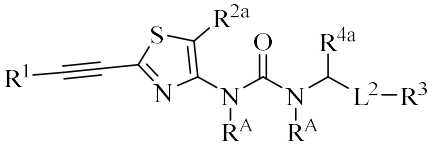
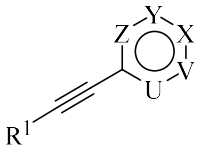
Claims

1. A compound of Formula (XLII) or (I):



(XLII)

or



(I)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; wherein:

each R^A in Formula (XLII) is independently hydrogen or $C_{1\text{-}6}$ alkyl;

R^{4a} in Formula (XLII) is $C_{1\text{-}6}$ alkyl or $–C(O)NR^{1b}R^{1c}$;

U, V, X, and Z are each independently $–C(R^{2a})=$, –N=, $–N(R^{2b})–$, –O–, –S–, or $–A–L^1–L^2–R^3$; with the proviso that at least one of U and Z is –N=, and one of U, V, X, and Z is $–A–L^1–L^2–R^3$;

Y is a bond, $–C(R^{2a})=$, or –N=;

A is $–C(O)–$, $–C(O)NR^{1a}–$, $–OC(O)NR^{1a}–$, $–NR^{1a}C(O)NR^{1d}–$, $–S(O)–$, $–S(O)_2–$, $–S(O)NR^{1a}–$, or $–S(O)_2NR^{1a}–$;

L^1 is a bond, $C_{1\text{-}6}$ alkylene, $C_{2\text{-}6}$ alkenylene, $C_{2\text{-}6}$ alkynylene, $C_{3\text{-}10}$ cycloalkylene, $C_{6\text{-}14}$ arylene, heteroarylene, or heterocyclylene;

L^2 is $C_{6\text{-}14}$ arylene, heteroarylene, or heterocyclylene;

R^1 is hydrogen, deuterium, $C_{1\text{-}6}$ alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, $C_{3\text{-}10}$ cycloalkyl, $C_{6\text{-}14}$ aryl, $C_{7\text{-}15}$ aralkyl, heteroaryl, or heterocyclyl;

R^3 is (i) hydrogen, deuterium, cyano, halo, or nitro; (ii) $C_{1\text{-}6}$ alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, $C_{3\text{-}10}$ cycloalkyl, $C_{6\text{-}14}$ aryl, $C_{7\text{-}15}$ aralkyl, heteroaryl, or heterocyclyl; or (iii) $–C(O)R^{1a}$, $–C(O)OR^{1a}$, $–C(O)NR^{1b}R^{1c}$, $–C(NR^{1a})NR^{1b}R^{1c}$, $–OR^{1a}$, $–OC(O)R^{1a}$, $–OC(O)OR^{1a}$, $–OC(O)NR^{1b}R^{1c}$, $–OC(NR^{1a})NR^{1b}R^{1c}$, $–OS(O)R^{1a}$, $–OS(O)_2R^{1a}$, $–OS(O)NR^{1b}R^{1c}$, $–OS(O)_2NR^{1b}R^{1c}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}C(O)OR^{1d}$, $–NR^{1a}C(O)NR^{1b}R^{1c}$,

$–NR^{1a}C(NR^{1d})NR^{1b}R^{1c}$, $–NR^{1a}S(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–NR^{1a}S(O)NR^{1b}R^{1c}$, $–NR^{1a}S(O)_2NR^{1b}R^{1c}$, $–SR^{1a}$, $–S(O)R^{1a}$, $–S(O)_2R^{1a}$, $–S(O)NR^{1b}R^{1c}$, or $–S(O)_2NR^{1b}R^{1c}$;

each R^{2a} is independently (i) hydrogen, deuterium, cyano, halo, or nitro; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl; or (iii) $–C(O)R^{1a}$, $–C(O)OR^{1a}$, $–C(O)NR^{1b}R^{1c}$, $–C(NR^{1a})NR^{1b}R^{1c}$, $–OR^{1a}$, $–OC(O)R^{1a}$, $–OC(O)OR^{1a}$, $–OC(O)NR^{1b}R^{1c}$, $–OC(NR^{1a})NR^{1b}R^{1c}$, $–OS(O)R^{1a}$, $–OS(O)_2R^{1a}$, $–OS(O)NR^{1b}R^{1c}$, $–OS(O)_2NR^{1b}R^{1c}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}C(O)OR^{1d}$, $–NR^{1a}C(O)NR^{1b}R^{1c}$, $–NR^{1a}C(NR^{1d})NR^{1b}R^{1c}$, $–NR^{1a}S(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–NR^{1a}S(O)NR^{1b}R^{1c}$, $–NR^{1a}S(O)_2NR^{1b}R^{1c}$, $–SR^{1a}$, $–S(O)R^{1a}$, $–S(O)_2R^{1a}$, $–S(O)NR^{1b}R^{1c}$, or $–S(O)_2NR^{1b}R^{1c}$;

each R^{2b} is independently (i) hydrogen, deuterium, cyano, halo, or nitro; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl; or (iii) $–C(O)R^{1a}$, $–C(O)OR^{1a}$, $–C(O)NR^{1b}R^{1c}$, $–C(NR^{1a})NR^{1b}R^{1c}$, $–OR^{1a}$, $–OC(O)R^{1a}$, $–OC(O)OR^{1a}$, $–OC(O)NR^{1b}R^{1c}$, $–OC(NR^{1a})NR^{1b}R^{1c}$, $–OS(O)R^{1a}$, $–OS(O)_2R^{1a}$, $–OS(O)NR^{1b}R^{1c}$, $–OS(O)_2NR^{1b}R^{1c}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}C(O)OR^{1d}$, $–NR^{1a}C(O)NR^{1b}R^{1c}$, $–NR^{1a}C(NR^{1d})NR^{1b}R^{1c}$, $–NR^{1a}S(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–NR^{1a}S(O)NR^{1b}R^{1c}$, $–NR^{1a}S(O)_2NR^{1b}R^{1c}$, $–S(O)R^{1a}$, $–S(O)_2R^{1a}$, $–S(O)NR^{1b}R^{1c}$, or $–S(O)_2NR^{1b}R^{1c}$; and

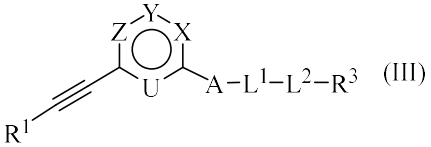
each R^{1a}, R^{1b}, R^{1c}, and R^{1d} is independently hydrogen, deuterium, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl;

wherein each alkyl, alkylene, alkenyl, alkenylene, alkynyl, alkynylene, cycloalkyl, cycloalkylene, aryl, arylene, aralkyl, heteroaryl, heteroarylene, heterocyclyl, and heterocyclylene is optionally substituted with one or more substituents Q, wherein each Q is independently selected from: (a) deuterium, cyano, halo, nitro, and oxo; (b) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, and heterocyclyl, each of which is further optionally substituted with one or more substituents Q^a; and (c) $–C(O)R^a$, $–C(O)OR^a$, $–C(O)NR^bR^c$, $–C(O)SR^a$, $–C(NR^a)NR^bR^c$, $–C(S)R^a$, $–C(S)OR^a$, $–C(S)NR^bR^c$, $–OR^a$, $–OC(O)R^a$, $–OC(O)OR^a$, $–OC(O)NR^bR^c$, $–OC(O)SR^a$, $–OC(NR^a)NR^bR^c$, $–OC(S)R^a$, $–OC(S)OR^a$, $–OC(S)NR^bR^c$, $–OS(O)R^a$, $–OS(O)_2R^a$, $–OS(O)NR^bR^c$, $–OS(O)_2NR^bR^c$, $–NR^bR^c$, $–NR^aC(O)R^d$, $–NR^aC(O)OR^d$, $–NR^aC(O)NR^bR^c$, $–NR^aC(O)SR^d$, $–NR^aC(NR^d)NR^bR^c$, $–NR^aC(S)R^d$, $–NR^aC(S)OR^d$, $–NR^aC(S)NR^bR^c$, $–NR^aS(O)R^d$, $–NR^aS(O)_2R^d$, $–NR^aS(O)NR^bR^c$,

–$NR^aS(O)_2NR^bR^c$, –SR^a, –$S(O)R^a$, –$S(O)_2R^a$, –$S(O)NR^bR^c$, and –$S(O)_2NR^bR^c$, wherein each R^a, R^b, R^c, and R^d is independently (i) hydrogen or deuterium; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl, each of which is optionally substituted with one or more substituents Q^a; or (iii) R^b and R^c together with the N atom to which they are attached form heterocyclyl optionally substituted with one or more substituents Q^a;

wherein each Q^a is independently selected from: (a) deuterium, cyano, halo, nitro, and oxo; (b) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, and heterocyclyl; and (c) –$C(O)R^e$, –$C(O)OR^e$, –$C(O)NR^fR^g$, –$C(O)SR^e$, –$C(NR^e)NR^fR^g$, –$C(S)R^e$, –$C(S)OR^e$, –$C(S)NR^fR^g$, –OR^e, –$OC(O)R^e$, –$OC(O)OR^e$, –$OC(O)NR^fR^g$, –$OC(O)SR^e$, –$OC(NR^e)NR^fR^g$, –$OC(S)R^e$, –$OC(S)OR^e$, –$OC(S)NR^fR^g$, –$OS(O)R^e$, –$OS(O)_2R^e$, –$OS(O)NR^fR^g$, –$OS(O)_2NR^fR^g$, –NR^fR^g, –$NR^eC(O)R^h$, –$NR^eC(O)OR^f$, –$NR^eC(O)NR^fR^g$, –$NR^eC(O)SR^f$, –$NR^eC(NR^h)NR^fR^g$, –$NR^eC(S)R^h$, –$NR^eC(S)OR^f$, –$NR^eC(S)NR^fR^g$, –$NR^eS(O)R^h$, –$NR^eS(O)_2R^h$, –$NR^eS(O)NR^fR^g$, –$NR^eS(O)_2NR^fR^g$, –SR^e, –$S(O)R^e$, –$S(O)_2R^e$, –$S(O)NR^fR^g$, and –$S(O)_2NR^fR^g$; wherein each R^e, R^f, R^g, and R^h is independently (i) hydrogen or deuterium; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl; or (iii) R^f and R^g together with the N atom to which they are attached form heterocyclyl.

2. The compound of claim 1, wherein the compound is a compound of Formula (III):



(III)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof.

3. The compound of claim 1 or 2,

wherein U is –N=, –S–, –O–, –N(H)–, or –$N(CH_3)$–; and/or

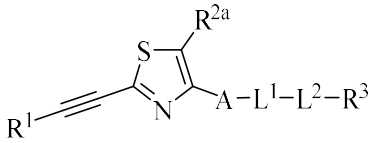
wherein X is –N=, –C(H)=, –$C(CH_3)$=, –C(phenyl)=, –S–, –O–, –N(H)–, or –$N(CH_3)$–; and/or

wherein Y is a bond, –C(H)=, or –N=; and/or

wherein Z is –N=, –S–, –O–, –N(H)–, or –N(CH_3)–.

4. The compound of claim 1 or 2,

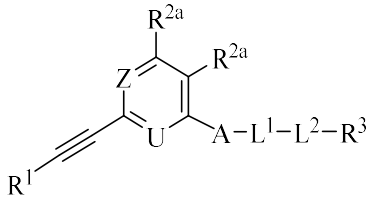
wherein the compound is a compound of Formula (IX):



(IX)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

wherein the compound is a compound of Formula (XII):



(XII)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; wherein U is –N= and Z is –C(R^{2a})= or –N=; or U is –C(R^{2a})= and Z is –N=.

5. The compound of claim 4, wherein U is –N= or –C(H)=; and/or wherein Z is –N= or –C(H)=.

6. The compound of any one of claims 1 to 5,

wherein L^1 is a bond; or C_{1-6} alkylene, C_{2-6} alkenylene, C_{3-10} cycloalkylene, or heterocyclylene, each of which is optionally substituted with one, two, or three substituents Q; or wherein L^1 is a bond; or wherein L^1 is C_{1-6} alkylene, optionally substituted with one, two, or three substituents Q; or wherein L^1 is methanediyl or ethanediyl, each of which is optionally substituted with amino, hydroxymethyl, or hydroxyl; or wherein L^1 is C_{2-6} alkenylene, optionally substituted with one, two, or three substituents Q; or wherein L^1 is ethenediyl; or wherein L^1 is C_{3-10} cycloalkylene, optionally substituted with one, two, or three substituents Q; or wherein L^1

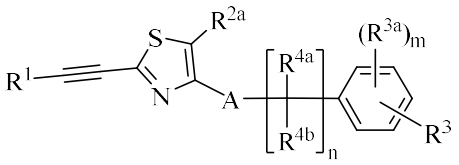
is cyclopropanediyl; or wherein L^1 is heterocyclylene, optionally substituted with one, two, or three substituents Q; or wherein L^1 is monocyclic heterocyclylene, optionally substituted with one, two, or three substituents Q; or wherein L^1 is 3 to 7 membered heterocyclylene, each optionally substituted with one, two, or three substituents Q; or wherein L^1 is azetidindiyl, pyrrolidindiyl, piperidindiyl, or piperazindiyl, each of which is optionally substituted with fluoro, hydroxymethyl, hydroxyl, or amino; or wherein L^1 is a bond, methanediyl, ethane-1,1-diyl, 2-hydroxyethane-1,1-diyl, ethane-1,2-diyl, 1-hydroxyethane-1,2-diyl, 1-aminoethane-1,2-diyl, ethene-1,2-diyl, cyclopropan-1,1-diyl, azetidin-1,3-diyl, pyrrolidin-1,2-diyl, piperidin-1,4-diyl, 4-fluropiperidin-1,4-diyl, 4-hydroxypiperidin-1,4-diyl, piperazin-1,4-diyl, or 2-hydroxymethylpiperazin-1,4-diyl; and/or

wherein L^2 is C_{6-14} arylene, optionally substituted with one, two, or three substituents Q; or wherein L^2 is monocyclic or bicyclic C_{6-14} arylene, each optionally substituted with one, two, or three substituents Q; or wherein L^2 is phendiyl, 2,3-dihydroindendiyl, or naphthdiyl, each optionally substituted with one, two, or three substituents Q; or wherein L^2 is phen-1,2-diyl, phen-1,3-diyl, phen-1,4-diyl, 2,3-dihydroinden-1,4-diyl, 2,3-dihydroinden-2,5-diyl, naphth-1,5-diyl, or naphth-2,6-diyl, each of which is optionally substituted with one or two substituents, where each substituent is independently cyano, fluoro, chloro, hydroxyl, or methoxy; or wherein L^2 is heteroarylene, optionally substituted with one, two, or three substituents Q; or wherein L^2 is monocyclic or bicyclic heteroarylene, each optionally substituted with one, two, or three substituents Q; or wherein L^2 is indoldiyl, indazoldiyl, benzothiazoldiyl, quinoldiyl, or quinoldiyl, each optionally substituted with one, two, or three substituents Q; or wherein L^2 is indol-2,5-diyl, indazol-3,7-diyl, benzothiazol-2,6-diyl, quinol-2,6-diyl, or quinol-3,7-diyl, each of which is optionally substituted with one or two substituents, where each substituent is independently cyano, fluoro, chloro, hydroxyl, or methoxy; or wherein L^2 is heterocyclylene, optionally substituted with one, two, or three substituents Q; or wherein L^2 is monocyclic or bicyclic heterocyclylene, each optionally substituted with one, two, or three substituents Q; or wherein L^2 is piperidindiyl, isoindolindiyl, 1,2,3,4-tetrahydroisoquinolindiyl, benzo[*d*][1,3]dioxoldiyl, or 2,3-dihydrobenzo[*b*][1,4]-dioxindiyl, each optionally substituted with one, two, or three substituents Q; or wherein L^2 is piperidin-1,2-diyl, piperidin-1,3-diyl, piperidin-1,4-diyl, isoindolin-2,5-diyl, 1,2,3,4-tetrahydroisoquinolin-2,6-diyl, benzo[*d*][1,3]dioxol-2,5-diyl, or 2,3-dihydrobenzo[*b*][1,4]dioxin-2,6-diyl, each of which is

optionally substituted with one or two substituents, where each substituent is independently cyano, fluoro, chloro, hydroxyl, or methoxy; or wherein L^2 is phen-1,2-diyl, phen-1,3-diyl, phen-1,4-diyl, 4-methoxyphen-1,3-diyl, 2-cyanophen-1,4-diyl, 2-fluorophen-1,4-diyl, 2-chlorophen-1,4-diyl, 2-hydroxyphen-1,4-diyl, 2,3-dihydroinden-1,4-diyl, 2,3-dihydroinden-2,5-diyl, naphth-1,5-diyl, naphth-2,6-diyl, pyrazol-1,3-diyl, pyrazol-1,4-diyl, pyridin-2,3-diyl, pyridin-2,5-diyl, indol-2,5-diyl, indazol-3,7-diyl, benzothiazol-2,6-diyl, quinol-2,6-diyl, quinol-3,7-diyl, piperidin-1,2-diyl, piperidin-1,3-diyl, piperidin-1,4-diyl, isoindolin-2,5-diyl, 1,2,3,4-tetrahydroisoquinolin-2,6-diyl, benzo[*d*][1,3]-dioxol-2,5-diyl, or 2,3-dihydrobenzo[*b*][1,4]-dioxin-2,6-diyl.

7. The compound of claim 1 or 4,

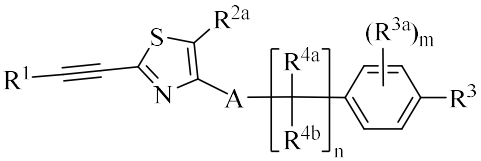
wherein the compound is a compound of Formula (XIII):



(XIII)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

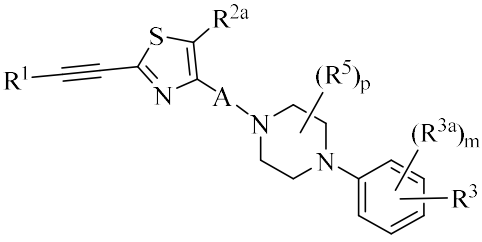
wherein the compound is a compound of Formula (XIV):



(XIV)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

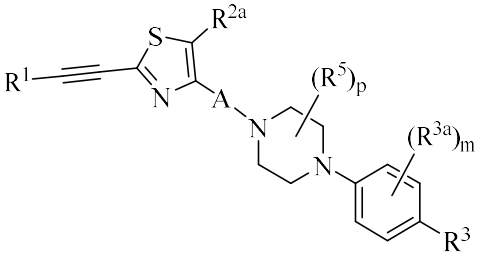
wherein the compound is a compound of Formula (XXI):



(XXI)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

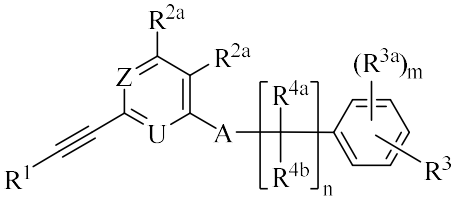
wherein the compound is a compound of Formula (XXII):



(XXII)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof;

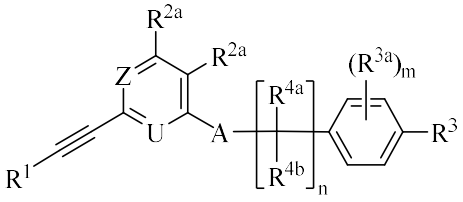
wherein the compound is a compound of Formula (XXVII):



(XXVII)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

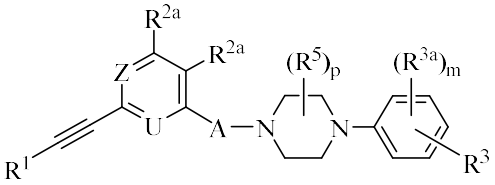
wherein the compound is a compound of Formula (XXVIII):



(XXVIII)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

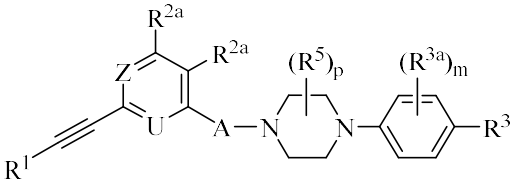
wherein the compound is a compound of Formula (XXXV):



(XXXV)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

wherein the compound is a compound of Formula (XXXVI):



(XXXVI)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof;

wherein:

each R^5 is independently (i) deuterium, cyano, halo, or nitro; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl; or (iii) $–C(O)R^{1a}$, $–C(O)OR^{1a}$, $–C(O)NR^{1b}R^{1c}$, $–C(NR^{1a})NR^{1b}R^{1c}$, $–OR^{1a}$, $–OC(O)R^{1a}$, $–OC(O)OR^{1a}$, $–OC(O)NR^{1b}R^{1c}$, $–OC(NR^{1a})NR^{1b}R^{1c}$, $–OS(O)R^{1a}$, $–OS(O)_2R^{1a}$, $–OS(O)NR^{1b}R^{1c}$, $–OS(O)_2NR^{1b}R^{1c}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}C(O)OR^{1d}$, $–NR^{1a}C(O)NR^{1b}R^{1c}$, $–NR^{1a}C(NR^{1d})NR^{1b}R^{1c}$, $–NR^{1a}S(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–NR^{1a}S(O)NR^{1b}R^{1c}$, $–NR^{1a}S(O)_2NR^{1b}R^{1c}$, $–SR^{1a}$, $–S(O)R^{1a}$, $–S(O)_2R^{1a}$, $–S(O)NR^{1b}R^{1c}$, or $–S(O)_2NR^{1b}R^{1c}$;

each R^{3a} is independently (i) deuterium, cyano, halo, or nitro; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl; or (iii) $–C(O)R^{1a}$, $–C(O)OR^{1a}$, $–C(O)NR^{1b}R^{1c}$, $–C(NR^{1a})NR^{1b}R^{1c}$, $–OR^{1a}$, $–OC(O)R^{1a}$, $–OC(O)OR^{1a}$, $–OC(O)NR^{1b}R^{1c}$, $–OC(NR^{1a})NR^{1b}R^{1c}$, $–OS(O)R^{1a}$, $–OS(O)_2R^{1a}$, $–OS(O)NR^{1b}R^{1c}$, $–OS(O)_2NR^{1b}R^{1c}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}C(O)OR^{1d}$, $–NR^{1a}C(O)NR^{1b}R^{1c}$, $–NR^{1a}C(NR^{1d})NR^{1b}R^{1c}$, $–NR^{1a}S(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–NR^{1a}S(O)NR^{1b}R^{1c}$, $–NR^{1a}S(O)_2NR^{1b}R^{1c}$, $–SR^{1a}$, $–S(O)R^{1a}$, $–S(O)_2R^{1a}$, $–S(O)NR^{1b}R^{1c}$, or $–S(O)_2NR^{1b}R^{1c}$;

each R^{4a} and R^{4b} is independently (i) hydrogen, deuterium, cyano, halo, or nitro; (b) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or

heterocyclyl; or (iii) $–C(O)R^{1a}$, $–C(O)OR^{1a}$, $–C(O)NR^{1b}R^{1c}$, $–C(NR^{1a})NR^{1b}R^{1c}$, $–OR^{1a}$, $–OC(O)R^{1a}$, $–OC(O)OR^{1a}$, $–OC(O)NR^{1b}R^{1c}$, $–OC(NR^{1a})NR^{1b}R^{1c}$, $–OS(O)R^{1a}$, $–OS(O)_2R^{1a}$, $–OS(O)NR^{1b}R^{1c}$, $–OS(O)_2NR^{1b}R^{1c}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}C(O)OR^{1d}$, $–NR^{1a}C(O)NR^{1b}R^{1c}$, $–NR^{1a}C(NR^{1d})NR^{1b}R^{1c}$, $–NR^{1a}S(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–NR^{1a}S(O)NR^{1b}R^{1c}$, $–NR^{1a}S(O)_2NR^{1b}R^{1c}$, $–SR^{1a}$, $–S(O)R^{1a}$, $–S(O)_2R^{1a}$, $–S(O)NR^{1b}R^{1c}$, or $–S(O)_2NR^{1b}R^{1c}$; or R^{4a} and R^{4b} together with the carbon atom to which they are attached form $C_{3\text{-}10}$ cycloalkyl;

m is an integer of 0, 1, 2, 3, or 4;

n is an integer of 0, 1, 2, 3, 4, 5, or 6; and

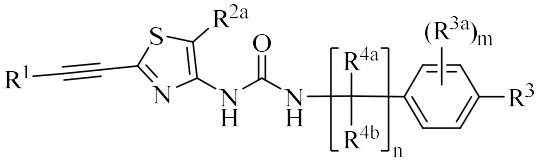
p is an integer of 0, 1, 2, 3, or 4;

wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, and heterocyclyl is optionally substituted with one or more substituents Q.

8. The compound of any one of claims 1 to 7, wherein A is $–C(O)–$, $–C(O)NR^{1a}–$, or $–NR^{1a}C(O)NR^{1d}–$; or wherein A is $–C(O)–$, $–C(O)NH–$, or $–C(O)N(CH_3)–$, or $–NHC(O)NNH–$.

9. The compound of claim 7,

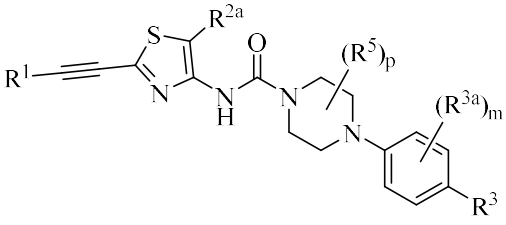
wherein the compound is a compound of Formula (XVI):



(XVI)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

wherein the compound is a compound of Formula (XXIV):



(XXIV)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or

a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof.

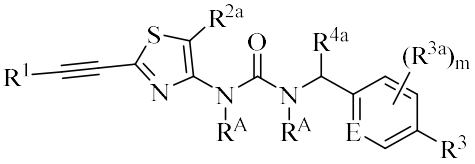
10. The compound of any one of claims 7 to 9,

wherein each R^{4a} and R^{4b} is independently hydrogen, C_{1-6} alkyl, or $–NR^{1b}R^{1c}$; or wherein each R^{4a} and R^{4b} is independently hydrogen, methyl, or amino; or wherein R^{4a} and R^{4b} together with the carbon atom to which they are attached form C_{3-10} cycloalkylene, optionally substituted with one, two, or three substituents Q; or wherein R^{4a} and R^{4b} together with the carbon atom to which they are attached form cyclopropanediyl, optionally substituted with one, two, or three substituents Q; and/or

wherein n is an integer of 1, 2, or 3.

11. The compound of claim 1,

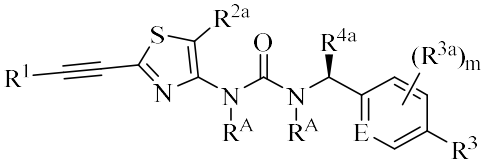
wherein the compound is a compound of Formula (XLIII):



(XLIII)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

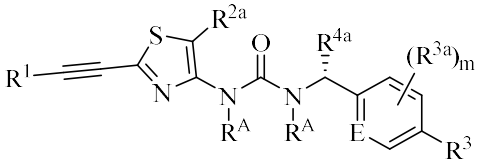
wherein the compound is a compound of Formula (XLIV):



(XLIV)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; or

wherein the compound is a compound of Formula (XLV):



(XLV)

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more

diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof;
wherein:

each E is independently –C(H)= or –N=;

each R^{3a} is independently (i) deuterium, cyano, halo, or nitro; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl, each optionally substituted with one or more substituents Q; or (iii) $–C(O)R^{1a}$, $–C(O)OR^{1a}$, $–C(O)NR^{1b}R^{1c}$, $–C(NR^{1a})NR^{1b}R^{1c}$, $–OR^{1a}$, $–OC(O)R^{1a}$, $–OC(O)OR^{1a}$, $–OC(O)NR^{1b}R^{1c}$, $–OC(NR^{1a})NR^{1b}R^{1c}$, $–OS(O)R^{1a}$, $–OS(O)_2R^{1a}$, $–OS(O)NR^{1b}R^{1c}$, $–OS(O)_2NR^{1b}R^{1c}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}C(O)OR^{1d}$, $–NR^{1a}C(O)NR^{1b}R^{1c}$, $–NR^{1a}C(NR^{1d})NR^{1b}R^{1c}$, $–NR^{1a}S(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–NR^{1a}S(O)NR^{1b}R^{1c}$, $–NR^{1a}S(O)_2NR^{1b}R^{1c}$, $–SR^{1a}$, $–S(O)R^{1a}$, $–S(O)_2R^{1a}$, $–S(O)NR^{1b}R^{1c}$, or $–S(O)_2NR^{1b}R^{1c}$; and

m is an integer of 0, 1, 2, 3, or 4.

12. The compound of claim 11,

wherein R^A is hydrogen; or wherein R^A is C_{1-6} alkyl, optionally substituted with one or more substituents Q; or wherein R^A is methyl; and/or

wherein E is –C(H)=; or wherein E is –N=; and/or

wherein each R^{3a} is independently cyano or halo; or wherein each R^{3a} is independently cyano, fluoro, or chloro; and/or

wherein m is an integer of 0, 1, or 2.

13. The compound of any one of claims 1 to 12,

wherein R^1 is hydrogen, deuterium, or C_{1-6} alkyl, optionally substituted with one or more substituents Q; or wherein R^1 is hydrogen; or wherein R^1 is C_{1-6} alkyl, optionally substituted with one or more substituents Q; or wherein R^1 is methyl or dimethylaminomethyl; and/or

wherein R^3 is (i) hydrogen, deuterium, cyano, halo, or nitro; (ii) C_{1-6} alkyl, C_{6-14} aryl, heteroaryl, or heterocyclyl, each optionally substituted with one or more substituents Q; or (iii) $–C(O)OR^{1a}$, $–OR^{1a}$, $–NR^{1b}R^{1c}$, $–NR^{1a}C(O)R^{1d}$, $–NR^{1a}S(O)_2R^{1d}$, $–S(O)_2R^{1a}$, or $–S(O)_2NR^{1b}R^{1c}$; or wherein R^3 is hydrogen, deuterium, cyano, halo, or nitro; or wherein R^3 is hydrogen, deuterium, cyano, chloro, bromo, or nitro; or wherein R^3 is C_{1-6} alkyl, monocyclic or bicyclic C_{6-14} aryl, monocyclic, bicyclic, or tricyclic heteroaryl, or bicyclic heterocyclyl; each of which is optionally

substituted with one, two, or three substituents Q; or wherein R^3 is C_{1-6} alkyl, optionally substituted with one, two, or three substituents Q; or wherein R^3 is methyl or ethyl; or wherein R^3 is monocyclic or bicyclic C_{6-14} aryl, each optionally substituted with one, two, or three substituents Q; or wherein R^3 is phenyl or 2,3-dihydroindenyl, each of which is optionally substituted with one, two, or three substituents, where each substituent is independently cyano, fluoro, oxo, methyl, cyclopropyl, 1-cyanocyclopropyl, 1-hydroxy-cyclopentyl, cyclopent-1-en-1-yl, azetidin-1-yl, 3-hydroxyazetidin-1-yl, pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, 2-oxoimidazolidin-1-yl, 2-oxooxazolidin-3-yl, methoxycarbonyl, carbamoyl, methylcarbamoyl, hydroxyl, (3-hydroxycyclobutyl)amino, oxetan-3-ylamino, methylsulfonyl, methylsulfamoyl, or dimethylsulfamoyl; or wherein R^3 is phenyl or 2,3-dihydroinden-4-yl, each of which is optionally substituted with one, two, or three substituents, where each substituent is independently cyano, fluoro, oxo, methyl, cyclopropyl, 1-cyanocyclopropyl, 1-hydroxycyclopentyl, cyclopent-1-en-1-yl, azetidin-1-yl, 3-hydroxyazetidin-1-yl, pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, 2-oxoimidazolidin-1-yl, 2-oxooxazolidin-3-yl, methoxycarbonyl, carbamoyl, methylcarbamoyl, hydroxyl, (3-hydroxycyclobutyl)amino, oxetan-3-ylamino, methylsulfonyl, methylsulfamoyl, or dimethylsulfamoyl; or wherein R^3 is monocyclic, bicyclic, or tricyclic heteroaryl, each optionally substituted with one, two, or three substituents Q; or wherein R^3 is pyrazolyl, thiazolyl, pyridinyl, benzo[*b*]thiophenyl, benzo[*d*][1,2,3]thiadiazolyl, benzo[*d*]thiazolyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,5-*a*]pyridinyl, indolyl, indazolyl, thiazolo[4,5-*c*]pyridinyl, [1,2,3]triazolo[1,5-*a*]-pyridinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, isoquinolinyl, quinolinyl, quinazolinyl, quinoxalinyl, or 7,8-dihydro-6*H*-thiazolo[5,4-*e*]isoindolyl, each of which is optionally substituted with one, two, or three substituents, where each substituent is independently cyano, fluoro, oxo, methyl, 3-hydroxyazetidin-1-yl, pyrrolidin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 2-oxooxazolidin-3-yl, methoxycarbonyl, carbamoyl, methylcarbamoyl, hydroxyl, (3-hydroxycyclobutyl)amino, oxetan-3-ylamino, methylsulfonyl, methylsulfamoyl, or dimethylsulfamoyl; or wherein R^3 is pyrazol-3-yl, pyrazol-4-yl, thiazol-4-yl, thiazol-5-yl, pyridin-3-yl, benzo[*b*]thiophen-7-yl, benzo[*d*][1,2,3]thiadiazol-7-yl, benzo[*d*]thiazol-4-yl, benzo[*d*]thiazol-5-yl, benzo[*d*]thiazol-6-yl, benzo[*d*]thiazol-7-yl, imidazo[1,2-*a*]pyridin-5-yl, imidazo[1,2-*a*]pyridin-8-yl, imidazo[1,5-*a*]pyridin-5-yl, imidazo[1,5-*a*]pyridin-8-yl, indol-4-yl, indazol-4-yl, thiazolo[4,5-*c*]pyridin-7-yl, [1,2,3]triazolo[1,5-*a*]pyridin-4-yl, [1,2,4]triazolo[1,5-

a]pyridin-5-yl, [1,2,4]triazolo[1,5-*a*]-pyridin-8-yl, [1,2,4]triazolo[4,3-*a*]pyridin-5-yl, [1,2,4]triazolo[4,3-*a*]pyridin-8-yl, isoquinolin-5-yl, isoquinolin-8-yl, quinolin-5-yl, quinazolin-5-yl, or quinoxalin-5-yl, or 7,8-dihydro-6*H*-thiazolo[5,4-*e*]isoindol-5-yl, each of which is optionally substituted with one, two, or three substituents, where each substituent is independently cyano, fluoro, oxo, methyl, 3-hydroxy-azetidin-1-yl, pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-oxooxazolidin-3-yl, methoxycarbonyl, carbamoyl, methylcarbamoyl, hydroxyl, (3-hydroxycyclobutyl)amino, oxetan-3-ylamino, methylsulfonyl, methylsulfamoyl, or dimethylsulfamoyl; or wherein R^3 is bicyclic heterocyclyl, optionally substituted with one, two, or three substituents Q; or wherein R^3 is 2,3-dihydrobenzo[*b*]-thiophenyl, isoindolinyl, indolinyl, 2,3-dihydroindazolyl, dihydrobenzo[*b*]thiophenyl, or 3,4-dihydroquinazolinyl, each of which is optionally substituted with one, two, or three substituents, where each substituent is independently cyano, fluoro, oxo, methyl, 3-hydroxyazetidin-1-yl, pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-oxooxazolidin-3-yl, methoxycarbonyl, carbamoyl, methylcarbamoyl, hydroxyl, (3-hydroxycyclobutyl)amino, oxetan-3-ylamino, methylsulfonyl, methylsulfamoyl, or dimethylsulfamoyl; or wherein R^3 is 2,3-dihydrobenzo[*b*]-thiophen-7-yl, isoindolin-4-yl, indolin-4-yl, 2,3-dihydroindazol-4-yl, dihydrobenzo[*b*]thiophen-7-yl, or 3,4-dihydroquinazolin-5-yl, each of which is optionally substituted with one, two, or three substituents, where each substituent is independently cyano, fluoro, oxo, methyl, 3-hydroxyazetidin-1-yl, pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-oxooxazolidin-3-yl, methoxycarbonyl, carbamoyl, methylcarbamoyl, hydroxyl, (3-hydroxycyclobutyl)amino, oxetan-3-ylamino, methylsulfonyl, methylsulfamoyl, or dimethylsulfamoyl; or wherein R^3 is (i) hydrogen, deuterium, cyano, chloro, bromo, or nitro; (ii) methyl, methoxycarbonylmethyl, carbamoyl-methyl, hydroxymethyl, 2-methoxycarbonylethyl, 2-hydroxylethyl, phenyl, 2-cyanophenyl, 3-cyclopropylphenyl, 3-(1-cyanocyclopropyl)phenyl, 3-(1-hydroxycyclopentyl)phenyl, 3-(cyclopent-1-en-1-yl)phenyl, 3-(azetidin-1-yl)phenyl, 3-(pyrrolidin-1-yl)phenyl, 3-(3-hydroxypyrrolidin-1-yl)phenyl, 3-(2-oxopyrrolidin-1-yl)phenyl, 3-(2-oxoimidazolidin-1-yl)phenyl, 3-(2-oxooxazolidin-3-yl)phenyl, 3-(3-hydroxycyclobutyl)-aminophenyl, 3-(oxetan-3-ylamino)phenyl, 3-(3-hydroxyazetidin-1-yl)phenyl, 3-carbamoylphenyl, 2-methylcarbamoyl-phenyl, 3-methylcarbamoylphenyl, 2-methylsulfamoylphenyl, 2-dimethylsulfamoylphenyl, 2-methyl-sulfonylphenyl, 3-oxo-2,3-dihydro-1*H*-inden-4-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-3-yl, 1-methylpyrazol-4-yl, thiazol-4-yl, thiazol-5-yl, pyridin-3-yl, 1,1-dioxidobenzo[*b*]-thiophen-7-yl,

benzo[*d*][1,2,3]thiadiazol-7-yl, benzo[*d*]thiazol-4-yl, benzo[*d*]thiazol-5-yl, benzo[*d*]thiazol-6-yl, benzo[*d*]thiazol-7-yl, 6-fluorobenzo[*d*]thiazol-5-yl, 6-cyanobenzo[*d*]thiazol-7-yl, 6-fluorobenzo[*d*]thiazol-7-yl, 5-methoxycarbonylbenzo[*d*]-thiazol-7-yl, 6-methoxycarbonylbenzo[*d*]thiazol-7-yl, 5-carbamoylbenzo[*d*]thiazol-7-yl, 6-carbamoylbenzo[*d*]thiazol-7-yl, 5-methylcarbamoylbenzo[*d*]thiazol-7-yl, 6-methylcarbamoyl-benzo[*d*]thiazol-7-yl, 2-aminobenzo[*d*]thiazol-7-yl, 2-amino-6-cyanobenzo[*d*]thiazol-7-yl, imidazo[1,2-*a*]pyridin-5-yl, imidazo[1,2-*a*]pyridin-8-yl, imidazo[1,5-*a*]pyridin-5-yl, imidazo[1,5-*a*]pyridin-8-yl, indol-4-yl, 1-methylindol-4-yl, indazol-4-yl, 1-methylindazol-4-yl, 2-methylindazol-4-yl, 1,5-dimethyl-indazol-4-yl, 1-methyl-6-methoxycarbonylindazol-4-yl, 1-methyl-6-carbamoylindazol-4-yl, 1-methyl-6-methylcarbamoylindazol-4-yl, 1-methyl-6-dimethylcarbamoylindazol-4-yl, thiazolo[4,5-*c*]pyridin-7-yl, [1,2,3]triazolo[1,5-*a*]pyridin-4-yl, [1,2,4]triazolo[1,5-*a*]pyridin-5-yl, 2-amino-[1,2,4]triazolo[1,5-*a*]pyridin-5-yl, [1,2,4]triazolo[1,5-*a*]pyridin-8-yl, [1,2,4]triazolo[4,3-*a*]pyridin-5-yl, [1,2,4]triazolo[4,3-*a*]pyridin-8-yl, isoquinolin-5-yl, 1-hydroxyisoquinolin-8-yl, quinolin-5-yl, quinazolin-5-yl, 4-hydroxy-quinazolin-5-yl, quinoxalin-5-yl, 8-oxo-7,8-dihydro-6*H*-thiazolo[5,4-*e*]isoindol-5-yl, 3-hydroxy-1,1-dioxido-2,3-dihydrobenzo[*b*]thiophen-7-yl, 1,1-dioxido-3-oxo-2,3-dihydrobenzo[*b*]-thiophen-7-yl, 1-oxoisoindolin-4-yl, 3-oxoisoindolin-4-yl, 2-methyl-1-oxoisoindolin-4-yl, 2,3-dioxoindolin-4-yl, 2-oxoindolin-4-yl, 1-methyl-2-oxoindolin-4-yl, 1-methyl-3-oxo-2,3-dihydro-1*H*-indazol-4-yl, 2,2-difluoro-1,1-dioxido-3-oxo-2,3-dihydrobenzo[*b*]-thiophen-7-yl, or 3-methyl-4-oxo-3,4-dihydroquinazolin-5-yl; or (iii) methoxycarbonyl, hydroxyl, methoxy, amino, acetamido, methylsulfonamido, methylsulfonyl, or methylsulfamoyl.

14. A compound of:

1-(4-(1,1-dioxidobenzo[*b*]thiophen-7-yl)benzyl)-3-(2-ethynylthiazol-4-yl)urea **A1**;

1-(2-ethynylthiazol-4-yl)-3-(4-(3-hydroxy-1,1-dioxido-2,3-dihydrobenzo[*b*]-thiophen-7-yl)benzyl)urea **A2**;

1-(4-(1,1-dioxido-3-oxo-2,3-dihydrobenzo[*b*]thiophen-7-yl)benzyl)-3-(2-ethynylthiazol-4-yl)urea **A3**;

1-(2-ethynylthiazol-4-yl)-3-(4-(8-oxo-7,8-dihydro-6*H*-thiazolo[5,4-*e*]isoindol-5-yl)-benzyl)urea **A4**;

(*S*)-1-(2-ethynylthiazol-4-yl)-3-((3'-(3-hydroxypyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)-methyl)urea **A5**;

1-(4-(benzo[*d*]thiazol-7-yl)benzyl)-3-(2-ethynylthiazol-4-yl)urea **A6**;

1-(2-ethynylthiazol-4-yl)-3-((3'-(pyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)methyl)urea **A7**;

1-([1,1'-biphenyl]-4-ylmethyl)-3-(2-ethynylthiazol-4-yl)urea **A8**;

1-(2-ethynylthiazol-4-yl)-3-(4-(4-hydroxyquinazolin-5-yl)benzyl)urea **A9**;

4'-((3-(2-ethynylthiazol-4-yl)ureido)methyl)-[1,1'-biphenyl]-3-carboxamide **A10**;

1-(2-ethynylthiazol-4-yl)-3-(4-(3-methyl-4-oxo-3,4-dihydroquinazolin-5-yl)benzyl)urea **A11**;

1-(2-ethynylthiazol-4-yl)-3-(4-(6-fluorobenzo[*d*]thiazol-5-yl)benzyl)urea **A12**;

4'-((3-(2-ethynylthiazol-4-yl)ureido)methyl)-*N*-methyl-[1,1'-biphenyl]-2-sulfonamide **A13**;

4'-((3-(2-ethynylthiazol-4-yl)ureido)methyl)-*N*-methyl-[1,1'-biphenyl]-3-carboxamide **A14**;

1-(4-(1,5-dimethyl-1*H*-indazol-4-yl)benzyl)-3-(2-ethynylthiazol-4-yl)urea **A15**;

1-(2-ethynylthiazol-4-yl)-3-(4-(1-methyl-1*H*-indazol-4-yl)benzyl)urea **A16**;

7-(4-((3-(2-ethynylthiazol-4-yl)ureido)methyl)phenyl)-*N*-methylbenzo[*d*]thiazole-6-carboxamide **A17**;

1-(2-ethynylthiazol-4-yl)-3-(4-(1-hydroxyisoquinolin-8-yl)benzyl)urea **A18**;

7-(4-((3-(2-ethynylthiazol-4-yl)ureido)methyl)phenyl)benzo[*d*]thiazole-6-carboxamide **A19**;

4-(4-((3-(2-ethynylthiazol-4-yl)ureido)methyl)phenyl)-1-methyl-1*H*-indazole-6-carboxamide **A20**;

4-(4-((3-(2-ethynylthiazol-4-yl)ureido)methyl)phenyl)-*N*,1-dimethyl-1*H*-indazole-6-carboxamide **A21**;

methyl 4-(4-((3-(2-ethynylthiazol-4-yl)ureido)methyl)phenyl)-1-methyl-1*H*-indazole-6-carboxylate **A22**; or

4-(4-((3-(2-ethynylthiazol-4-yl)ureido)methyl)phenyl)-*N*,*N*,1-trimethyl-1*H*-indazole-6-carboxamide **A23**;

1-(2-ethynylthiazol-4-yl)-3-(4-(1-methyl-3-oxo-2,3-dihydro-1*H*-indazol-4-yl)benzyl)urea **A24**;

(*S*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)ethyl)-3-(2-ethynylthiazol-4-yl)urea **A25**;

(*R*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)ethyl)-3-(2-ethynylthiazol-4-yl)urea **A26**;

1-(4-(2,2-difluoro-1,1-dioxido-3-oxo-2,3-dihydrobenzo[*b*]thiophen-7-yl)benzyl)-3-(2-ethynylthiazol-4-yl)urea **A27**;

1-(2-ethynylthiazol-4-yl)-3-((3'-(oxetan-3-ylamino)-[1,1'-biphenyl]-4-yl)methyl)urea **A28**;

1-((2'-cyano-[1,1'-biphenyl]-4-yl)methyl)-3-(2-ethynylthiazol-4-yl)urea **A29**;

1-(2-ethynylthiazol-4-yl)-3-(4-(pyrrolidin-1-yl)benzyl)urea **A30**;

1-(4-((3-(2-ethynylthiazol-4-yl)ureido)methyl)phenyl)pyrrolidine-2-carboxamide **A31**;

(*S*)-1-(4-(2-cyanopyrrolidin-1-yl)benzyl)-3-(2-ethynylthiazol-4-yl)urea **A32**;

(*R*)-1-(4-(2-cyanopyrrolidin-1-yl)benzyl)-3-(2-ethynylthiazol-4-yl)urea **A33**;

1-(2-(3-(2-cyanophenyl)azetidin-1-yl)-2-oxoethyl)-3-(2-ethynylthiazol-4-yl)urea **A34**;

1-(2-(4-(2-cyanophenyl)piperidin-1-yl)-2-oxoethyl)-3-(2-ethynylthiazol-4-yl)urea **A35**;

1-(2-(4-(2-cyanophenyl)piperazin-1-yl)-2-oxoethyl)-3-(2-ethynylthiazol-4-yl)urea **A36**;

1-((1-(2-cyanophenyl)piperidin-4-yl)methyl)-3-(2-ethynylthiazol-4-yl)urea **A37**;

1-(adamantan-1-ylmethyl)-3-(2-ethynylthiazol-4-yl)urea **A38**;

1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)piperidin-4-yl)-3-(2-ethynylthiazol-4-yl)urea **A39**;

(*R*)-1-(1-(4-(benzo[d]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A40**;

(*S*)-1-(1-(4-(benzo[d]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A41**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(3'-(pyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)-ethyl)urea **A42**;

(*R*)-2-(4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)-*N*-methylacetamide **A43**;

(*R*)-1-(1-(2'-cyano-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A44**;

(*R*)-1-(1-(5-(2-cyanophenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A45**;

(*R*)-2-(2'-cyano-[1,1'-biphenyl]-4-yl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl carbamate **A46**;

(*R*)-2-(4-(3-cyanopyridin-2-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl carbamate **A47**;

(*R*)-2-(4-(4-cyanopyridin-2-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl carbamate **A48**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(isoquinolin-8-yl)phenyl)ethyl carbamate **A49**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(quinazolin-8-yl)phenyl)ethyl carbamate **A50**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(quinoxalin-5-yl)phenyl)ethyl carbamate **A51**;

(*R*)-1-(1-(4-(7-cyanoquinolin-8-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A52**;

(*R*)-1-(1-(4-(3-cyano-1-methyl-1*H*-indazol-4-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A53**;

(*R*)-1-(1-(2'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A54**;

(*R*)-2-(2'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-ethyl carbamate **A55**;

(*R*)-2-(4-(6-(1-cyanocyclopropyl)pyridin-2-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethyl carbamate **A56**;

(*R*)-2-(4-(4-(1-cyanocyclopropyl)pyridin-2-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethyl carbamate **A57**;

(*R*)-2-(4-(3-(1-cyanocyclopropyl)pyridin-2-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethyl carbamate **A58**;

(*R*)-1-(1-(6-(2-(1-cyanocyclopropyl)phenyl)pyridin-3-yl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A59**;

(*R*)-2-(5-(2-(1-cyanocyclopropyl)phenyl)pyridin-2-yl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethyl carbamate **A60**;

(*S*)-2-(5-(2-(1-cyanocyclopropyl)phenyl)pyridin-2-yl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethyl carbamate **A61**;

(*R*)-1-(1-(4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A62**;

(*R*)-2-(4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-

ureido)ethyl carbamate **A63**;

(*R*)-1-(1-(4-(2-(1-cyanocyclopropyl)-5-fluoropyridin-3-yl)phenyl)-2-hydroxy-ethyl)-3-(2-ethynylthiazol-4-yl)urea **A64**;

(*R*)-1-(1-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-hydroxy-ethyl)-3-(2-ethynylthiazol-4-yl)urea **A65**;

(*S*)-1-(1-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-hydroxy-ethyl)-3-(2-ethynylthiazol-4-yl)urea **A66**;

(*R*)-1-(1-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-hydroxy-ethyl)-3-(2-ethynylthiazol-4-yl)-1-methylurea **A67**;

(*R*)-1-(1-(4-(2-(1-cyanocyclopropyl)pyridin-3-yl)-3-fluorophenyl)-2-hydroxy-ethyl)-3-(2-ethynylthiazol-4-yl)urea **A68**;

(*R*)-2-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-(3-(2-ethynyl-thiazol-4-yl)ureido)ethyl carbamate **A69**;

(*R*)-2-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-(3-(2-ethynyl-thiazol-4-yl)-1-methylureido)ethyl carbamate **A70**;

(*R*)-1-(1-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-hydroxy-ethyl)-3-(5-ethynyl-1,3,4-thiadiazol-2-yl)urea **A71**;

(*R*)-1-(1-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-(methyl-sulfonyl)-ethyl)-3-(2-ethynylthiazol-4-yl)urea **A72**;

(*R*)-2-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-(3-(2-ethynyl-thiazol-4-yl)ureido)ethanesulfonamide **A73**;

(*R*)-2-(3-chloro-4-(2-(1-cyanocyclopropyl)pyridin-3-yl)phenyl)-2-(3-(2-ethynyl-thiazol-4-yl)ureido)-N-methylacetamide **A74**;

(*R*)-1-(1-(5-(2-(1-cyanocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-hydroxy-ethyl)-3-(2-ethynylthiazol-4-yl)urea **A75**;

(*R*)-2-(5-(2-(1-cyanocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-(3-(2-ethynyl-thiazol-4-yl)ureido)ethyl carbamate **A76**;

(*R*)-1-(1-(5-(2-(1-cyanocyclopropyl)-5-fluorophenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A77**;

(*R*)-1-(1-(5-(2-(1-cyanocyclopropyl)-6-fluorophenyl)pyridin-2-yl)-2-hydroxy-ethyl)-3-(2-ethynylthiazol-4-yl)urea **A78**;

(*R*)-1-(1-(5-(2-(1-cyanocyclopropyl)-4,6-difluorophenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A79**;

1-((1*R*)-1-(5-(2-(2,2-difluorocyclopropyl)phenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A80**;

1-((1*R*)-1-(5-(2-(2,2-difluorocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A81**;

1-((1*R*)-1-(5-(2-(2,2-difluorocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)-1-methylurea **A82**;

(2*R*)-2-(5-(2-(2,2-difluorocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-(3-(2-ethynyl-thiazol-4-yl)ureido)ethyl carbamate **A83**;

(2*R*)-2-(5-(2-(2,2-difluorocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-(3-(2-ethynyl-thiazol-4-yl)-1-methylureido)ethyl carbamate **A84**;

1-((1*R*)-1-(5-(2-(2,2-difluorocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(5-ethynyl-1,3,4-thiadiazol-2-yl)urea **A85**;

1-((1*R*)-1-(5-(2-(2,2-difluorocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-hydroxyethyl)-3-(5-ethynyl-1,3,4-thiadiazol-2-yl)-1-methylurea **A86**;

(2*R*)-2-(5-(2-(2,2-difluorocyclopropyl)-4-fluorophenyl)pyridin-2-yl)-2-(3-(5-ethynyl-1,3,4-thiadiazol-2-yl)ureido)ethyl carbamate **A87**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(6-(pyrrolidin-1-yl)pyridin-2-yl)phenyl)-ethyl)urea **A88**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(6-(pyrrolidin-1-yl)-[2,3'-bipyridin]-6'-yl)-ethyl)urea **A89**;

(*R*)-2-(3-(2-ethynylthiazol-5-yl)ureido)-2-(6-(pyrrolidin-1-yl)-[2,3'-bipyridin]-6'-yl)ethyl carbamate **A90**;

(*R*)-3-(2-ethynylthiazol-4-yl)-1-(2-hydroxy-1-(6-(pyrrolidin-1-yl)-[2,3'-bipyridin]-6'-yl)-ethyl)-1-methylurea **A91**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)-1-methylureido)-2-(6-(pyrrolidin-1-yl)-[2,3'-bipyridin]-6'-yl)ethyl carbamate **A92**;

(*R*)-1-(5-ethynyl-1,3,4-thiadiazol-2-yl)-3-(2-hydroxy-1-(4-(6-(pyrrolidin-1-yl)-pyridin-2-yl)phenyl)ethyl)urea **A93**;

(*R*)-2-(3-(5-ethynyl-1,3,4-thiadiazol-2-yl)ureido)-2-(4-(6-(pyrrolidin-1-yl)-pyridin-2-yl)-

phenyl)ethyl carbamate **A94**;

(*R*)-2-(3-(5-ethynyl-1,3,4-thiadiazol-2-yl)-1-methylureido)-2-(4-(6-(pyrrolidin-1-yl)-pyridin-2-yl)phenyl)ethyl carbamate **A95**;

(*R*)-1-(5-ethynyl-1,3,4-thiadiazol-2-yl)-3-(2-hydroxy-1-(6-(pyrrolidin-1-yl)-[2,3'-bipyridin]-6'-yl)ethyl)urea **A96**;

(*R*)-2-(3-(5-ethynyl-1,3,4-thiadiazol-2-yl)ureido)-2-(6-(pyrrolidin-1-yl)-[2,3'-bipyridin]-6'-yl)ethyl carbamate **A97**;

(*R*)-1-(1-(4-(2-(dimethylamino)pyridin-3-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A98**;

(*R*)-2-(4-(2-(dimethylamino)pyridin-3-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)-ethyl carbamate **A99**;

(*R*)-1-(1-(3-chloro-4-(2-(dimethylamino)pyridin-3-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A100**;

(*R*)-2-(3-chloro-4-(2-(dimethylamino)pyridin-3-yl)phenyl)-2-(3-(2-ethynyl-thiazol-4-yl)-ureido)ethyl carbamate **A101**;

(*R*)-1-(1-(4-(2-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A102**;

(*R*)-2-(4-(2-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)phenyl)-2-(3-(2-ethynyl-thiazol-4-yl)-ureido)ethyl carbamate **A103**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(1-hydroxyisoquinolin-8-yl)-phenyl)-ethyl)urea **A104**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(1-hydroxyisoquinolin-8-yl)phenyl)-ethyl carbamate **A105**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(5-(1-hydroxyisoquinolin-8-yl)-pyridin-2-yl)ethyl)urea **A106**;

(*R*)-1-(1-(3-chloro-4-(1-hydroxyisoquinolin-8-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A107**;

(*R*)-1-(5-ethynyl-1,3,4-thiadiazol-2-yl)-3-(2-hydroxy-1-(4-(1-hydroxyisoquinolin-8-yl)-phenyl)ethyl)urea **A108**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(4-hydroxyquinazolin-5-yl)phenyl)-ethyl)urea **A109**;

(*R*)-1-(1-(3-chloro-4-(4-hydroxyquinazolin-5-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A110**;

(*R*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)-1-methylurea **A111**;

(*R*)-3-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-1-(2-ethynylthiazol-4-yl)-1-methylurea **A112**;

(*R*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)-1,3-dimethylurea **A113**;

(*R*)-1-(1-(5-(benzo[*d*]thiazol-7-yl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A114**;

(*R*)-2-(3-chloro-4-(4-fluorobenzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethane-1-sulfonamide **A115**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl L-valinate **A116**;

(5*Z*,8*Z*,11*Z*,14*Z*)-(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethyl icosa-5,8,11,14-tetraenoate **A117**;

(*R*)-1-(1-(4-(Benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-5-yl)urea **A118**;

(*R*)-1-(1-(4-(Benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-5-methyl-thiazol-4-yl)urea **A119**;

(*R*)-1-(1-(4-(Benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(5-ethynyl-1,3,4-thiadiazol-2-yl)urea **A120**;

(*R*)-1-(1-(4-(Benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(3-ethynyl-1,2,4-thiadiazol-5-yl)urea **A121**;

(*R*)-1-(1-(4-(Benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(5-ethynyl-1,2,4-thiadiazol-3-yl)urea **A122**;

(*R*)-1-(4-ethynylpyrimidin-2-yl)-3-(2-hydroxy-1-(4-(6-(pyrrolidin-1-yl)pyridin-2-yl)-phenyl)ethyl)urea **A123**;

(*R*)-1-(6-ethynylpyridin-2-yl)-3-(2-hydroxy-1-(4-(6-(pyrrolidin-1-yl)pyridin-2-yl)-phenyl)ethyl)urea **A124**;

(*R*)-1-(2-ethynylpyrimidin-4-yl)-3-(2-hydroxy-1-(4-(6-(pyrrolidin-1-yl)pyridin-2-yl)-

phenyl)ethyl)urea **A125**;

(*R*)-1-(1-(4-(3,3-difluoroazetidin-1-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A126**;

(*R*)-2-(4-(3,3-difluoroazetidin-1-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-ethyl carbamate **A127**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(pyrrolidin-1-yl)phenyl)ethyl)-urea **A128**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(2-oxopyrrolidin-1-yl)phenyl)-ethyl)urea **A129**;

(*R*)-1-(1-(4-(3,3-difluoropyrrolidin-1-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A130**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(2-oxopiperidin-1-yl)phenyl)-ethyl)urea **A131**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(2-oxopyridin-1(2*H*)-yl)phenyl)-ethyl)-urea **A132**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-morpholinophenyl)ethyl)urea **A133**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(3-oxomorpholino)phenyl)-ethyl)urea **A134**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(5-(piperidin-1-yl)pyridin-2-yl)-ethyl)urea **A135**;

(*R*)-1-(1-(5-(3,3-difluoropiperidin-1-yl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A136**;

(*R*)-1-(1-(4-(azepan-1-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A137**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(2-oxoazepan-1-yl)phenyl)-ethyl)urea **A138**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(1-methyl-1,5,6,7-tetrahydro-4*H*-pyrazolo[4,3-*b*]pyridin-4-yl)phenyl)ethyl)urea **A139**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(2-methyl-2,5,6,7-tetrahydro-4*H*-pyrazolo[4,3-*b*]pyridin-4-yl)phenyl)ethyl)urea **A140**;

(*R*)-1-(1-(6'-cyano-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A141**;

(*R*)-1-(1-(5-(2-cyanocyclohex-1-en-1-yl)pyridin-2-yl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A142**;

1-((1*R*)-1-(4-(1-acetylpiperidin-2-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)-urea **A143**;

(*R*)-1-(1-(3-(2-cyanophenyl)azetidin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A144**;

(*S*)-1-(1-(3-(2-cyanophenyl)azetidin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A145**;

(*R*)-1-(1-(4-(2-cyanophenyl)piperidin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A146**;

(*S*)-1-(1-(4-(2-cyanophenyl)piperidin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A147**;

(*R*)-1-(1-(4-(2-cyanophenyl)piperazin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A148**;

(*S*)-1-(1-(4-(2-cyanophenyl)piperazin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A149**;

(*R*)-1-(1-(1-(2-cyanophenyl)piperidin-4-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)-urea **A150**;

(*S*)-1-(1-(1-(2-cyanophenyl)piperidin-4-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)-urea **A151**;

(*S*)-1-(2-ethynylthiazol-4-yl)-3-(3-hydroxy-1-oxo-1-(6-azaspiro[2.5]octan-6-yl)propan-2-yl)urea **A152**;

(*S*)-1-(2-ethynylthiazol-4-yl)-3-(3-hydroxy-1-oxo-1-(7-azaspiro[3.5]nonan-7-yl)propan-2-yl)urea **A153**;

(*S*)-1-(2-ethynylthiazol-4-yl)-3-(3-hydroxy-1-oxo-1-(8-azaspiro[4.5]decan-8-yl)propan-2-yl)urea **A154**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(3-hydroxy-1-oxo-1-(8-azaspiro[4.5]decan-8-yl)propan-2-yl)urea **A155**;

(*S*)-1-(2-ethynylthiazol-5-yl)-3-(3-hydroxy-1-oxo-1-(1-oxo-8-azaspiro[4.5]decan-8-yl)-propan-2-yl)urea **A156**;

(*S*)-1-(2-ethynylthiazol-4-yl)-3-(3-hydroxy-1-oxo-1-(3-azaspiro[5.5]undecan-3-yl)-

propan-2-yl)urea **A157**;

(*S*)-1-(1-(9,9-difluoro-3-azaspiro[5.5]undecan-3-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynylthiazol-4-yl)urea **A158**;

(*S*)-1-(1-(4-(3,3-difluoroazetidin-1-yl)piperidin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynylthiazol-4-yl)urea **A159**;

(*R*)-1-(1-(4-(3,3-difluoroazetidin-1-yl)piperidin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynylthiazol-4-yl)urea **A160**;

(*S*)-1-(1-(4,4-difluoropiperidin-1-yl)-3-hydroxy-1-oxopropan-2-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A161**;

1-(6-chloro-8-fluoro-7-(2-fluoro-6-methoxyphenyl)quinazolin-4-yl)-3-(2-ethynylthiazol-4-yl)urea **A162**;

1-(2-ethynylthiazol-4-yl)-3-(7-(2-fluoro-6-hydroxyphenyl)quinazolin-4-yl)urea **A163**;

1-(2-ethynylthiazol-4-yl)-3-(7-(2-fluoro-6-methoxyphenyl)quinazolin-4-yl)urea **A164**;

1-(7-(benzo[*d*]thiazol-7-yl)-6-chloro-8-fluoroquinazolin-4-yl)-3-(2-ethynyl-thiazol-4-yl)urea **A165**;

1-(7-(2-(1-cyanocyclopropyl)pyridin-3-yl)quinazolin-4-yl)-3-(2-ethynylthiazol-4-yl)urea **A166**;

1-((3'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)methyl)-3-(2-ethynylthiazol-4-yl)urea **A167**;

1-(2-ethynylthiazol-4-yl)-3-((3'-(1-hydroxycyclopropyl)-[1,1'-biphenyl]-4-yl)methyl)urea **A168**;

1-(2-ethynylthiazol-4-yl)-3-((3'-propionyl-[1,1'-biphenyl]-4-yl)methyl)urea **A169**;

1-(2-ethynylthiazol-4-yl)-3-((3'-(1-hydroxycyclobutyl)-[1,1'-biphenyl]-4-yl)-methyl)urea **A170**;

1-(4-(2-(3,3-difluoroazetidin-1-yl)-4-hydroxyquinazolin-5-yl)benzyl)-3-(2-ethynyl-thiazol-4-yl)urea **A171**;

1-(2-ethynylthiazol-4-yl)-3-(4-(4-hydroxy-2-(2-hydroxyethoxy)quinazolin-5-yl)-benzyl)-urea **A172**;

1-(2-ethynylthiazol-4-yl)-3-(4-(4-(pyrrolidin-1-yl)pyridin-2-yl)benzyl)urea **A173**;

1-(2-ethynylthiazol-4-yl)-3-(4-(5-(pyrrolidin-1-yl)pyridin-3-yl)benzyl)urea **A174**;

1-(2-ethynylthiazol-4-yl)-3-(4-(2-(pyrrolidin-1-yl)pyridin-4-yl)benzyl)urea **A175**;

1-(2-ethynylthiazol-4-yl)-3-(4-(6-(pyrrolidin-1-yl)pyridin-2-yl)benzyl)urea **A176**;

1-(4-(benzo[*d*]thiazol-7-yl)-2-cyanobenzyl)-3-(2-ethynylthiazol-4-yl)urea **A177**;

1-(4-(benzo[*d*]thiazol-7-yl)-2-cyanobenzyl)-3-(2-ethynylthiazol-4-yl)urea **A178**;

1-((5-(benzo[*d*]thiazol-7-yl)pyridin-2-yl)methyl)-3-(2-ethynylthiazol-4-yl)urea **A179**;

1-((6-(3-(1-cyanocyclopropyl)phenyl)pyridin-3-yl)methyl)-3-(2-ethynylthiazol-4-yl)urea **A180**;

(*R*)-1-(1-(3'-(3,3-difluoropyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A181**;

(*R*)-1-(1-(4-cyclohexylphenyl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A182**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(2',3',4',5'-tetrahydro-[1,1'-biphenyl]-4-yl)-ethyl)urea **A183**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(1-methylpiperidin-4-yl)phenyl)-ethyl)-urea **A184**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(1-methyl-1,2,3,6-tetrahydro-pyridin-4-yl)phenyl)ethyl)urea **A185**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)ethyl)urea **A186**;

(*R*)-1-(1-(3'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A187**;

1-((1*R*)-1-(3'-(2,2-difluorocyclopropyl)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A188**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(3'-(1-hydroxycyclobutyl)-[1,1'-biphenyl]-4-yl)ethyl)urea **A189**;

(*R*)-1-(1-(3'-(azetidin-1-yl)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A190**;

(*R*)-1-(1-(3'-(3,3-difluoroazetidin-1-yl)-[1,1'-biphenyl]-4-yl)-2-hydroxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A191**;

1-(2-ethynylthiazol-4-yl)-3-((1*R*)-2-hydroxy-1-(4-(1-methylpiperidin-3-yl)-phenyl)ethyl)-urea **A192**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(1-methyl-1,2,5,6-tetrahydro-pyridin-3-yl)phenyl)ethyl)urea **A193**;

1-((1*R*)-1-(4-(1-acetylpiperidin-3-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-thiazol-4-yl)-urea **A194**;

(*R*)-1-(2-ethynylthiazol-4-yl)-3-(2-hydroxy-1-(4-(piperidin-1-yl)phenyl)ethyl)-urea **A195**;

(*S*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-cyanoethyl)-3-(2-ethynylthiazol-4-yl)urea **A196**;

(*R*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(methylsulfonyl)ethyl)-3-(2-ethynyl-thiazol-4-yl)urea **A197**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-ethane-1-sulfonamide **A198**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-*N*-methyl-ethane-1-sulfonamide **A199**;

(*R*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-methoxyethyl)-3-(2-ethynylthiazol-4-yl)urea **A200**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl acetate **A201**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl pivalate **A202**;

(*R*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxy-2-methylpropyl)-3-(2-ethynyl-thiazol-4-yl)urea **A203**;

1-((1*R*)-1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxypropyl)-3-(2-ethynyl-thiazol-4-yl)-urea **A204**;

1-(4-(benzo[*d*]thiazol-7-yl)benzyl)-1-(2-cyanoethyl)-3-(2-ethynylthiazol-4-yl)urea **A205**;

1-(4-(benzo[*d*]thiazol-7-yl)benzyl)-3-(2-ethynylthiazol-4-yl)-1-(2-hydroxyethyl)-urea **A206**;

1-(4-(benzo[*d*]thiazol-7-yl)benzyl)-3-(2-ethynylthiazol-4-yl)-1-(2-(methylsulfonyl)-ethyl)urea **A207**;

1-(4-(benzo[*d*]thiazol-7-yl)benzyl)-1-(cyanomethyl)-3-(2-ethynylthiazol-4-yl)urea **A208**;

2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)acetamide **A209**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-acetamide **A210**;

(*S*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-acetamide **A211**;

(*R*)-2-(3'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-acetamide **A212**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-N-methyl-2-(4-(4-oxo-3,4-dihydro-quinazolin-5-yl)phenyl)acetamide **A213**;

2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-*N*-methyl-acetamide **A214**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-*N*-methyl-acetamide **A215**;

(*S*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-*N*-methyl-acetamide **A216**;

(*R*)-2-(3'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-*N*-methylacetamide **A217**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(3'-(1-hydroxycyclopropyl)-[1,1'-biphenyl]-4-yl)-*N*-methylacetamide **A218**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-*N*-methyl-2-(3'-propionyl-[1,1'-biphenyl]-4-yl)-acetamide **A219**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-*N*,*N*-dimethylacetamide **A220**;

(*R*)-2-(3'-cyano-[1,1'-biphenyl]-4-yl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl carbamate **A221**;

(*R*)-2-(3'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)-2-(3-(2-ethynylthiazol-4-yl)ureido)-ethyl carbonate **A222**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl carbamate **A223**;

(*R*)-2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)ureido)ethyl methyl-carbamate **A224**;

(*R*)-2-(4-(benzo[*d*][1,2,3]thiadiazol-7-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)-ethyl carbamate **A225**;

(*R*)-2-(4-(benzo[*c*][1,2,5]thiadiazol-4-yl)phenyl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)-

ethyl carbamate **A226**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(quinolin-8-yl)phenyl)ethyl carbamate **A227**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(isoquinolin-8-yl)phenyl)ethyl carbamate **A228**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(isoquinolin-5-yl)phenyl)ethyl carbamate **A229**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(quinolin-5-yl)phenyl)ethyl carbamate **A230**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(1-methyl-1H-indazol-4-yl)phenyl)-ethyl carbamate **A231**;

(2*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(1-methyl-4,5,6,7-tetrahydro-1*H*-indazol-4-yl)phenyl)ethyl carbamate **A232**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(1-methyl-6,7-dihydro-1*H*-indazol-4-yl)-phenyl)ethyl carbamate **A233**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(6-(pyrrolidin-1-yl)pyridin-2-yl)-phenyl)-ethyl carbamate **A234**;

(*R*)-2-(3-(2-ethynylthiazol-4-yl)ureido)-2-(4-(2-(pyrrolidin-1-yl)pyridin-4-yl)-phenyl)-ethyl carbamate **A235**;

(*R*)-2-(5-(3-(1-cyanocyclopropyl)phenyl)pyridin-2-yl)-2-(3-(2-ethynylthiazol-4-yl)-ureido)ethyl carbamate **A236**;

1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)piperidin-4-yl)-3-(2-ethynylthiazol-4-yl)urea **A237**;

1-((4-(3-(1-cyanocyclopropyl)phenyl)cyclohexyl)methyl)-3-(2-ethynylthiazol-4-yl)urea **A238**;

1-((3'-(1-cyanocyclopropyl)-2,3,4,5-tetrahydro-[1,1'-biphenyl]-4-yl)methyl)-3-(2-ethynylthiazol-4-yl)urea **A239**;

1-((1-(3-(1-cyanocyclopropyl)phenyl)piperidin-4-yl)methyl)-3-(2-ethynylthiazol-4-yl)-urea **A240**;

(*R*)-1-(1-(4-(benzo[*d*]thiazol-7-yl)phenyl)-2-hydroxyethyl)-3-(2-ethynyl-pyrimidin-4-yl)-urea **A241**;

2-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)pyrrolidine-1-carboxamide

B1;

3-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)azetidine-1-carboxamide **B2**;

6-(benzo[*d*]thiazol-7-yl)-*N*-(2-ethynylthiazol-4-yl)-3,4-dihydroisoquinoline-2(1*H*)-carboxamide **B3**;

5-(benzo[*d*]thiazol-7-yl)-*N*-(2-ethynylthiazol-4-yl)isoindoline-2-carboxamide **B2**;

4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B5**;

4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperidine-1-carboxamide **B6**;

N-(2-ethynylthiazol-4-yl)-4-(5-(3-(2-oxooxazolidin-3-yl)phenyl)pyridin-2-yl)piperazine-1-carboxamide **B7**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(oxetan-3-ylamino)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B8**;

N-(2-ethynylthiazol-4-yl)-4-(3'-((3-hydroxycyclobutyl)amino)-[1,1'-biphenyl]-4-yl)-piperazine-1-carboxamide **B9**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(3-hydroxyazetidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B10**;

N-(2-ethynylthiazol-4-yl)-4-(4-(imidazo[1,5-*a*]pyridin-5-yl)phenyl)piperazine-1-carboxamide **B11**;

4-(4-([1,2,4]triazolo[4,3-*a*]pyridin-5-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B12**;

N-(2-ethynylthiazol-4-yl)-4-(4-(imidazo[1,5-*a*]pyridin-8-yl)phenyl)piperazine-1-carboxamide **B13**;

4-(4-([1,2,3]triazolo[1,5-*a*]pyridin-4-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B14**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(pyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B15**;

(*S*)-*N*-(2-ethynylthiazol-4-yl)-4-(3'-(3-hydroxypyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)-piperazine-1-carboxamide **B16**;

4-(4-(1,1-dioxido-3-oxo-2,3-dihydrobenzo[*b*]thiophen-7-yl)phenyl)-*N*-(2-ethynylthiazol-

4-yl)piperazine-1-carboxamide **B17**;

N-(2-ethynylthiazol-4-yl)-4-(4-(1-methyl-1*H*-indazol-4-yl)phenyl)piperazine-1-carboxamide **B18**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(pyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B19**;

N-(2-ethynylthiazol-4-yl)-4-(4-(1-oxo-1,2-dihydroisoquinolin-8-yl)phenyl)piperazine-1-carboxamide **B20**;

N-(2-ethynylthiazol-4-yl)-4-(4-(3-hydroxy-1,1-dioxido-2,3-dihydrobenzo[*b*]thiophen-7-yl)phenyl)piperazine-1-carboxamide **B21**;

N-(2-ethynylthiazol-4-yl)-4-(4-(4-oxo-3,4-dihydroquinazolin-5-yl)phenyl)piperazine-1-carboxamide **B22**;

(*S*)-4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)-piperazine-1-carboxamide **B23**;

(*R*)-4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)-piperazine-1-carboxamide **B24**;

4-(4-(2-amino-6-cyanobenzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B25**;

4-(4-(6-cyanobenzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B26**;

4-(4-(2-aminobenzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B27**;

4-(4-(benzo[*d*][1,2,3]thiadiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B28**;

4-(4-([1,2,4]triazolo[1,5-*a*]pyridin-8-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B29**;

4-(4-([1,2,4]triazolo[4,3-*a*]pyridin-8-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B30**;

4-(2'-cyano-[1,1'-biphenyl]-4-yl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B31**;

4-(4-([1,2,4]triazolo[4,3-*a*]pyridin-5-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B32**;

N-(2-ethynylthiazol-4-yl)-4-(4-(imidazo[1,2-*a*]pyridin-5-yl)phenyl)piperazine-1-carboxamide **B33**;

4-(4-([1,2,4]triazolo[1,5-*a*]pyridin-5-yl)phenyl)-N-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B34**;

N-(2-ethynylthiazol-4-yl)-4-(4-(imidazo[1,2-*a*]pyridin-8-yl)phenyl)piperazine-1-carboxamide **B35**;

(*R*)-4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)-3-(hydroxymethyl)-piperazine-1-carboxamide **B36**;

(*S*)-4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)-3-(hydroxymethyl)-piperazine-1-carboxamide **B37**;

4-(3'-(1-cyanocyclopropyl)-[1,1'-biphenyl]-4-yl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B38**;

4-(3'-cyano-[1,1'-biphenyl]-4-yl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B39**;

4-(4-(benzo[*d*]thiazol-7-yl)-2-cyanophenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B40**;

4-(4-(benzo[*d*]thiazol-7-yl)-3-cyanophenyl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B41**;

4-(3'-cyclopropyl-[1,1'-biphenyl]-4-yl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B42**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(2-oxopyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B43**;

4-((4-(benzo[*d*]thiazol-7-yl)phenyl)amino)-*N*-(2-ethynylthiazol-4-yl)piperidine-1-carboxamide **B44**;

4-(4-(2-amino-[1,2,4]triazolo[1,5-*a*]pyridin-5-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)-piperazine-1-carboxamide **B45**;

4-(3'-(cyclopent-1-en-1-yl)-[1,1'-biphenyl]-4-yl)-*N*-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B46**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(2-oxoimidazolidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B47**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(1-hydroxycyclopentyl)-[1,1'-biphenyl]-4-yl)piperazine-

1-carboxamide **B48**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(3-hydroxyazetidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B49**;

N-(2-ethynylthiazol-4-yl)-4-(3'-(3-hydroxypyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)-piperazine-1-carboxamide **B50**;

4-(3'-(azetidin-1-yl)-[1,1'-biphenyl]-4-yl)-N-(2-ethynylthiazol-4-yl)piperazine-1-carboxamide **B51**;

(*S*)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)-4-(3'-(pyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B52**;

(*R*)-4-(3-cyano-3'-(pyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)piperazine-1-carboxamide **B53**;

(*R*)-*N*-(*2*-ethynylthiazol-4-yl)-2-(hydroxymethyl)-4-(3'-(pyrrolidin-1-yl)-[1,1'-biphenyl]-4-yl)piperazine-1-carboxamide **B54**;

(*R*)-4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)-piperazine-1-carboxamide **B55**;

(*R*)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)-4-(5-(3-(pyrrolidin-1-yl)phenyl)pyridin-2-yl)piperazine-1-carboxamide **B56**;

N-(2-ethynylthiazol-4-yl)-4-(5-(3-(2-oxooxazolidin-3-yl)phenyl)pyridin-2-yl)piperazine-1-carboxamide **B57**;

(*R*)-4-(5-(benzo[*d*]thiazol-7-yl)pyridin-2-yl)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)piperazine-1-carboxamide **B58**;

(*R*)-4-(5-(benzo[*d*]thiazol-7-yl)-3-cyanopyridin-2-yl)-*N*-(2-ethynylthiazol-4-yl)-2-(hydroxymethyl)piperazine-1-carboxamide **B59**;

2-ethynyl-*N*-(4-(6-fluorobenzo[*d*]thiazol-5-yl)phenethyl)thiazole-4-carboxamide **C1**;

N-(4-(benzo[*d*]thiazol-7-yl)-3-fluorophenethyl)-2-ethynylthiazole-4-carboxamide **C2**;

7-(4-(2-(2-ethynylthiazole-4-carboxamido)ethyl)phenyl)benzo[*d*]thiazole-6-carboxamide **C3**;

2-ethynyl-*N*-(2-(3'-(methylcarbamoyl)-[1,1'-biphenyl]-4-yl)ethyl)thiazole-4-carboxamide **C4**;

2-ethynyl-*N*-(4-(6-fluorobenzo[*d*]thiazol-7-yl)phenethyl)thiazole-4-carboxamide **C5**;

N-(2-(2'-(*N*,*N*-dimethylsulfamoyl)-[1,1'-biphenyl]-4-yl)ethyl)-2-ethynylthiazole-4-

carboxamide **C6**;

methyl 2-(2-ethynylthiazole-4-carboxamido)-5-(4-(2-(2-ethynylthiazole-4-carboxamido)-ethyl)phenyl)benzo[*d*]thiazole-7-carboxylate **C7**;

7-(4-(2-(2-ethynylthiazole-4-carboxamido)ethyl)phenyl)benzo[*d*]thiazole-5-carboxamide **C8**;

7-(4-(2-(2-ethynylthiazole-4-carboxamido)ethyl)phenyl)-*N*-methylbenzo[*d*]thiazole-5-carboxamide **C9**;

methyl 7-(4-(2-(2-ethynylthiazole-4-carboxamido)ethyl)phenyl)benzo[*d*]thiazole-5-carboxylate **C10**;

2-ethynyl-*N*-(4-(quinoxalin-5-yl)phenethyl)thiazole-4-carboxamide **C11**;

2-ethynyl-*N*-(2-(2'-(methylcarbamoyl)-[1,1'-biphenyl]-4-yl)ethyl)thiazole-4-carboxamide **C12**;

2-ethynyl-*N*-(4-(3-oxoisoindolin-4-yl)phenethyl)thiazole-4-carboxamide **C13**;

N-(4-(2,3-dioxoindolin-4-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C14**;

2-ethynyl-*N*-(2-(2'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)ethyl)thiazole-4-carboxamide **C15**;

2-ethynyl-*N*-(4-(1-hydroxyisoquinolin-8-yl)phenethyl)thiazole-4-carboxamide **C16**;

2-ethynyl-*N*-(4-(1-oxoisoindolin-4-yl)phenethyl)thiazole-4-carboxamide **C17**;

2-ethynyl-*N*-(4-(3-oxo-2,3-dihydro-1*H*-inden-4-yl)phenethyl)thiazole-4-carboxamide **C18**;

2-ethynyl-*N*-(4-(thiazolo[4,5-*c*]pyridin-7-yl)phenethyl)thiazole-4-carboxamide **C19**';

2-ethynyl-*N*-(2-(2'-(*N*-methylsulfamoyl)-[1,1'-biphenyl]-4-yl)ethyl)thiazole-4-carboxamide **C20**;

2-ethynyl-*N*-(4-(isoquinolin-5-yl)phenethyl)thiazole-4-carboxamide **C21**;

2-ethynyl-*N*-(4-(2-methyl-1-oxoisoindolin-4-yl)phenethyl)thiazole-4-carboxamide **C22**;

2-ethynyl-*N*-(4-(quinolin-5-yl)phenethyl)thiazole-4-carboxamide **C23**;

2-ethynyl-*N*-(4-(quinazolin-5-yl)phenethyl)thiazole-4-carboxamide **C24**;

N-(4-(benzo[*d*]thiazol-5-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C25**;

2-ethynyl-*N*-(3-(1-methyl-2-oxoindolin-4-yl)phenethyl)thiazole-4-carboxamide **C26**;

2-ethynyl-*N*-(3-(2-oxoindolin-4-yl)phenethyl)thiazole-4-carboxamide **C27**;

N-(4-(1*H*-indol-4-yl)benzyl)-2-ethynylthiazole-4-carboxamide **C28**;

2-ethynyl-*N*-(3-(2-methyl-2*H*-indazol-4-yl)phenethyl)thiazole-4-carboxamide **C29**;
2-ethynyl-*N*-(3-(1-methyl-1*H*-indazol-4-yl)phenethyl)thiazole-4-carboxamide **C30**;
N-(4-(benzo[*d*]thiazol-4-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C31**;
2-ethynyl-*N*-(4-(2-methyl-2*H*-indazol-4-yl)phenethyl)thiazole-4-carboxamide **C32**;
2-ethynyl-*N*-(4-(1-methyl-1*H*-indazol-4-yl)phenethyl)thiazole-4-carboxamide **C33**;
N-(4-(benzo[*d*]thiazol-7-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C34**;
2-ethynyl-*N*-(3-(1-methyl-1*H*-indol-4-yl)phenethyl)thiazole-4-carboxamide **C35**;
N-(3-(1*H*-indol-4-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C36**;
2-ethynyl-*N*-(4-(2-oxoindolin-4-yl)benzyl)thiazole-4-carboxamide **C37**;
2-ethynyl-*N*-(3-(pyridin-3-yl)phenethyl)thiazole-4-carboxamide **C38**;
N-(3-(1*H*-indazol-4-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C39**;
N-(4-(1*H*-indazol-4-yl)benzyl)-2-ethynylthiazole-4-carboxamide **C40**;
2-ethynyl-*N*-(4-(1-methyl-1*H*-pyrazol-3-yl)phenethyl)thiazole-4-carboxamide **C41**;
N-(4-(benzo[*d*]thiazol-6-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C42**;
2-ethynyl-*N*-(4-(1-methyl-2-oxoindolin-4-yl)phenethyl)thiazole-4-carboxamide **C43**;
2-ethynyl-*N*-(quinolin-2-ylmethyl)thiazole-4-carboxamide **C44**;
N-(2-cyanophenethyl)-2-ethynylthiazole-4-carboxamide **C45**;
methyl 2-(3-((2-ethynylthiazole-4-carboxamido)methyl)phenyl)acetate **C46**;
N-(3-(2-amino-2-oxoethyl)benzyl)-2-ethynylthiazole-4-carboxamide **C47**;
2-ethynyl-*N*-(4-(2-oxoindolin-4-yl)phenethyl)thiazole-4-carboxamide **C48**;
N-(4-(1*H*-indazol-4-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C49**;
2-ethynyl-*N*-(4-(1-methyl-1*H*-indol-4-yl)phenethyl)thiazole-4-carboxamide **C50**;
N-(4-(1*H*-indol-4-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C51**;
N-(3-chlorobenzyl)-2-ethynyl-5-methylthiazole-4-carboxamide **C52**;
2-ethynyl-*N*-(4-(thiazol-4-yl)phenethyl)thiazole-4-carboxamide **C53**;
2-ethynyl-*N*-(4-(1-methyl-1*H*-pyrazol-3-yl)benzyl)thiazole-4-carboxamide **C54**;
2-ethynyl-*N*-(4-(thiazol-4-yl)benzyl)thiazole-4-carboxamide **C55**;
N-(3-chlorobenzyl)-2-ethynyl-5-phenylthiazole-4-carboxamide **C56**;
2-ethynyl-*N*-(4-(thiazol-5-yl)phenethyl)thiazole-4-carboxamide **C57**;
N-(3-(1*H*-pyrazol-4-yl)benzyl)-2-ethynylthiazole-4-carboxamide **C58**;
2-ethynyl-*N*-(3-(1-methyl-1*H*-pyrazol-4-yl)benzyl)thiazole-4-carboxamide **C59**;

N-(3-(1*H*-pyrazol-3-yl)benzyl)-2-ethynylthiazole-4-carboxamide **C60**;
2-ethynyl-*N*-(4-(thiazol-5-yl)benzyl)thiazole-4-carboxamide **C61**;
N-(2,3-dihydro-1*H*-inden-2-yl)-2-ethynylthiazole-4-carboxamide **C62**;
N-(2-cyanobenzyl)-2-ethynylthiazole-4-carboxamide **C63**;
2-ethynyl-*N*-(naphthalen-2-ylmethyl)thiazole-4-carboxamide **C64**;
2-ethynyl-*N*-(3-(pyridin-3-yl)benzyl)thiazole-4-carboxamide **C65**;
N-(benzo[*d*]thiazol-6-ylmethyl)-2-ethynylthiazole-4-carboxamide **C66**;
(*R*)-*N*-(1-(3-chlorophenyl)ethyl)-2-ethynylthiazole-4-carboxamide **C67**;
N-(1-(3-chlorophenyl)cyclopropyl)-2-ethynylthiazole-4-carboxamide **C68**;
(*S*)-*N*-(1-(3-chlorophenyl)ethyl)-2-ethynylthiazole-4-carboxamide **C69**;
2-ethynyl-*N*-(2-(hydroxymethyl)benzyl)thiazole-4-carboxamide **C70**;
(*S*)-*N*-(2,3-dihydro-1*H*-inden-1-yl)-2-ethynylthiazole-4-carboxamide **C71**;
(*R*)-*N*-(2,3-dihydro-1*H*-inden-1-yl)-2-ethynylthiazole-4-carboxamide **C72**;
methyl 3-(4-((2-ethynylthiazole-4-carboxamido)methyl)phenyl)propanoate **C73**;
methyl 2-((2-ethynylthiazole-4-carboxamido)methyl)benzoate **C74**;
2-ethynyl-*N*-(4-(1-methyl-1*H*-pyrazol-4-yl)phenethyl)thiazole-4-carboxamide **C75**;
N-(4-(1*H*-pyrazol-4-yl)phenethyl)-2-ethynylthiazole-4-carboxamide **C76**;
N-(2-ethynylthiazol-4-yl)-2-phenylacetamide **C77**;
2-ethynyl-*N*-(1-phenylpiperidin-4-yl)thiazole-4-carboxamide **C78**;
2-ethynyl-*N*-(4-(pyridin-3-yl)phenethyl)thiazole-4-carboxamide **C79**;
N-(4-bromophenethyl)-2-ethynylthiazole-4-carboxamide **C80**;
2-ethynyl-*N*-(3-(methylsulfonamido)phenethyl)thiazole-4-carboxamide **C81**;
N-(3-acetamidophenethyl)-2-ethynylthiazole-4-carboxamide **C82**;
2-ethynyl-*N*-(4-(1-methyl-1*H*-pyrazol-4-yl)benzyl)thiazole-4-carboxamide **C83**;
methyl 4-(2-(2-ethynylthiazole-4-carboxamido)ethyl)benzoate **C84**;
N-(3-aminophenethyl)-2-ethynylthiazole-4-carboxamide **C85**;
N-((2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)methyl)-2-ethynylthiazole-4-carboxamide **C86**;
2-ethynyl-*N*-(3-nitrophenethyl)thiazole-4-carboxamide **C87**;
N-(4-acetamidophenethyl)-2-ethynylthiazole-4-carboxamide **C88**;
N-(4-acetamidobenzyl)-2-ethynylthiazole-4-carboxamide **C89**;
N-benzyl-2-cyanothiazole-4-carboxamide **C90**;

N-(4-(1*H*-pyrazol-3-yl)benzyl)-2-ethynylthiazole-4-carboxamide **C91**;
N-(4-(1*H*-pyrazol-4-yl)benzyl)-2-ethynylthiazole-4-carboxamide **C92**;
2-ethynyl-*N*-(4-(pyridin-3-yl)benzyl)thiazole-4-carboxamide **C93**;
N-(3-acetamidobenzyl)-2-ethynylthiazole-4-carboxamide **C94**;
N-(3-aminobenzyl)-2-ethynylthiazole-4-carboxamide **C95**;
2-ethynyl-*N*-(quinolin-6-ylmethyl)thiazole-4-carboxamide **C96**;
methyl 3-(2-(2-ethynylthiazole-4-carboxamido)ethyl)benzoate **C97**;
N-benzyl-2-ethynyl-1-methyl-1*H*-imidazole-4-carboxamide **C98**;
2-ethynyl-*N*-(4-(methylsulfonamido)phenethyl)thiazole-4-carboxamide **C99**;
2-ethynyl-*N*-methyl-*N*-(4-nitrophenethyl)thiazole-4-carboxamide **C100**;
2-ethynyl-*N*-(4-(methylsulfonyl)phenethyl)thiazole-4-carboxamide **C101**;
N-(4-cyanophenethyl)-2-ethynylthiazole-4-carboxamide **C102**;
2-ethynyl-*N*-(4-nitrobenzyl)thiazole-4-carboxamide **C103**;
N-(4-cyanobenzyl)-2-ethynylthiazole-4-carboxamide **C104**;
2-ethynyl-*N*-(3-(methylsulfonyl)phenethyl)thiazole-4-carboxamide **C105**;
N-(2-chlorophenethyl)-2-ethynylthiazole-4-carboxamide **C106**;
2-ethynyl-*N*-(3-nitrobenzyl)thiazole-4-carboxamide **C107**;
2-ethynyl-*N*-(4-(methylsulfonyl)benzyl)thiazole-4-carboxamide **C108**;
N-((3-chloropyridin-2-yl)methyl)-2-ethynylthiazole-4-carboxamide **C109**;
N-(3-chlorophenethyl)-2-ethynylthiazole-4-carboxamide **C110**;
N-benzyl-2-ethynyl-1*H*-imidazole-4-carboxamide **C111**;
N-([1,1'-biphenyl]-2-ylmethyl)-2-ethynylthiazole-4-carboxamide **C112**;
2-ethynyl-*N*-(naphthalen-1-ylmethyl)thiazole-4-carboxamide **C113**;
N-([1,1'-biphenyl]-4-ylmethyl)-2-ethynylthiazole-4-carboxamide **C114**;
N-([1,1'-biphenyl]-3-ylmethyl)-2-ethynylthiazole-4-carboxamide **C115**;
ethyl 3-(*N*-benzyl-2-ethynylthiazole-4-carboxamido)propanoate **C116**;
methyl 4-((2-ethynylthiazole-4-carboxamido)methyl)benzoate **C117**;
N-(4-aminobenzyl)-2-ethynylthiazole-4-carboxamide **C118**;
2-ethynyl-*N*-((1-methyl-1*H*-pyrazol-3-yl)methyl)thiazole-4-carboxamide **C119**;
2-ethynyl-*N*-((1-methyl-1*H*-pyrazol-4-yl)methyl)thiazole-4-carboxamide **C120**;
2-ethynyl-*N*-(4-hydroxybenzyl)thiazole-4-carboxamide **C121**;

2-ethynyl-*N*-(4-hydroxy-3-methoxyphenethyl)thiazole-4-carboxamide **C122**;

N-(2-ethynylthiazol-4-yl)-3-phenylpropanamide **C123**;

methyl 3-((2-ethynylthiazole-4-carboxamido)methyl)benzoate **C124**;

N-(3-chlorobenzyl)-2-ethynylthiazole-4-carboxamide **C125**;

2-ethynyl-*N*-(pyridin-2-ylmethyl)thiazole-4-carboxamide **C126**;

N-(3-cyanobenzyl)-2-ethynylthiazole-4-carboxamide **C127**;

N-(4-aminophenethyl)-2-ethynylthiazole-4-carboxamide **C128**;

2-ethynyl-*N*-(4-nitrophenethyl)thiazole-4-carboxamide **C129**;

2-ethynyl-*N*-(1*H*-indazol-4-yl)thiazole-4-carboxamide **C130**;

ethyl *N*-benzyl-*N*-(2-ethynylthiazole-4-carbonyl)glycinate **C133**;

N-benzyl-2-ethynyl-1-methyl-1*H*-imidazole-5-carboxamide **C134**;

N-benzyl-2-ethynyl-*N*-(2-hydroxyethyl)thiazole-4-carboxamide **C135**;

2-ethynyl-*N*-(1*H*-indazol-7-yl)thiazole-4-carboxamide **C136**;

(*S*)-2-ethynyl-*N*-(2-hydroxy-2-phenylethyl)thiazole-4-carboxamide **C137**;

N-(2-acetamidobenzyl)-2-ethynylthiazole-4-carboxamide **C138**;

N-benzyl-2-ethynyl-*N*-methylthiazole-4-carboxamide **C139**;

2-ethynyl-*N*-phenethylthiazole-4-carboxamide **C140**;

N-((1*H*-indol-4-yl)methyl)-2-ethynylthiazole-4-carboxamide **C141**;

N-(2-aminobenzyl)-2-ethynylthiazole-4-carboxamide **C142**;

N-benzyl-2-ethynylthiazole-5-carboxamide **C143**;

N-benzyl-2-ethynyloxazole-4-carboxamide **C144**;

N-(2-chlorobenzyl)-2-ethynylthiazole-4-carboxamide **C145**;

2-ethynyl-*N*-(2-methoxybenzyl)thiazole-4-carboxamide **C146**;

N-benzyl-4-ethynylthiazole-2-carboxamide **C147**;

N-benzyl-2-ethynylpyrimidine-4-carboxamide **C148**;

N-benzyl-6-ethynylpicolinamide **C149**;

N-benzyl-2-ethynylthiazole-4-carboxamide **C150**;

N-benzyl-2-ethynylisonicotinamide **C151**;

(4-(4-(1,5-dimethyl-1*H*-indazol-4-yl)phenyl)piperazin-1-yl)(2-ethynylthiazol-4-yl)methanone **D1**;

methyl 4-(4-(4-(2-ethynylthiazole-4-carbonyl)piperazin-1-yl)phenyl)-1-methyl-1*H*-

indazole-6-carboxylate **D2**;

7-(4-(4-(2-ethynylthiazole-4-carbonyl)piperazin-1-yl)phenyl)-*N*-methylbenzo[*d*]thiazole-5-carboxamide **D3**;

methyl 7-(4-(4-(2-ethynylthiazole-4-carbonyl)piperazin-1-yl)phenyl)benzo[*d*]-thiazole-5-carboxylate **D4**;

7-(4-(4-(2-ethynylthiazole-4-carbonyl)piperazin-1-yl)phenyl)benzo[*d*]thiazole-5-carboxamide **D5**;

7-(4-(4-(2-ethynylthiazole-4-carbonyl)piperazin-1-yl)phenyl)-*N*,*N*-dimethylbenzo[*d*]-thiazole-5-carboxamide **D6**;

(4-(4-(benzo[*d*]thiazol-7-yl)phenyl)piperazin-1-yl)(2-ethynylthiazol-5-yl)methanone **D7**;

(4-(4-(benzo[*d*]thiazol-4-yl)phenyl)piperazin-1-yl)(2-ethynylthiazol-5-yl)methanone **D8**;

(4-(4-(benzo[*d*]thiazol-7-yl)-2-chlorophenyl)piperazin-1-yl)(2-ethynylthiazol-4-yl)methanone **D9**;

(4-(5-(benzo[*d*]thiazol-7-yl)pyridin-2-yl)piperazin-1-yl)(2-ethynylthiazol-4-yl)methanone **D10**;

(4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-4-fluoropiperidin-1-yl)(2-ethynylthiazol-4-yl)methanone **D11**;

5-(benzo[*d*]thiazol-7-yl)-2-(4-(2-ethynylthiazole-4-carbonyl)piperazin-1-yl)benzonitrile **D12**;

(3-(4-(benzo[*d*]thiazol-7-yl)phenyl)azetidin-1-yl)(2-ethynylthiazol-4-yl)methanone **D13**;

(4-(4-(benzo[*d*]thiazol-7-yl)phenyl)-4-hydroxypiperidin-1-yl)(2-ethynylthiazol-4-yl)methanone **D14**;

(4-(3-(benzo[*d*]thiazol-7-yl)phenyl)piperidin-1-yl)(2-ethynylthiazol-4-yl)methanone **D15**;

(4-(3-(benzo[*d*]thiazol-7-yl)phenyl)piperazin-1-yl)(2-ethynylthiazol-4-yl)methanone **D16**;

(4-(4-(benzo[*d*]thiazol-7-yl)phenyl)piperazin-1-yl)(2-ethynylthiazol-4-yl)methanone **D17**;

(4-(4-(benzo[*d*]thiazol-7-yl)phenyl)piperidin-1-yl)(2-ethynylthiazol-4-yl)methanone **D18**;

(2-ethynylthiazol-4-yl)(4-(4-(2-methyl-2*H*-indazol-4-yl)phenyl)piperidin-1-yl)methanone **D19**;

(2-ethynylthiazol-4-yl)(4-(4-(1-methyl-1*H*-indazol-4-yl)phenyl)piperidin-1-yl)methanone

D20;

(4-(4-(1*H*-indazol-4-yl)phenyl)piperidin-1-yl)(2-ethynylthiazol-4-yl)methanone **D21**;

(2-ethynylthiazol-4-yl)(4-(4-(1-methyl-1*H*-indazol-4-yl)phenyl)piperazin-1-yl)methanone **D22**;

(2-ethynylthiazol-4-yl)(4-(4-(2-methyl-2*H*-indazol-4-yl)phenyl)piperazin-1-yl)methanone **D23**;

4-(1-(2-ethynylthiazole-4-carbonyl)piperidin-4-yl)benzonitrile **D24**;

(4-(4-(1*H*-indazol-4-yl)phenyl)piperazin-1-yl)(2-ethynylthiazol-4-yl)methanone **D25**;

4-(4-(2-ethynylthiazole-4-carbonyl)piperazin-1-yl)benzonitrile **D26**;

(2-ethynylthiazol-4-yl)(4-(4-nitrophenyl)piperazin-1-yl)methanone **D27**;

(2-ethynylthiazol-4-yl)(4-phenylpiperazin-1-yl)methanone **D28**;

(2-ethynylthiazol-4-yl)(4-phenylpiperidin-1-yl)methanone **D29**;

(3,4-dihydroisoquinolin-2(1*H*)-yl)(2-ethynylthiazol-4-yl)methanone **D30**;

(2-ethynylthiazol-4-yl)(4-hydroxypiperidin-1-yl)methanone **D31**;

(2-ethynylthiazol-4-yl)(2-(2-hydroxyethyl)piperidin-1-yl)methanone **D32**;

(2-ethynylthiazol-4-yl)(3-(hydroxymethyl)piperidin-1-yl)methanone **D33**;

(2-ethynylthiazol-4-yl)(3-hydroxypiperidin-1-yl)methanone **D34**;

methyl 1-(2-ethynylthiazole-4-carbonyl)piperidine-4-carboxylate **D35**;

methyl 1-(2-ethynylthiazole-4-carbonyl)piperidine-3-carboxylate **D36**;

methyl 1-(2-ethynylthiazole-4-carbonyl)piperidine-2-carboxylate **D37**;

3-(4-(benzo[*d*]thiazol-7-yl)phenyl)-*N*-(2-ethynylthiazol-4-yl)propanamide **E1**;

(*S*)-2-amino-*N*-(2-ethynylthiazol-4-yl)-3-phenylpropanamide **E2**;

(*R*)-2-amino-*N*-(2-ethynylthiazol-4-yl)-3-phenylpropanamide **E3**;

N-(2-ethynylthiazol-4-yl)-3-(4-(1-methyl-1*H*-indazol-4-yl)phenyl)propanamide **E4**;

(*R*)-2-amino-3-(2-cyanophenyl)-*N*-(2-ethynylthiazol-4-yl)propenamide **E5**;

2-ethynyl-*N*-(3-(thiazol-5-yl)phenethyl)thiazole-4-carboxamide **E6**;

2-ethynyl-*N*-(3-(thiazol-4-yl)phenethyl)thiazole-4-carboxamide **E7**;

(*S*)-2-amino-3-(2-cyanophenyl)-*N*-(2-ethynylthiazol-4-yl)propenamide **E8**;

3-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(2-ethynylthiazol-4-yl)propanamide **E9**;

N-(2-ethynylthiazol-4-yl)quinoline-2-carboxamide **E10**;

N-(2-ethynylthiazol-4-yl)cinnamamide **E11**; or

N-(2-ethynylthiazol-4-yl)benzamide **E12**;

or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof.

15. A pharmaceutical composition comprising the compound of any one of claims 1 to 14, or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; and a pharmaceutically acceptable excipient.

16. Use of a compound of any one of claims 1 to 14, or an enantiomer, a mixture of enantiomers, a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof, in the manufacture of a medicament for treating a proliferative disease or a disorder, disease, or condition mediated by a glutathione peroxidase 4.