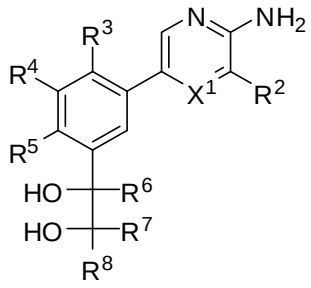
~~WHAT IS CLAIMED IS:~~

CLAIMS:

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof; wherein:

X^1 is N or CR^1;

R^1 is selected from H, D, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, CN, OH, and NH_2;

R^2 is $C(O)NR^{c1}R^{d1}$;

R^3, R^4 and R^5 are each independently selected from H, D, halo, CN, OH, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, cyano-C_{1-6} alkyl, HO-C_{1-6} alkyl, C_{1-6} alkoxy-C_{1-6} alkyl, C_{3-6} cycloalkyl, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, and $C(O)NR^cR^d$, wherein the C_{1-6} alkyl is optionally substituted by 1, 2, 3, 4, 5, or 6 D;

R^6, R^7 and R^8 are each independently selected from H, D, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, $C(O)R^{b3}$, $C(O)NR^{c3}R^{d3}$, $C(O)NR^{c3}(OR^{a3})$, $C(O)OR^{a3}$, $C(=NR^{e3})R^{b3}$, $C(=NOH)R^{b3}$, $C(=NCN)R^{b3}$, and $C(=NR^{e3})NR^{c3}R^{d3}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^6, R^7, and R^8 are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^B substituents; and wherein the C_{1-6} haloalkyl of R^6, R^7, or R^8 is optionally substituted by 1, 2, 3, or 4 independently selected Y substituents;

each Y is independently selected from D, halo, C_{1-6} alkyl, and C_{1-6} haloalkyl;

or R^6 and R^7 substituents, together with the ring atoms to which they are attached, form a C_{3-10} cycloalkyl or 4-7 membered heterocycloalkyl, each of which is optionally substituted with 1, 2, 3, or 4 independently selected R^B substituents;

or R^7 and R^8 substituents, together with the ring atoms to which they are attached, form a C_{3-10} cycloalkyl or 4-7 membered heterocycloalkyl, each of which is optionally substituted with 1, 2, 3, or 4 independently selected R^B substituents;

R^c and R^d are each independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^c and R^d, are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^M substituents;

each R^{c1} and R^{d1} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{c1} and R^{d1} are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^A substituents;

or, any R^{c1} and R^{d1}, attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^A substituents;

each R^{a3}, R^{b3}, R^{c3}, and R^{d3} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{a3}, R^{b3}, R^{c3}, and R^{d3} are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^B substituents;

or, any R^{c3} and R^{d3}, attached to the same N atom, together with the N atom to which they are attached, form a 5- or 6-membered heteroaryl or a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 5- or 6-membered heteroaryl or 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^B substituents;

each R^{e3} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^A is independently selected from D, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, CN, NO_2, OR^{a4}, SR^{a4}, $NHOR^{a4}$, $C(O)R^{b4}$, $C(O)NR^{c4}R^{d4}$, $C(O)NR^{c4}(OR^{b4})$, $C(O)OR^{a4}$, $OC(O)R^{b4}$, $OC(O)NR^{c4}R^{d4}$, $NR^{c4}R^{d4}$, $NR^{c4}NR^{c4}R^{d4}$, $NR^{c4}C(O)R^{b4}$, $NR^{c4}C(O)OR^{a4}$, $NR^{c4}C(O)NR^{c4}R^{d4}$, $C(=NR^{e4})R^{b4}$, $C(=NOH)R^{b4}$, $C(=NCN)R^{b4}$, $C(=NR^{e4})NR^{c4}R^{d4}$, $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$, $NR^{c4}C(=NR^{e4})R^{b4}$, $NR^{c4}C(=NOH)NR^{c4}R^{d4}$, $NR^{c4}C(=NCN)NR^{c4}R^{d4}$, $NR^{c4}S(O)R^{b4}$, $NR^{c4}S(O)NR^{c4}R^{d4}$, $NR^{c4}S(O)_2R^{b4}$, $NR^{c4}S(O)_2NR^{c4}R^{d4}$, $S(O)R^{b4}$, $S(O)NR^{c4}R^{d4}$, $S(O)_2R^{b4}$, $S(O)_2NR^{c4}R^{d4}$, $OS(O)(=NR^{e4})R^{b4}$, $OS(O)_2R^{b4}$, SF_5, $P(O)R^{f4}R^{g4}$, $OP(O)(OR^{h4})(OR^{i4})$, $P(O)(OR^{h4})(OR^{i4})$, and $BR^{j4}R^{k4}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^A is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^D substituents;

each R^B is independently selected from D, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, CN, NO_2, OR^{a2}, SR^{a2}, $NHOR^{a2}$, $C(O)R^{b2}$, $C(O)NR^{c2}R^{d2}$, $C(O)NR^{c2}(OR^{b2})$, $C(O)OR^{a2}$, $OC(O)R^{b2}$, $OC(O)NR^{c2}R^{d2}$, $NR^{c2}R^{d2}$, $NR^{c2}NR^{c2}R^{d2}$, $NR^{c2}C(O)R^{b2}$, $NR^{c2}C(O)OR^{a2}$, $NR^{c2}C(O)NR^{c2}R^{d2}$, $C(=NR^{e2})R^{b2}$, $C(=NOH)R^{b2}$, $C(=NCN)R^{b2}$, $C(=NR^{e2})NR^{c2}R^{d2}$, $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$, $NR^{c2}C(=NR^{e2})R^{b2}$, $NR^{c2}C(=NOH)NR^{c2}R^{d2}$, $NR^{c2}C(=NCN)NR^{c2}R^{d2}$, $NR^{c2}S(O)R^{b2}$, $NR^{c2}S(O)NR^{c2}R^{d2}$, $NR^{c2}S(O)_2R^{b2}$, $NR^{c2}S(O)_2NR^{c2}R^{d2}$, $S(O)R^{b2}$, $S(O)NR^{c2}R^{d2}$, $S(O)_2R^{b2}$, $S(O)_2NR^{c2}R^{d2}$, $OS(O)(=NR^{e2})R^{b2}$, $OS(O)_2R^{b2}$, SF_5, $P(O)R^{f2}R^{g2}$, $OP(O)(OR^{h2})(OR^{i2})$, $P(O)(OR^{h2})(OR^{i2})$, and $BR^{j2}R^{k2}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^B is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^M substituents;

each R^{a2}, R^{b2}, R^{c2}, and R^{d2} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{a2}, R^{b2}, R^{c2}, and R^{d2} are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^M substituents;

or, any R^{c2} and R^{d2} attached to the same N atom, together with the N atom to which they are attached, form a 5- or 6-membered heteroaryl or a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 5- or 6-membered heteroaryl or 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^M substituents;

each R^{e2} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{f2} and R^{g2} is independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{h2} and R^{i2} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{j2} and R^{k2} is independently selected from OH, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

or any R^{j2} and R^{k2} attached to the same B atom, together with the B atom to which they are attached, form a 5- or 6-membered heterocycloalkyl group optionally substituted with 1, 2, 3, or 4 substituents independently selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

each R^{a4}, R^{b4}, R^{c4}, and R^{d4} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered

heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{a4}, R^{b4}, R^{c4}, and R^{d4} are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^D substituents;

or, any R^{c4} and R^{d4} attached to the same N atom, together with the N atom to which they are attached, form a 5- or 6-membered heteroaryl or a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 5- or 6-membered heteroaryl or 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^D substituents;

each R^{e4} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{f4} and R^{g4} is independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{h4} and R^{i4} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{j4} and R^{k4} is independently selected from OH, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

or any R^{j4} and R^{k4} attached to the same B atom, together with the B atom to which they are attached, form a 5- or 6-membered heterocycloalkyl group optionally substituted with 1, 2, 3, or 4 substituents independently selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

each R^D is independently selected from H, D, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, CN, NO_2, OR^{a5}, SR^{a5}, $NHOR^{a5}$, $C(O)R^{b5}$, $C(O)NR^{c5}R^{d5}$, $C(O)NR^{c5}(OR^{b5})$, $C(O)OR^{a5}$, $OC(O)R^{b5}$, $OC(O)NR^{c5}R^{d5}$, $NR^{c5}R^{d5}$, $NR^{c5}NR^{c5}R^{d5}$, $NR^{c5}C(O)R^{b5}$, $NR^{c5}C(O)OR^{a5}$, $NR^{c5}C(O)NR^{c5}R^{d5}$, $C(=NR^{e5})R^{b5}$,

$C(=NOH)R^{b5}$, $C(=NCN)R^{b5}$, $C(=NR^{e5})NR^{c5}R^{d5}$, $NR^{c5}C(=NR^{e5})NR^{c5}R^{d5}$, $NR^{c5}C(=NR^{e5})R^{b5}$, $NR^{c5}C(=NOH)NR^{c5}R^{d5}$, $NR^{c5}C(=NCN)NR^{c5}R^{d5}$, $NR^{c5}S(O)R^{b5}$, $NR^{c5}S(O)NR^{c5}R^{d5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$, $S(O)R^{b5}$, $S(O)NR^{c5}R^{d5}$, $S(O)_2R^{c5}$, $S(O)_2NR^{c5}R^{d5}$, $OS(O)(=NR^{e5})R^{b5}$, $OS(O)_2R^{b5}$, SF_5, $P(O)R^{f5}R^{g5}$, $OP(O)(OR^{h5})(OR^{i5})$, $P(O)(OR^{h5})(OR^{i5})$, and $BR^{j5}R^{k5}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^D are each optionally substituted with 1, 2, 3, or 4 independently selected R^E substituents;

each R^{a5}, R^{b5}, R^{c5}, and R^{d5} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{a5}, R^{b5}, R^{c5}, and R^{d5} are each optionally substituted with 1, 2, 3, or 4 independently selected R^E substituents;

or, any R^{c5} and R^{d5} attached to the same N atom, together with the N atom to which they are attached, form a 5- or 6-membered heteroaryl or a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 5- or 6-membered heteroaryl or 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, or 4 independently selected R^E substituents;

each R^{e5} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{f5} and R^{g5} is independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{h5} and R^{i5} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered

~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{j5} and R^{k5} is independently selected from OH, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

or any R^{j5} and R^{k5} attached to the same B atom, together with the B atom to which they are attached, form a 5- or 6-membered heterocycloalkyl group optionally substituted with 1, 2, 3, or 4 substituents independently selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

each R^E is independently selected from H, D, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, CN, NO_2, OR^{a6}, SR^{a6}, $NHOR^{a6}$, $C(O)R^{b6}$, $C(O)NR^{c6}R^{d6}$, $C(O)NR^{c6}(OR^{b6})$, $C(O)OR^{a6}$, $OC(O)R^{b6}$, $OC(O)NR^{c6}R^{d6}$, $NR^{c6}R^{d6}$, $NR^{c6}NR^{c6}R^{d6}$, $NR^{c6}C(O)R^{b6}$, $NR^{c6}C(O)OR^{a6}$, $NR^{c6}C(O)NR^{c6}R^{d6}$, $C(=NR^{e6})R^{b6}$, $C(=NOH)R^{b6}$, $C(=NCN)R^{b6}$, $C(=NR^{e6})NR^{c6}R^{d6}$, $NR^{c6}C(=NR^{e6})NR^{c6}R^{d6}$, $NR^{c6}C(=NR^{e6})R^{b6}$, $NR^{c6}C(=NOH)NR^{c6}R^{d6}$, $NR^{c6}C(=NCN)NR^{c6}R^{d6}$, $NR^{c6}S(O)R^{b6}$, $NR^{c6}S(O)NR^{c6}R^{d6}$, $NR^{c6}S(O)_2R^{b6}$, $NR^{c6}S(O)_2NR^{c6}R^{d6}$, $S(O)R^{b6}$, $S(O)NR^{c6}R^{d6}$, $S(O)_2R^{c6}$, $S(O)_2NR^{c6}R^{d6}$, $OS(O)(=NR^{e6})R^{b6}$, $OS(O)_2R^{b6}$, SF_5, $P(O)R^{f6}R^{g6}$, $OP(O)(OR^{h6})(OR^{i6})$, $P(O)(OR^{h6})(OR^{i6})$, and $BR^{j6}R^{k6}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^E are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^G substituents;

each R^{a6}, R^{b6}, R^{c6}, and R^{d6} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{a6}, R^{b6}, R^{c6}, and R^{d6} are each optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^G substituents;

or, any R^{c6} and R^{d6} attached to the same N atom, together with the N atom to which they are attached, form a 5- or 6-membered heteroaryl or a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 5- or 6-membered heteroaryl or 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^G substituents;

each R^{e6} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{f6} and R^{g6} is independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{h6} and R^{i6} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered ~~hetereocycloalkyl~~heterocycloalkyl)-C_{1-6} alkyl-;

each R^{j6} and R^{k6} is independently selected from OH, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

or any R^{j6} and R^{k6} attached to the same B atom, together with the B atom to which they are attached, form a 5- or 6-membered heterocycloalkyl group optionally substituted with 1, 2, 3, or 4 substituents independently selected from C_{1-6} alkyl and C_{1-6} haloalkyl;

each R^{G} is independently selected from H, D, halo, CN, NO_2, SF_5, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl; and

each R^{M} is independently selected from H, D, OH, NO_2, CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, cyano-C_{1-6} alkyl, HO-C_{1-6} alkyl, C_{1-6} alkoxy-C_{1-6} alkyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-7} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, thio, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, carbamyl, C_{1-6} alkylcarbamyl, di(C_{1-6} alkyl)carbamyl, carboxy, C_{1-6} alkylcarbonyl, C_{1-4} alkoxycarbonyl, C_{1-6} alkylcarbonylamino, C_{1-6} alkylsulfonylamino, aminosulfonyl, C_{1-6} alkylaminosulfonyl, di(C_{1-6} alkyl)aminosulfonyl, aminosulfonylamino, C_{1-6} alkylaminosulfonylamino, di(C_{1-6} alkyl)aminosulfonylamino, aminocarbonylamino, C_{1-6} alkylaminocarbonylamino, and di(C_{1-6} alkyl)aminocarbonylamino.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is H, D or C_{1-6} alkyl.

3. The compound of any one of claims 1 and 2, wherein each R^A is independently selected from D, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, ~~C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl C_{1-6} alkyl , C_{3-7} cycloalkyl C_{1-6} alkyl , (5-10 membered heteroaryl) C_{1-6} alkyl , (4-10 membered heterocycloalkyl) C_{1-6} alkyl , CN, NO_2~~CN, OR^{a4}, ~~SR^{a4}, $NHOR^{a4}$, $C(O)R^{b4}$, $C(O)$~~and $NR^{c4}R^{d4}$, ~~$C(O)NR^{c4}(OR^{b4})$, $C(O)OR^{a4}$, $OC(O)R^{b4}$, $OC(O)NR^{c4}R^{d4}$, $NR^{c4}R^{d4}$, $NR^{c4}NR^{c4}R^{d4}$, $NR^{c4}C(O)R^{b4}$, $NR^{c4}C(O)OR^{a4}$, $NR^{c4}C(O)NR^{c4}R^{d4}$, $NR^{c4}S(O)R^{b4}$, $NR^{c4}S(O)NR^{c4}R^{d4}$, $NR^{c4}S(O)_2R^{b4}$, $NR^{c4}S(O)_2NR^{c4}R^{d4}$, $S(O)R^{b4}$, $S(O)NR^{c4}R^{d4}$, $S(O)_2R^{b4}$, $S(O)_2NR^{c4}R^{d4}$, and $OS(O)_2R^{b4}$,~~; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, ~~C_{2-6} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl C_{1-6} alkyl , C_{3-7} cycloalkyl C_{1-6} alkyl , (5-10 membered heteroaryl) C_{1-6} alkyl ,~~ and ~~(4-10 membered heterocycloalkyl) C_{1-6} alkyl~~ C_{2-6} alkynyl of R^A are each optionally substituted with 1, 2, 3, ~~4, 5, 6, 7,~~ or ~~8~~4 independently selected R^D substituents;

each R^{a4}, ~~R^{b4},~~ R^{c4}, and R^{d4} is independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl, ~~C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, C_{3-7} cycloalkyl, 5-6 membered heteroaryl, 4-7 membered heterocycloalkyl, phenyl C_{1-6} alkyl , C_{3-7} cycloalkyl C_{1-6} alkyl , (5-6 membered heteroaryl) C_{1-6} alkyl , and (4-7 membered heterocycloalkyl) C_{1-6} alkyl ,~~ wherein the C_{1-6} alkyl~~, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, C_{3-7} cycloalkyl, 5-6 membered heteroaryl, 4-7 membered heterocycloalkyl, phenyl C_{1-6} alkyl , C_{3-7} cycloalkyl C_{1-6} alkyl , (5-6 membered heteroaryl) C_{1-6} alkyl , and (4-7 membered heterocycloalkyl) C_{1-6} alkyl~~ of R^{a4}, ~~R^{b4},~~ R^{c4}, and R^{d4} are each optionally substituted with 1, 2, 3, ~~4, 5, 6, 7,~~ or ~~8~~4 independently selected R^D substituents; and

~~or, any R^{c4} and R^{d4} attached to the same N atom, together with the N atom to which they are attached, form a 5- or 6-membered heteroaryl or a 4 , 5 , 6 , or 7-membered heterocycloalkyl group, wherein the 5- or 6-membered heteroaryl or 4 , 5 , 6 , or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, 6, 7, or 8 independently selected R^D substituents; and~~

each R^D is independently selected from D, OH, ~~NO_2,~~ CN, halo, C_{1-6} alkyl, ~~C_{2-6} alkenyl, C_{2-6} alkynyl,~~ C_{1-6} haloalkyl, ~~cyano C_{1-6} alkyl, HO C_{1-6} alkyl, C_{1-6} alkoxy C_{1-6} alkyl, C_{3-7} cycloalkyl,~~ C_{1-6} alkoxy, C_{1-6} haloalkoxy, amino, C_{1-6} alkylamino, and di(C_{1-6} alkyl)amino~~, thio, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, carbamyl, C_{1-6} alkylcarbamyl, di(C_{1-6} alkyl)carbamyl, carboxy, C_{1-6} alkylcarbonyl, C_{1-4} alkoxycarbonyl, C_{1-6} alkylcarbonylamino, C_{1-6} alkylsulfonylamino, aminosulfonyl, C_{1-6} alkylaminosulfonyl, di(C_{1-6} alkyl)aminosulfonyl,~~

~~aminosulfonylamino, C_{1-6} alkylaminosulfonylamino, di(C_{1-6} alkyl)aminosulfonylamino, aminocarbonylamino, C_{1-6} alkylaminocarbonylamino, and di(C_{1-6} alkyl)aminocarbonylamino~~.

~~4. The compound of any one of claims 1-3, wherein each R^A is independently selected from D, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, CN, OR^{a4}, and $NR^{c4}R^{d4}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl of R^A are each optionally substituted with 1, 2, 3, or 4 independently selected R^D substituents;~~

~~each R^{a4}, R^{c4}, and R^{d4} is independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl, wherein the C_{1-6} alkyl of R^{a4}, R^{c4}, and R^{d4} are each optionally substituted with 1, 2, 3, or 4 independently selected R^D substituents; and~~

~~each R^D is independently selected from D, OH, CN, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, amino, C_{1-6} alkylamino, and di(C_{1-6} alkyl)amino.~~

~~5~~4. The compound of any one of claims 1 and 2, or a pharmaceutically acceptable salt thereof, wherein each R^{c1} and R^{d1} is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{c1} and R^{d1} are each optionally substituted with 1, 2, 3, or 4 independently selected R^A substituents;

or, any R^{c1} and R^{d1}, attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, or 4 independently selected R^A substituents.

~~6. The compound of any one of claims 1 and 2, or a pharmaceutically acceptable salt thereof, wherein:~~

~~each R^{c1} and R^{d1} is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl C_{1-6} alkyl , C_{3-10} cycloalkyl C_{1-6} alkyl , (5-10 membered heteroaryl) C_{1-6} alkyl , and (4-10 membered heterocycloalkyl) C_{1-6} alkyl , wherein the C_{1-6} alkyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl C_{1-6} alkyl , C_{3-10} cycloalkyl C_{1-6} alkyl , (5-10 membered~~

heteroaryl)-C_{1-6}-alkyl-, and (4-10-membered heterocycloalkyl)-C_{1-6}-alkyl- of R^{c1} and R^{d1} are each optionally substituted with 1, 2, 3, or 4 independently selected R^A substituents;

or, any R^{c1} and R^{d1}, attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1, 2, 3, or 4 independently selected R^A substituents;

each R^A is independently selected from D, halo, oxo, C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{2-6}-alkenyl, and C_{2-6}-alkynyl, CN, NO_2, and OR^{a4}, wherein the C_{1-6}-alkyl, C_{2-6}-alkenyl, and C_{2-6}-alkynyl of R^A is optionally substituted with 1 or 2 independently selected R^D substituents;

each R^{a4} is independently selected from H and C_{1-6}-alkyl, wherein the C_{1-6}-alkyl is optionally substituted CN, NO_2, or OH; and

each R^D is OH.

7. The compound of any one of claims 1 and 2, or a pharmaceutically acceptable salt thereof, wherein:

R^{c1} is H;

R^{d1} is selected from C_{1-6}-alkyl, C_{3-7}-cycloalkyl, 4-7-membered heterocycloalkyl, phenyl-C_{1-4}-alkyl-, and C_{3-7}-cycloalkyl-C_{1-4}-alkyl-, wherein the C_{1-6}-alkyl, C_{3-7}-cycloalkyl, 4-7-membered heterocycloalkyl, phenyl-C_{1-4}-alkyl-, and C_{3-7}-cycloalkyl-C_{1-4}-alkyl- of R^{c1} and R^{d1} are each optionally substituted with 1 or 2 independently selected R^A substituents;

or, any R^{c1} and R^{d1}, attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1 or 2 independently selected R^A substituent; and

each R^A is independently selected from oxo, methyl, CH_2F, CHF_2, CF_3, OCH_3, CH_2OH, CN and OH.

8. The compound of any one of claims 1 and 2, or a pharmaceutically acceptable salt thereof, wherein:

R^{c1} is H;

R^{d1} is selected from ethyl, propyl, isopropyl, butyl, tert-butyl, cyclobutyl, cyclohexyl, bicyclo[1.1.1]pentanyl, bicyclo[2.1.1]hexanyl, bicyclo[2.2.1]heptanyl, methyl-cyclopropyl, methyl-cyclopbutyl, methyl-phenyl, ethyl-phenyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, pyrorolidinyl, and thianyl, wherein the ethyl, propyl, isopropyl, tert-butyl, cyclobutyl, cyclohexyl, bicyclo[1.1.1]pentanyl, bicyclo[2.1.1]hexanyl, bicyclo[2.2.1]heptanyl,

~~methyl-cyclopropyl, methyl-cyclopbutyl, methyl-phenyl, ethyl-phenyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, pyrorolidinyl and thianyl of R^{d1} are each optionally substituted with 1 or 2 independently selected R^A substituents;~~

~~or, any R^{e1} and R^{d1}, attached to the same N atom, together with the N atom to which they are attached, for a azetidinyl or pyrrolidinyl, wherein the azetidinyl or pyrrolidinyl is optionally substituted with 1 or 2 independently selected R^A substituents; and~~

~~each R^A is independently selected from oxo, methyl, CH_2F, CHF_2, CF_3, OCH_3, CH_2OH, CN and OH.~~

~~9. The compound of any claims 1-8, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from H, D, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, CN, OH, and NH_2, wherein C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.~~

~~10. The compound of any claims 1-8, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_{1-6} alkyl, which is optionally substituted with 1, 2, or 3 D.~~

~~11. The compound of any claims 1-8, or a pharmaceutically acceptable salt thereof, wherein R^3 is methyl or CD_3.~~

~~12. The compound of any claims 1-8, or a pharmaceutically acceptable salt thereof, wherein R_3 is methyl.~~

~~13. The compound of any claims 1-8, or a pharmaceutically acceptable salt thereof, wherein R^3 is CD_3.~~

~~14~~5. The compound of any one of claims 1-~~13~~4, or a pharmaceutically acceptable salt thereof, wherein R^4 is H, D, or C_{1-6} alkyl, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.

~~15. The compound of any claims 1-13, or a pharmaceutically acceptable salt thereof, wherein R^4 is H.~~

~~16~~6. The compound of any one of claims 1-~~13~~4, or a pharmaceutically acceptable salt thereof, wherein R^5 is H, D, or C_{1-6} alkyl, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.

~~17~~7. The compound of any one of claims 1-~~13~~4, or a pharmaceutically acceptable salt thereof, wherein R^5 is H.

~~18. The compound of any claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R^6 is selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl C_{1-6} alkyl , C_{3-10} cycloalkyl C_{1-6} alkyl , (5-10 membered heteroaryl) C_{1-6} alkyl , (4-10 membered heterocycloalkyl) C_{1-6} alkyl , CN, NO_2, OH, COOH, and NH_2, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.~~

~~19. The compound of any claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R^6 is selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, CN, NO_2, OH, COOH and NH_2, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.~~

~~20~~8. The compound of any one of claims 1-~~17~~7, or a pharmaceutically acceptable salt thereof, wherein R^6 is H, D, C_{1-6} alkyl or C_{1-6} haloalkyl, wherein each halogen is F, wherein the haloalkyl is optionally substituted with 1 or 2 independently selected Y substituents, wherein each Y substituent is independently selected from D, halo, C_{1-6} alkyl, and C_{1-6} haloalkyl.

~~21. The compound of any claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R^6 is C_{1-6} haloalkyl, wherein each halogen is F.~~

~~22. The compound of any claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R^6 is H, CH_2F, CHF_2 or CF_3.~~

~~23. The compound of any claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R^6 is CH_2F, CHF_2 or CF_3.~~

~~24. The compound of any claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R^6 is CF_3.~~

~~25~~9. The compound of any one of claims 1-~~24~~8, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.

~~26. The compound of any claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^7 is H, D or C_{1-6} alkyl, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.~~

~~27. The compound of any claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^7 is methyl or ethyl.~~

~~28. The compound of any claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^7 is H.~~

~~29~~10. The compound of any one of claims 1-~~28~~9, or a pharmaceutically acceptable salt thereof, wherein R^8 is selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D.

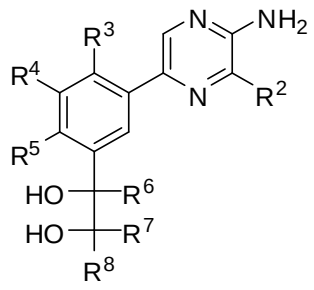
~~30.~~11. The compound of any one of claims 1-~~28~~9, or a pharmaceutically acceptable salt thereof, wherein R^8 is H~~, D or C_{1-6} alkyl, wherein the C_{1-6} alkyl is optionally substituted with 1, 2, or 3 D~~.

~~31. The compound of any claims 1-28, or a pharmaceutically acceptable salt thereof, wherein R^8 is methyl or ethyl.~~

~~32. The compound of any claims 1-28, or a pharmaceutically acceptable salt thereof, wherein R^8 is H.~~

~~33. The compound of any claims 1-32, or a pharmaceutically acceptable salt thereof, wherein R^7 and R^8, together with the C atom to which they are attached, form a cyclopropyl or cyclobutyl.~~

~~34~~12. The compound of any one of claims 1-~~33~~11, having Formula (II):



(II)

or a pharmaceutically acceptable salt thereof.

~~35. The compound of any claims 1-33, having Formula (III):~~

~~(III)~~

~~or a pharmaceutically acceptable salt thereof.~~

~~36. The compound of claim 1, having Formula (VI):~~

~~(VI)~~

~~or a pharmaceutically acceptable salt thereof.~~

~~37. The compound of claim 1, having Formula (VII):~~

~~(VII)~~

~~or a pharmaceutically acceptable salt thereof.~~

~~38~~13. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

X^1 is N or CH;

R^2 is $C(O)NR^{c1}R^{d1}$;

each R^{c1} and R^{d1} is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- of R^{c1} and R^{d1} are each optionally substituted with 1, 2, 3, or 4 independently selected R^A substituents;

or, any R^{c1} and R^{d1}, attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group, wherein the 4-, 5-, 6-, or 7-membered heterocycloalkyl group is optionally substituted with 1 or 2 independently selected R^A substituents;

each R^A is independently selected from D, halo, oxo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, CN, NO_2 and OR^{a4}, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl of R^A is optionally substituted with 1 or 2 independently selected R^D substituents;

each R^{a4} is independently selected from H and C_{1-6} alkyl, wherein the C_{1-6} alkyl is optionally substituted CN, NO_2 or OH;

each R^D is OH;

each R^3, R^4, and R^5 is independently selected from H, D, halo, CN, OH, C_{1-3} alkyl, and C_{1-3} haloalkyl, wherein the C_{1-3} alkyl is optionally substituted by 1, 2, 3, 4, 5, or 6 D; and

each R^6, R^7, and R^8 is independently selected from H, D, C_{1-6} alkyl and C_{1-6} haloalkyl.

~~39~~14. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

X^1 is N;

R^2 is $C(O)NR^{c1}R^{d1}$;

R^{c1} is H;

R^{d1} is selected from ethyl, propyl, isopropyl, butyl, tert-butyl, cyclobutyl, cyclohexyl, bicyclo[1.1.1]pentanyl, bicyclo[2.1.1]hexanyl, bicyclo[2.2.1]heptanyl, methyl-cyclopropyl, methyl-~~cyclopbutyl~~cyclobutyl, methyl-phenyl, ethyl-phenyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, ~~pyrorolidinyl~~pyrrolidinyl, and thianyl, wherein the ethyl, propyl, isopropyl, tert-butyl, cyclobutyl, cyclohexyl, bicyclo[1.1.1]pentanyl, bicyclo[2.1.1]hexanyl, bicyclo[2.2.1]heptanyl, methyl-cyclopropyl, methyl-~~cyclopbutyl~~cyclobutyl, methyl-phenyl, ethyl-phenyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, ~~pyrorolidinyl~~pyrrolidinyl, and thianyl of R^{d1} is optionally substituted with 1 or 2 independently selected R^A substituents;

or, any R^{c1} and R^{d1}, attached to the same N atom, together with the N atom to which they are attached, form an azetidinyl or pyrrolidinyl, wherein the azetidinyl or pyrrolidinyl is optionally substituted with 1 or 2 independently selected R^A substituents;

each R^A is independently selected from oxo, methyl, CH_2F, CHF_2, CF_3, $-OCH_3$, $-CH_2OH$, CN, and OH;

R^3 is selected from H, methyl, and CD_3;

R^4 and R^5 are each H;

R^6 is selected from CH_2F, CHF_2 and CF_3; and

R^7 and R^8 are each H.

~~40~~15. The compound of claim 1, selected from:

3-Amino-6-(2-(methyl-d_3)-5-(1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)-*N*-(tetrahydro-2*H*-pyran-4-yl)pyrazine-2-carboxamide;

3-Amino-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-(methyl-d_3)phenyl)-*N*-(4-hydroxybicyclo[2.2.1]heptan-1-yl)pyrazine-2-carboxamide;

3-Amino-6-(2-(methyl-d_3)-5-(1,1,1-trifluoro-2,3-dihydroxybutan-2-yl)phenyl)-*N*-(tetrahydro-2*H*-pyran-4-yl)pyrazine-2-carboxamide;

3-Amino-6-(2-methyl-5-(1,1,1-trifluoro-2,3-dihydroxy-3-methylbutan-2-yl)phenyl)-*N*-(tetrahydro-2*H*-pyran-4-yl)pyrazine-2-carboxamide;

3-amino-*N*-((1*s*,3*R*)-3-cyanocyclobutyl)-6-(2-(methyl-d_3)-5-((*S*)-1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

3-amino-*N*-((1*S*,2*S*)-2-hydroxycyclohexyl)-6-(2-(methyl-d_3)-5-((*S*)-1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

3-amino-*N*-((*trans*)-3-hydroxytetrahydro-2*H*-pyran-4-yl)-6-(2-(methyl-d_3)-5-((*S*)-1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

3-amino-*N*-((1*s*,3*R*)-3-hydroxy-3-(trifluoromethyl)cyclobutyl)-6-(2-(methyl-d_3)-5-((*S*)-1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

3-amino-*N*-((1*s*,3*R*)-3-hydroxy-1-methylcyclobutyl)-6-(2-(methyl-d_3)-5-((*S*)-1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

(*S*)-3-amino-*N*-(4-(hydroxymethyl)bicyclo[2.1.1]hexan-1-yl)-6-(2-(methyl-d_3)-5-(1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

(*S*)-3-amino-*N*-(3-(hydroxymethyl)bicyclo[1.1.1]pentan-1-yl)-6-(2-(methyl-d_3)-5-(1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

3-amino-*N*-((*S*)-1-hydroxypropan-2-yl)-6-(2-(methyl-d_3)-5-((*S*)-1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

(*S*)-3-amino-*N*-(2-cyano-2-methylpropyl)-6-(2-(methyl-d_3)-5-(1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

(*S*)-3-amino-*N*-(4-hydroxybicyclo[2.2.1]heptan-1-yl)-6-(2-(methyl-d_3)-5-(1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

3-amino-*N*-((*R*)-1-hydroxypropan-2-yl)-6-(2-(methyl-d_3)-5-((*S*)-1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

(*S*)-3-amino-*N*-(4-hydroxybicyclo[2.1.1]hexan-1-yl)-6-(2-(methyl-d_3)-5-(1,1,1-trifluoro-2,3-dihydroxypropan-2-yl)phenyl)pyrazine-2-carboxamide;

3-amino-6-(5-((*S*)-1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-(methyl-d_3)phenyl)-*N*-((1*S*,2*S*)-2-hydroxycyclohexyl)pyrazine-2-carboxamide;

3-amino-6-(5-((*S*)-1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-(methyl-d_3)phenyl)-*N*-((1*R*,2*R*)-2-hydroxycyclohexyl)pyrazine-2-carboxamide;

(*S*)-3-amino-*N*-(4-cyanobicyclo[2.1.1]hexan-1-yl)-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-(methyl-d_3)phenyl)pyrazine-2-carboxamide;

(*S*)-3-amino-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-(methyl-d3)phenyl)-N-(tetrahydro-2H-pyran-4-yl)pyrazine-2-carboxamide;

(*S*)-3-amino-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)-*N*-(tetrahydro-2*H*-pyran-4-yl)pyrazine-2-carboxamide;

3-amino-6-(5-((*S*)-1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)-*N*-((*S*)-1-hydroxypropan-2-yl)pyrazine-2-carboxamide;

3-amino-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)-*N*-(4-hydroxybicyclo[2.2.1]heptan-1-yl)pyrazine-2-carboxamide;

(3-amino-6-(5-((*S*)-1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)pyrazin-2-yl)((*R*)-2-(hydroxymethyl)pyrrolidin-1-yl)methanone;

(*S*)-3-amino-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)-*N*-isopropylpyrazine-2-carboxamide;

3-amino-6-(5-((*S*)-1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)-N-(3-methyltetrahydrofuran-3-yl)pyrazine-2-carboxamide; and

3-Amino-N-(4-cyanobicyclo[2.1.1]hexan-1-yl)-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)pyrazine-2-carboxamide;

or an ~~enationmer~~enantiomer, diastereomer or tautomer thereof;

or a pharmaceutically acceptable salt thereof.

16. The compound of claim 1, which is (S)-3-amino-N-(4-cyanobicyclo[2.1.1]hexan-1-yl)-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-(methyl-d3)phenyl)pyrazine-2-carboxamide; or an enantiomer, diastereomer or tautomer thereof; or a pharmaceutically acceptable salt thereof.

17. The compound of claim 1, which is (S)-3-amino-6-(5-(1,1-difluoro-2,3-dihydroxypropan-2-yl)-2-methylphenyl)-N-(tetrahydro-2H-pyran-4-yl)pyrazine-2-carboxamide; or an enantiomer, diastereomer or tautomer thereof; or a pharmaceutically acceptable salt thereof.

~~41~~18. A pharmaceutical composition comprising a compound of any one of claims 1 to ~~40~~17, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient or carrier.

~~42~~19. A ~~method of inhibiting an activity of PI3Kγ kinase, comprising contacting the kinase with a~~ compound of any one of claims 1 to ~~40~~17, or a pharmaceutically acceptable salt thereof~~.~~.

~~43. The method of claim 42, wherein the compound, or a pharmaceutically acceptable salt thereof, is a selective inhibitor for PI3Kγ over one or more of PI3Kα, PI3Kβ, and PI3Kδ.~~

~~44.~~ for use in ~~A~~ a method of treating a disease or disorder in a patient, wherein the disease or disorder is associated with abnormal expression or activity of PI3Kγ kinase, the method comprising administering to the patient a therapeutically effective amount of a compound of any one of claims 1 to ~~40~~17, or a pharmaceutically acceptable salt thereof~~.~~, wherein the disease or disorder is selected from:

~~45. The method of claim 44, wherein the disease or disorder is~~(a) an autoimmune disease or disorder, cancer, cardiovascular disease, or neurodegenerative disease~~.~~; or

~~46. The method of claim 44, wherein disease or disorder is~~(b) lung cancer, melanoma, pancreatic cancer, breast cancer, prostate cancer, liver cancer, ~~color~~colon cancer, endometrial cancer, bladder cancer, skin cancer, cancer of the uterus, renal cancer, gastric cancer, seminoma, teratocarcinoma, astrocytoma, neuroblastoma, glioma, or sarcoma~~.~~; or

~~47. The method of claim 46, wherein the sarcoma is Askin's~~(c) Askin's tumor, sarcoma botryoides, chondrosarcoma, ~~Ewing's~~Ewing's sarcoma, malignant hemangioendothelioma, malignant schwannoma, osteosarcoma, alveolar soft part sarcoma, angiosarcoma, cystosarcoma phyllodes, dermatofibrosarcoma protuberans, desmoid tumor, desmoplastic small round cell tumor, epithelioid sarcoma, extraskeletal chondrosarcoma, extraskeletal osteosarcoma, fibrosarcoma, gastrointestinal stromal tumor (GIST), hemangiopericytoma, hemangiosarcoma, ~~Kaposi's~~Kaposi's sarcoma, leiomyosarcoma, liposarcoma, lymphangiosarcoma, lymphosarcoma, malignant peripheral nerve sheath tumor (MPNST), neurofibrosarcoma, rhabdomyosarcoma, synovial sarcoma, or undifferentiated pleomorphic sarcoma~~.~~; or

~~48. The method of claim 44, wherein the disease or disorder is~~(d) acute myeloid leukemia, acute monocytic leukemia, small ~~lymphocytic~~lymphocytic lymphoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), multiple myeloma, T-cell ~~actute lymphoblasic~~acute lymphoblastic leukemia (T-ALL), cutaneous T-cell lymphoma, large granular lymphocytic leukemia, mature (peripheral) t-cell neoplasm (PTCL), anaplastic large cell lymphoma (ALCL), or lymphoblastic lymphoma~~.~~; or

~~49. The method of claim 48, wherein the mature (peripheral) t-cell neoplasm (PTCL) is~~(e) T-cell prolymphocytic leukemia, T-cell granular lymphocytic leukemia, aggressive NK-cell leukemia, mycosis fungoides/Sezary syndrome, ~~naplastic~~anaplastic large cell lymphoma (T-cell type), enteropathy type T-cell lymphoma, adult T-cell leukemia/lymphoma, or angioimmunoblastic T-cell lymphoma~~.~~; or

~~50. The method of claim 48, wherein the anaplastic large cell lymphoma (ALCL) is~~(f) systemic ALCL or primary cutaneous ALCL; or~~.~~

~~51. The method of claim 44, wherein the disease or disorder is Burkitt's~~
(g) Burkitt's lymphoma, acute myeloblastic leukemia, chronic myeloid leukemia, non-Hodgkin's lymphoma, Hodgkin's lymphoma, hairy cell leukemia, Mantle cell lymphoma, small lymphocytic lymphoma, follicular lymphoma, ~~xenoderoma~~xeroderoma pigmentosum, ~~keratoctanthoma~~keratoacanthoma, lymphoplasmacytic lymphoma, extranodal marginal zone lymphoma, ~~Waldenstrom's~~Waldenstrom's macroglobulinemia, prolymphocytic leukemia, acute lymphoblastic leukemia, myelofibrosis, mucosa-associated lymphatic tissue (MALT) lymphoma, mediastinal (thymic) large B-cell lymphoma, lymphomatoid granulomatosis, splenic marginal zone lymphoma, primary effusion lymphoma, intravascular large B-cell lymphoma, plasma cell leukemia, extramedullary

plasmacytoma, ~~smoulderingsmoldering~~ myeloma (aka asymptomatic myeloma), monoclonal gammopathy of undetermined significance (MGUS), or diffuse large B cell lymphoma~~.~~; or

~~52. The method of claim 51, wherein the non-Hodgkin's lymphoma (NHL) is~~(h) relapsed NHL, refractory NHL, ~~recucurrent~~recurrent follicular NHL, indolent NHL (iNHL), or aggressive NHL (aNHL~~).~~); or

~~53. The method of claim 51, wherein the diffuse large B-cell lymphoma is~~(i) activated B-cell like (ABC) diffuse large B cell lymphoma, or germinal center B cell (GCB) diffuse large B cell lymphoma~~.~~; or

~~54. The method of claim 51, wherein the~~ (j) endemic Burkitt's lymphoma ~~is endemic Burkitt's lymphoma~~, sporadic ~~Burkitt's~~Burkitt's lymphoma, or ~~Burkitt's~~Burkitt's-like lymphoma; or~~.~~

~~55. The method of claim 44, wherein the disease or disorder is~~

(k) rheumatoid arthritis, multiple sclerosis, systemic lupus erythematous, asthma, allergy, allergic rhinitis, pancreatitis, psoriasis, anaphylaxis, glomerulonephritis, inflammatory bowel disease, thrombosis, meningitis, encephalitis, diabetic retinopathy, benign prostatic hypertrophy, myasthenia gravis, Sjögren's syndrome, osteoarthritis, restenosis, or atherosclerosis~~.~~; or

~~56. The method of claim 44, wherein the disease or disorder is heart hypertropy~~(l) heart hypertrophy, cardiac myocyte dysfunction, acute coronary syndrome, chronic obstructive pulmonary disease (COPD), chronic bronchitis, elevated blood pressure, ischemia, ischemia-reperfusion, vasoconstriction, anemia, bacterial infection, viral infection, graft rejection, kidney disease, anaphylactic shock fibrosis, skeletal muscle atrophy, skeletal muscle hypertrophy, angiogenesis, sepsis, graft-versus-host disease, allogeneic or xenogeneic transplantation, glomerulosclerosis, progressive renal fibrosis, idiopathic thrombocytopenic purpura (ITP), autoimmune hemolytic anemia, vasculitis, systemic lupus erythematosus, lupus nephritis, pemphigus, or membranous nephropathy~~.~~; or

~~57. The method of claim 56, wherein the idiopathic thrombocytopenic purpura (ITP) is~~(m) relapsed ITP or refractory ITP~~.~~; or

~~58. The method of claim 56, wherein the vasculitis is Behçet's~~(n) Behçet’s disease, ~~Cogan's~~Cogan’s syndrome, giant cell arteritis, polymyalgia rheumatica (PMR), ~~Takayasu's~~Takayasu’s arteritis, ~~Buerger's~~Buerger’s

disease (thromboangiitis obliterans), central nervous system vasculitis, Kawasaki disease, polyarteritis nodosa, Churg-Strauss syndrome, mixed cryoglobulinemia vasculitis (essential or hepatitis C virus (HCV)-induced), Henoch-Schönlein purpura (HSP), hypersensitivity vasculitis, microscopic polyangiitis, ~~Wegener's~~Wegener's granulomatosis, or anti-neutrophil cytoplasm antibody associated (ANCA) systemic vasculitis (AASV~~).~~); or

~~59. The method of claim 44, wherein the disease or disorder is Alzheimer's~~(o) Alzheimer's disease, central nervous system trauma, or stroke.

20. Use of a compound of any one claims 1 to 17, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disease or disorder in a patient, wherein the disease or disorder is associated with abnormal expression or activity of PI3Kγ kinase and wherein the disease or disorder is selected from:

(a) an autoimmune disease or disorder, cancer, cardiovascular disease, or neurodegenerative disease; or

(b) lung cancer, melanoma, pancreatic cancer, breast cancer, prostate cancer, liver cancer, colon cancer, endometrial cancer, bladder cancer, skin cancer, cancer of the uterus, renal cancer, gastric cancer, seminoma, teratocarcinoma, astrocytoma, neuroblastoma, glioma, or sarcoma; or

(c) Askin's tumor, sarcoma botryoides, chondrosarcoma, Ewing's sarcoma, malignant hemangioendothelioma, malignant schwannoma, osteosarcoma, alveolar soft part sarcoma, angiosarcoma, cystosarcoma phyllodes, dermatofibrosarcoma protuberans, desmoid tumor, desmoplastic small round cell tumor, epithelioid sarcoma, extraskeletal chondrosarcoma, extraskeletal osteosarcoma, fibrosarcoma, gastrointestinal stromal tumor (GIST), hemangiopericytoma, hemangiosarcoma, Kaposi's sarcoma, leiomyosarcoma, liposarcoma, lymphangiosarcoma, lymphosarcoma, malignant peripheral nerve sheath tumor (MPNST), neurofibrosarcoma, rhabdomyosarcoma, synovial sarcoma, or undifferentiated pleomorphic sarcoma; or

(d) acute myeloid leukemia, acute monocytic leukemia, small lymphocytic lymphoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), multiple myeloma, T-cell acute lymphoblastic leukemia (T-ALL), cutaneous T-cell lymphoma, large granular lymphocytic leukemia, mature (peripheral) t-cell neoplasm (PTCL), anaplastic large cell lymphoma (ALCL), or lymphoblastic lymphoma; or

(e) T-cell prolymphocytic leukemia, T-cell granular lymphocytic leukemia, aggressive NK-cell leukemia, mycosis fungoides/Sezary syndrome, anaplastic large cell lymphoma (T-cell type), enteropathy type T-cell lymphoma, adult T-cell leukemia/lymphoma, or angioimmunoblastic T-cell lymphoma; or

(f) systemic ALCL or primary cutaneous ALCL; or

(g) Burkitt's lymphoma, acute myeloblastic leukemia, chronic myeloid leukemia, non-Hodgkin's lymphoma, Hodgkin's lymphoma, hairy cell leukemia, Mantle cell lymphoma, small lymphocytic lymphoma, follicular lymphoma, xeroderoma pigmentosum, keratoacanthoma, lymphoplasmacytic lymphoma, extranodal marginal zone lymphoma, Waldenstrom's macroglobulinemia, prolymphocytic leukemia, acute lymphoblastic leukemia, myelofibrosis, mucosa-associated lymphatic tissue (MALT) lymphoma, mediastinal (thymic) large B-cell lymphoma, lymphomatoid granulomatosis, splenic marginal zone lymphoma, primary effusion lymphoma, intravascular large B-cell lymphoma, plasma cell leukemia, extramedullary plasmacytoma, smoldering myeloma (aka asymptomatic myeloma), monoclonal gammopathy of undetermined significance (MGUS), or diffuse large B cell lymphoma; or

(h) relapsed NHL, refractory NHL, recurrent follicular NHL, indolent NHL (iNHL), or aggressive NHL (aNHL); or

(i) activated B-cell like (ABC) diffuse large B cell lymphoma, or germinal center B cell (GCB) diffuse large B cell lymphoma; or

(j) endemic Burkitt's lymphoma, sporadic Burkitt's lymphoma, or Burkitt's-like lymphoma; or

(k) rheumatoid arthritis, multiple sclerosis, systemic lupus erythematous, asthma, allergy, allergic rhinitis, pancreatitis, psoriasis, anaphylaxis, glomerulonephritis, inflammatory bowel disease, thrombosis, meningitis, encephalitis, diabetic retinopathy, benign prostatic hypertrophy, myasthenia gravis, Sjögren's syndrome, osteoarthritis, restenosis, or atherosclerosis; or

(l) heart hypertrophy, cardiac myocyte dysfunction, acute coronary syndrome, chronic obstructive pulmonary disease (COPD), chronic bronchitis, elevated blood pressure, ischemia, ischemia-reperfusion, vasoconstriction, anemia, bacterial infection, viral infection, graft rejection, kidney disease, anaphylactic shock fibrosis, skeletal muscle atrophy, skeletal muscle hypertrophy, angiogenesis, sepsis, graft-versus-host disease, allogeneic or xenogeneic transplantation, glomerulosclerosis, progressive renal fibrosis,

idiopathic thrombocytopenic purpura (ITP), autoimmune hemolytic anemia, vasculitis, systemic lupus erythematosus, lupus nephritis, pemphigus, or membranous nephropathy; or

(m) relapsed ITP or refractory ITP; or

(n) Behçet's disease, Cogan's syndrome, giant cell arteritis, polymyalgia rheumatica (PMR), Takayasu's arteritis, Buerger's disease (thromboangiitis obliterans), central nervous system vasculitis, Kawasaki disease, polyarteritis nodosa, Churg-Strauss syndrome, mixed cryoglobulinemia vasculitis (essential or hepatitis C virus (HCV)-induced), Henoch-Schönlein purpura (HSP), hypersensitivity vasculitis, microscopic polyangiitis, Wegener's granulomatosis, or anti-neutrophil cytoplasm antibody associated (ANCA) systemic vasculitis (AASV); or

(o) Alzheimer's disease, central nervous system trauma, or stroke.