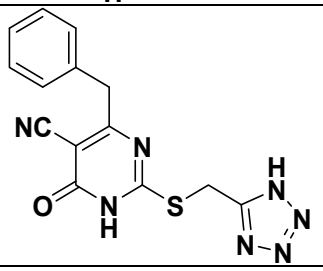
35. The compound of any one of claims 1-30, wherein R^7 is C.

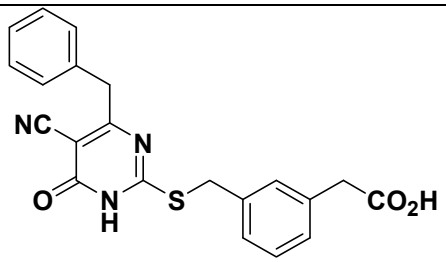
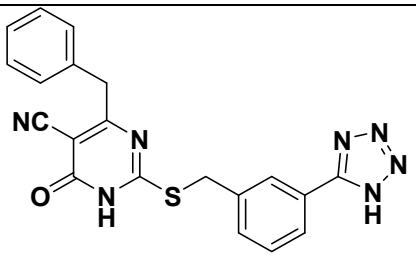
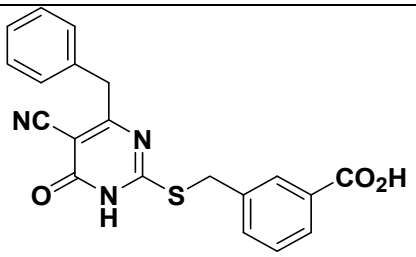
36. The compound of claim 35, wherein C is $–(CH_2)_rCN$, $–(CH_2)_sOH$, or $-(C(R^6)_2)_rC_6$-C_{10} aryl, wherein the aryl is substituted with one to three substituents each independently selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, and OH.

37. A compound, or a pharmaceutically acceptable salt or tautomer thereof, selected from the group consisting of:

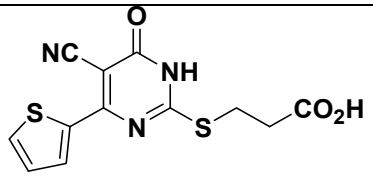
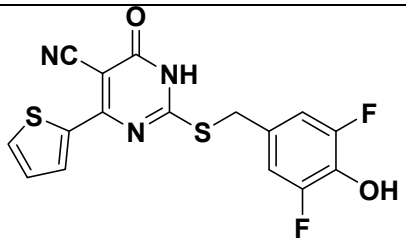
Cpd No.	Structure
I-1	 ,
I-2	 ,
I-3	 ,
I-4	 ,
I-5	 ,
I-6	 ,
I-8	 ,
I-9	 ,

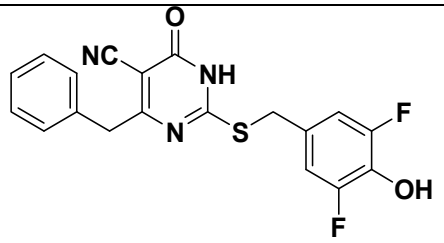
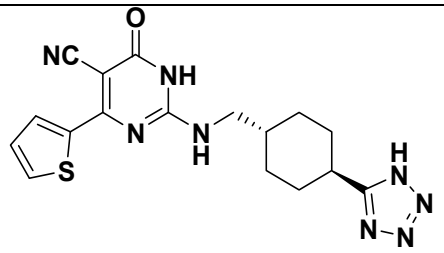
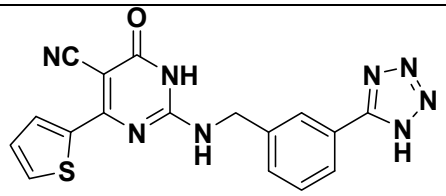
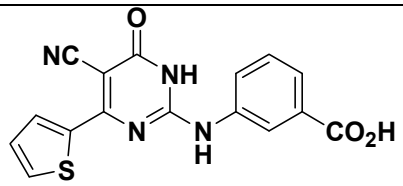
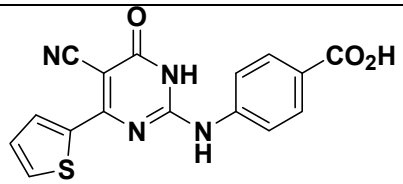
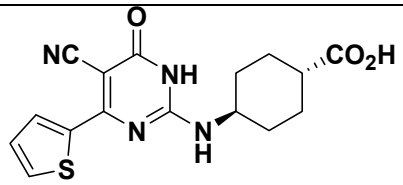
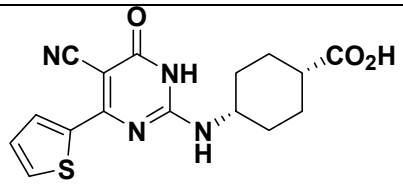
Cpd No.	Structure
I-10	 ,
I-11	 ,
I-12	 ,
I-13	 ,
I-14	 ,
I-15	 ,
I-16	 ,
I-17	 ,

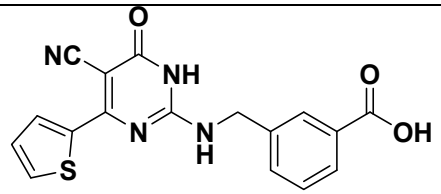
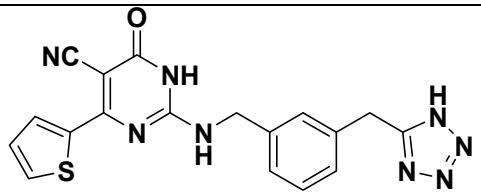
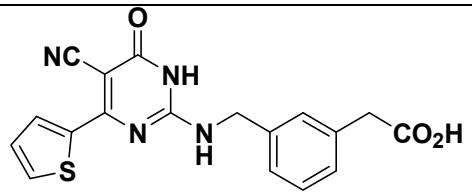
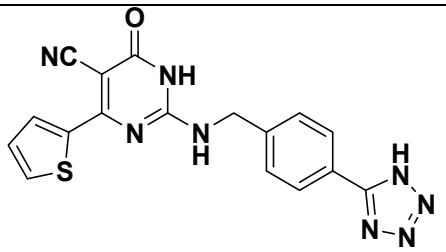
Cpd No.	Structure
I-18	 ,
I-21	 ,
I-22	 ,
I-24	 ,
I-25	 ,
I-30	 ,
I-32	 ,

Cpd No.	Structure
I-33	 ,
I-34	 , and
I-35	 ,

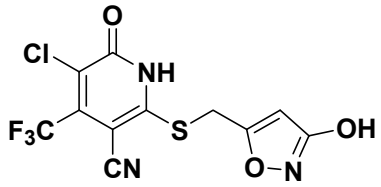
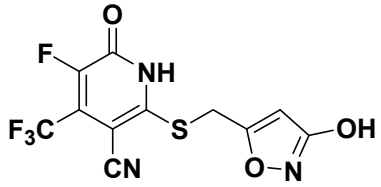
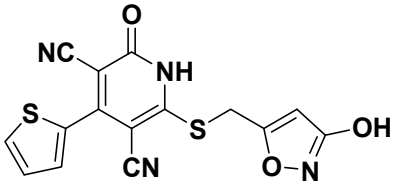
38. A compound, or a pharmaceutically acceptable salt or tautomer thereof, selected from the group consisting of:

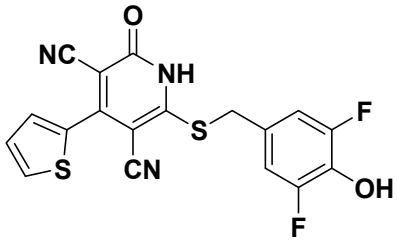
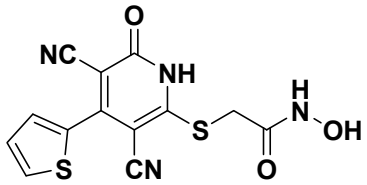
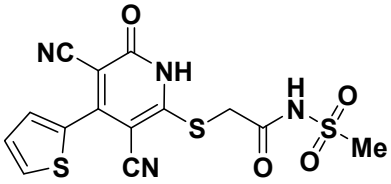
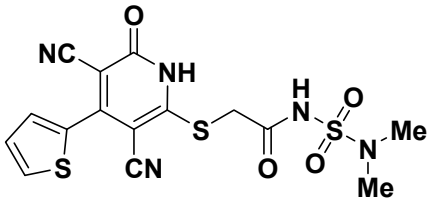
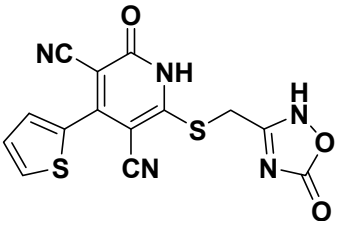
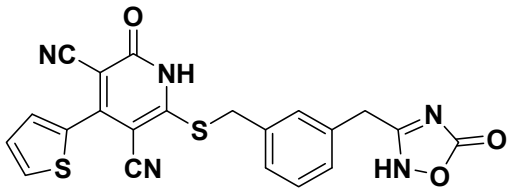
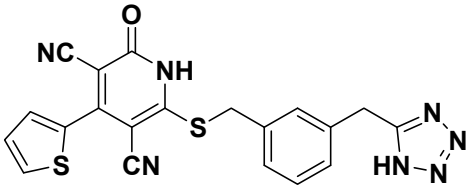
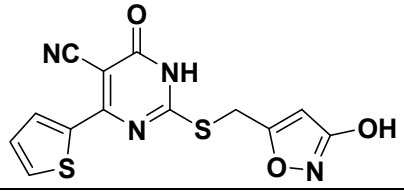
I-37	 ,
I-39	 ,

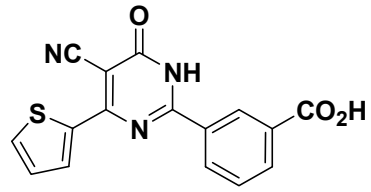
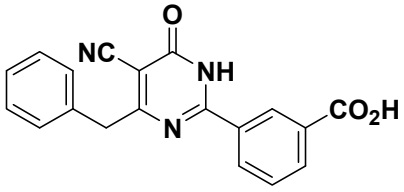
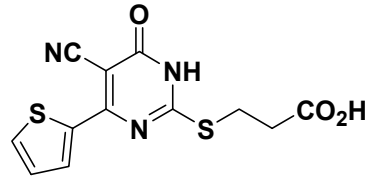
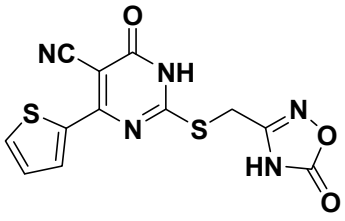
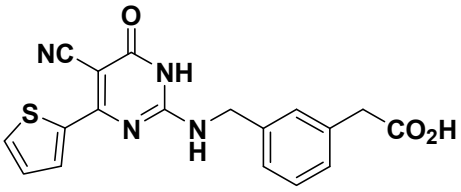
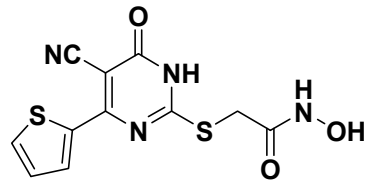
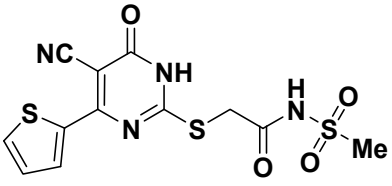
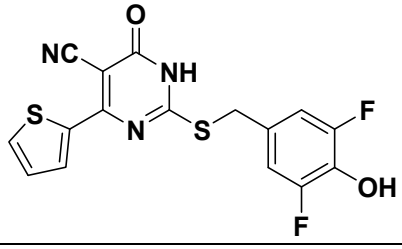
I-41	 ,
I-42	 ,
I-43	 ,
I-44	 ,
I-45	 ,
I-46	 ,
I-47	 ,

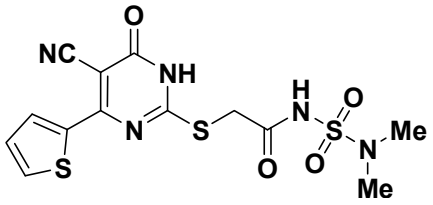
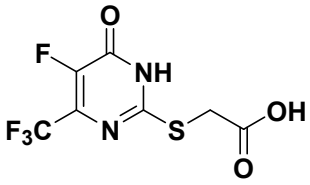
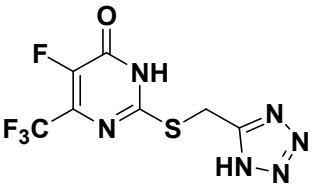
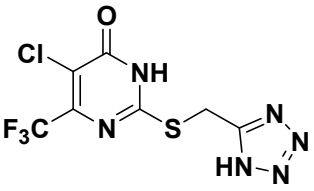
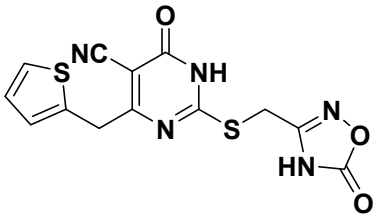
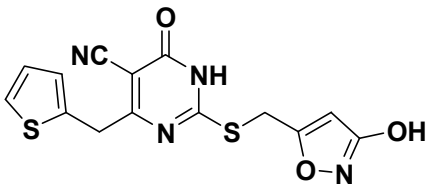
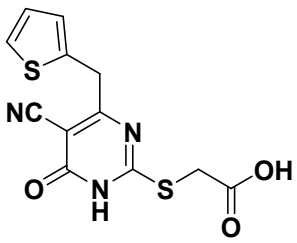
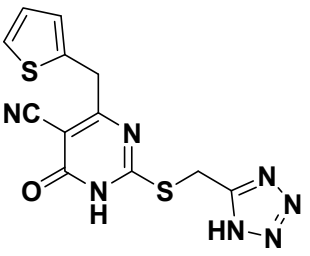
I-48		,
I-49		,
I-50		, and
I-51		.

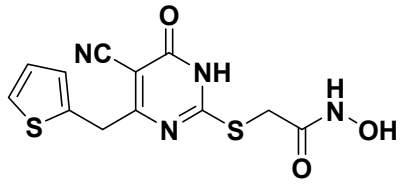
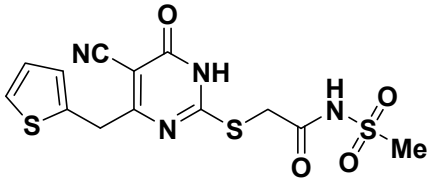
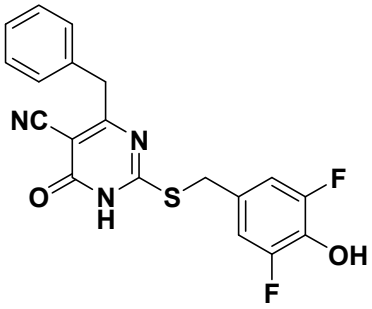
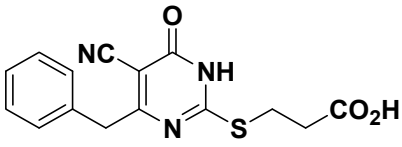
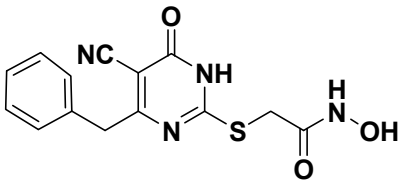
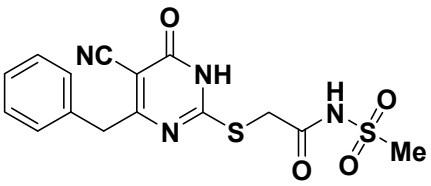
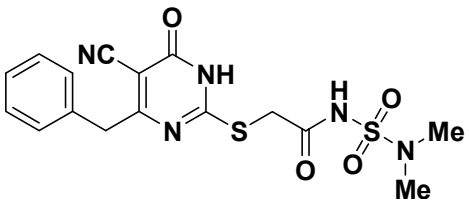
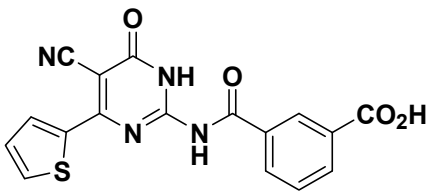
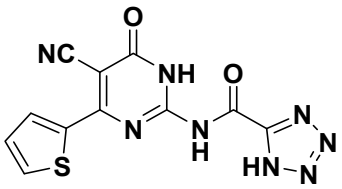
39. A compound, or a pharmaceutically acceptable salt or tautomer thereof, selected from the group consisting of:

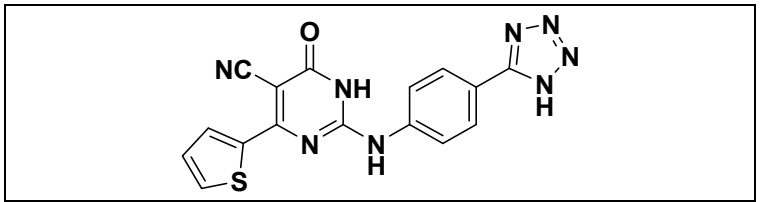
	,
	,
	,

 ,
 ,
 ,
 ,
 ,
 ,
 ,
 ,

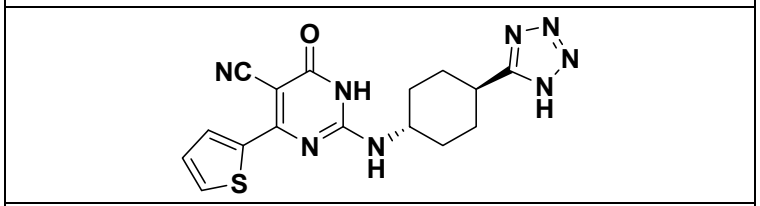
	,
	,
	,
	,
	,
	,
	,
	,

 ,
 ,
 ,
 ,
 ,
 ,
 ,
 ,

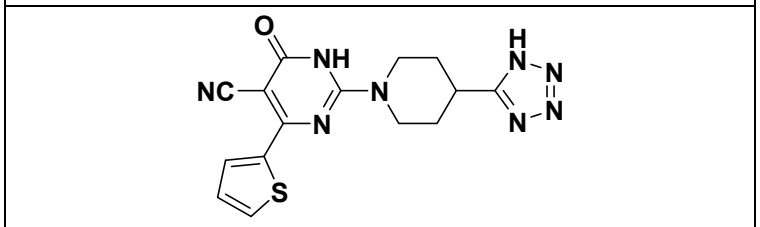
 ,
 ,
 ,
 ,
 ,
 ,
 ,
 ,
 ,



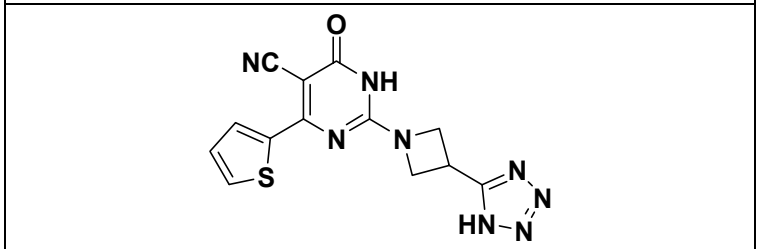
,



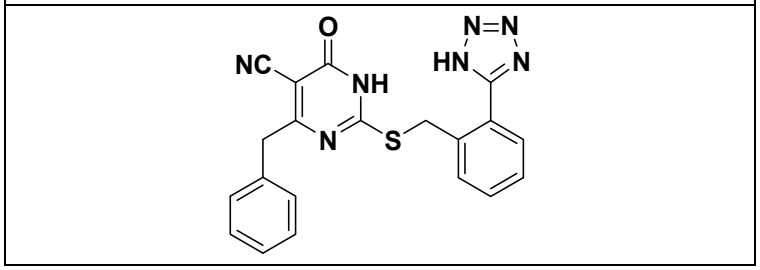
,



,



, and



.

40. A pharmaceutical composition comprising a compound of any one of claims 1-39, or a pharmaceutically acceptable salt thereof, and at least one of a pharmaceutically acceptable carrier, diluent, or excipient.

41. The pharmaceutical composition according to claim 40, which comprises one or more further therapeutic agents.

42. A compound of any of claims 1-39, or a pharmaceutically acceptable salt thereof, for use as a medicament.

43. A compound of any of claims 1-39, or a pharmaceutically acceptable salt thereof, for use in treating, preventing, or reducing the risk of a disease or disorder associated with reduced nicotinamide adenine dinucleotide (NAD^+) levels, wherein the disease is chronic liver disease selected from primary biliary cirrhosis (PBC), cerebrotendinous

xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune hepatitis, chronic viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome, Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, and alpha 1-antitrypsin deficiency.

44. A compound of any of claims 1-39, or a pharmaceutically acceptable salt thereof, for use in for treating, preventing, or reducing the risk of a disorder associated with mitochondrial dysfunction, wherein said disorder associated with mitochondrial dysfunction is an inherited mitochondrial disease, a common metabolic disorder, a neurodegenerative disease, an aging related disorder, a kidney disorder, or a chronic inflammatory disease.

45. Use of a compound of any of claims 1-39, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, preventing, or reducing the risk of a disease or disorder by inhibition of α-amino-β-carboxymuconate-ε-semialdehyde decarboxylase (ACMSD) dysfunction, wherein the disease is chronic liver disease selected from primary biliary cirrhosis (PBC), cerebrotendinous xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune hepatitis, chronic viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome, Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, and alpha 1-antitrypsin deficiency.

46. Use of a compound of any of claims 1-39, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, preventing, or reducing the risk of a disease or disorder associated with reduced nicotinamide adenine dinucleotide (NAD^+) levels, wherein the disease is chronic liver disease selected from primary biliary cirrhosis (PBC), cerebrotendinous xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune

hepatitis, chronic viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome, Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, and alpha 1-antitrypsin deficiency.

47. Use of a compound of any of claims 1-39, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, preventing, or reducing the risk of a disorder associated with mitochondrial dysfunction, wherein said disorder associated with mitochondrial dysfunction is an inherited mitochondrial disease, a common metabolic disorder, a neurodegenerative disease, an aging related disorder, a kidney disorder, or a chronic inflammatory disease.

48. A pharmaceutical composition of claim 40 for use as a medicament.

49. A pharmaceutical composition of claim 40 for use in treating, preventing, or reducing the risk of a disease or disorder associated with reduced nicotinamide adenine dinucleotide (NAD^+) levels, wherein the disease is chronic liver disease selected from primary biliary cirrhosis (PBC), cerebrotendinous xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune hepatitis, chronic viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome, Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, and alpha 1-antitrypsin deficiency.

50. A pharmaceutical composition of claim 40 for use in for treating, preventing, or reducing the risk of a disorder associated with mitochondrial dysfunction, wherein said disorder associated with mitochondrial dysfunction is an inherited mitochondrial disease, a common metabolic disorder, a neurodegenerative disease, an aging related disorder, a kidney disorder, or a chronic inflammatory disease.

51. Use of pharmaceutical composition of claim 40 in the manufacture of a medicament for treating, preventing, or reducing the risk of a disease or disorder by

inhibition of α-amino-β-carboxymuconate-ε-semialdehyde decarboxylase (ACMSD), wherein the disease is chronic liver disease selected from primary biliary cirrhosis (PBC), cerebrotendinous xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune hepatitis, chronic viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome, Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, and alpha 1-antitrypsin deficiency.

52. Use of pharmaceutical composition of claim 40 in the manufacture of a medicament for treating, preventing, or reducing the risk of a disease or disorder associated with reduced nicotinamide adenine dinucleotide (NAD^+) levels, wherein the disease is chronic liver disease selected from primary biliary cirrhosis (PBC), cerebrotendinous xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune hepatitis, chronic viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome, Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, and alpha 1-antitrypsin deficiency.

53. Use of pharmaceutical composition of claim 40 in the manufacture of a medicament for treating, preventing, or reducing the risk of a disorder associated with mitochondrial dysfunction, wherein said disorder associated with mitochondrial dysfunction is an inherited mitochondrial disease, a common metabolic disorder, a neurodegenerative disease, an aging related disorder, a kidney disorder, or a chronic inflammatory disease.

54. The use of any one of claims 45-46 or 51-52, wherein the disease is chronic liver disease selected from primary biliary cirrhosis (PBC), cerebrotendinous xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune hepatitis, chronic viral hepatitis,

alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome, Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, and alpha 1-antitrypsin deficiency.

55. The compound for use of claim 44 or 47, or the use of claim 50 or 53, wherein the common metabolic disorder is obesity or type II diabetes.