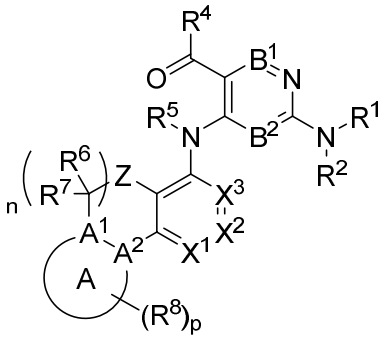
CLAIMS

What is claimed is:

1. A compound of Formula (I):



Formula (I),

or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein:

Ring A is an unsubstituted or substituted carbocyclic ring wherein A^1 and A^2 are both C, or an unsubstituted or substituted 5- or 6-membered heterocyclic ring wherein A^1 and A^2 are independently N or C, wherein if Ring A is substituted then Ring A is substituted with p instances of R^8;

each R^8 is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, -OR^{17}, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$N(R^{16})_2$, -$NR^{16}C(=O)R^{17}$, -SR^{16}, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$; wherein if R^8 is attached to a nitrogen atom, then R^8 is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$; or two R^8 attached to the same carbon atom are taken together to form =O, =S, or =NH;

Z is -NR^{10}-, -O-, -S-, -S(=O)-, or -SO_2-;

R^{10} is hydrogen, C_1-C_6 alkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, C_3-C_6 cycloalkyl, or monocyclic heterocycle;

X^1, X^2, and X^3 are each independently CR^{11} or N;

each R^{11} is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

B^1 is N or CR^{12a};

B^2 is N or CR^{12b};

R^{12a} and R^{12b} are each independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

R^1 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

R^2 is a Ring B that is an unsubstituted or substituted heterocycle or unsubstituted or substituted carbocycle, wherein if Ring B is substituted then Ring B is substituted with q instances of R^{13};

each R^{13} is independently halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

or two R^{13} groups on adjacent atoms of Ring B are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

or R^2 is $-C(=O)R^{14}$, $-C(=O)NR^{14}R^{15}$, or $-C(=O)OR^{14}$;

R^{14} is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted bicyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, or unsubstituted or substituted bicyclic heterocycle;

R^{15} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

or R^{14} and R^{15} are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4- to 6-membered monocyclic heterocycle;

or R^1 and R^{15} are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

R^4 is hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, or C_3-C_6 cycloalkyl;

or R^4 and R^{12a} are taken together with the intervening atoms to which they are attached to form a substituted or unsubstituted C_5-C_6 cycloalkyl;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_3-C_6 cycloalkyl, or monocyclic heterocycle;

each R^6 and R^7 is independently hydrogen, deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, C_3-C_6 cycloalkyl, monocyclic heterocycle, -CN, -OH, -OR^{17}, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$N(R^{16})_2$, -$NR^{16}C(=O)R^{17}$, -SR^{16}, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$;

or one R^6 and one R^7 attached to the same carbon atom are taken together with the carbon atom to which they are attached to form C=O, an unsubstituted or substituted C_3-C_6 cycloalkane, or an unsubstituted or substituted 3- to 6-membered heterocycloalkyl, wherein when the C_3-C_6 cycloalkane or 3- to 6-membered heterocycloalkyl is substituted, the C_3-C_6 cycloalkane or 3- to 6-membered heterocycloalkyl is substituted with m instances of R^3, wherein:

m is 0, 1, 2, 3, 4, 5, or 6; and

each R^3 is independently deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, -CN, -OH, -OR^{17}, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$N(R^{16})_2$, -$NR^{16}C(=O)R^{17}$, -SR^{16}, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$; wherein if R^3 is attached to a nitrogen atom, then R^3 is hydrogen, deuterium, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$;

provided that at least one R^6 and one R^7 attached to the same carbon atom are taken together with the carbon atom to which they are attached to form a substituted cyclopropyl, an unsubstituted or substituted C_4-C_6 cycloalkane, or an unsubstituted or substituted 3- to 6-membered heterocycloalkyl;

each R^{16} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^{16} on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle; and

each R^{17} is independently substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

wherein each substituted alkyl, substituted fluoroalkyl, substituted deuteroalkyl, substituted alkoxy, substituted fluoroalkoxy, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of deuterium, halogen, C_1-C_6 alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -CH_2CN, -OR^{18}, -CH_2OR^{18}, -CO_2R^{18}, -$CH_2CO_2R^{18}$, -$C(=O)N(R^{18})_2$, -$CH_2C(=O)N(R^{18})_2$, -$N(R^{18})_2$, -$CH_2N(R^{18})_2$, -$NR^{18}C(=O)R^{18}$, -$CH_2NR^{18}C(=O)R^{18}$, -$NR^{18}SO_2R^{19}$, -$CH_2NR^{18}SO_2R^{19}$, -SR^{18}, -CH_2SR^{18}, -$S(=O)R^{19}$, -$CH_2S(=O)R^{19}$, -SO_2R^{19}, -$CH_2SO_2R^{19}$, -$SO_2N(R^{18})_2$, or -$CH_2SO_2N(R^{18})_2$;

each R^{18} is independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl;

or two R^{18} groups are taken together with the N atom to which they are attached to form a N-containing heterocycle;

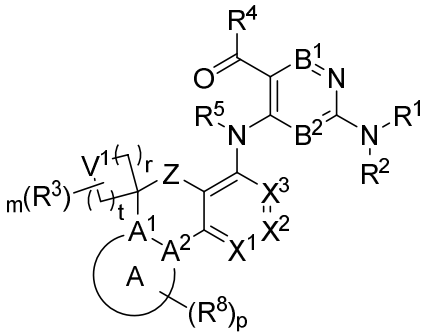
each R^{19} is independently selected from C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl;

n is 1, 2, or 3;

p is 1, 2, 3, or 4; and

q is 0, 1, 2, 3, or 4.

2. The compound of claim 1 further defined by Formula (I-A):



Formula (I-A),

or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein:

m is 0, 1, 2, 3, 4, 5, or 6;

r and t are each independently 0, 1, or 2, provided the sum of t and r is at least 2;

V^1 is $-NR^3-$, -O-, -S-, -S(=O)-, or $-SO_2-$;

Ring A is an unsubstituted or substituted carbocyclic ring wherein A^1 and A^2 are both C, or an unsubstituted or substituted 5- or 6-membered heterocyclic ring wherein A^1 and A^2 are independently N or C, wherein if Ring A is substituted then Ring A is substituted with p instances of R^8;

each R^8 is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$; wherein if R^8 is attached to a nitrogen atom, then R^8 is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$; or two R^8 attached to the same carbon atom are taken together to form =O, =S, or =NH;

Z is $-NR^{10}-$, -O-, -S-, -S(=O)-, or $-SO_2-$;

R^{10} is hydrogen, C_1-C_6 alkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, C_3-C_6 cycloalkyl, or monocyclic heterocycle;

X^1, X^2, and X^3 are each independently CR^{11} or N;

each R^{11} is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

B^1 is N or CR^{12a};

B^2 is N or CR^{12b};

R^{12a} and R^{12b} are each independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

R^1 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

R^2 is a Ring B that is an unsubstituted or substituted heterocycle or unsubstituted or substituted carbocycle, wherein if Ring B is substituted then Ring B is substituted with q instances of R^{13};

each R^{13} is independently halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

or two R^{13} groups on adjacent atoms of Ring B are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

or R^2 is $-C(=O)R^{14}$, $-C(=O)NR^{14}R^{15}$, or $-C(=O)OR^{14}$;

R^{14} is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted monocyclic carbocycle,

unsubstituted or substituted bicyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, or unsubstituted or substituted bicyclic heterocycle;

R^{15} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

or R^{14} and R^{15} are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4- to 6-membered monocyclic heterocycle;

or R^1 and R^{15} are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

each R^3 is independently deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, -CN, -OH, -OR^{17}, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$N(R^{16})_2$, -$NR^{16}C(=O)R^{17}$, -SR^{16}, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$; wherein if R^3 is attached to a nitrogen atom, then R^3 is hydrogen, deuterium, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$;

R^4 is hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, or C_3-C_6 cycloalkyl;

or R^4 and R^{12a} are taken together with the intervening atoms to which they are attached to form a substituted or unsubstituted C_5-C_6 cycloalkyl;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_3-C_6 cycloalkyl, or monocyclic heterocycle;

each R^{16} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^{16} on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle; and

each R^{17} is independently substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

wherein each substituted alkyl, substituted fluoroalkyl, substituted deuteroalkyl, substituted alkoxy, substituted fluoroalkoxy, substituted heteroalkyl, substituted

carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of deuterium, halogen, C_1-C_6 alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -CH_2CN, -OR^{18}, -CH_2OR^{18}, -CO_2R^{18}, -$CH_2CO_2R^{18}$, -$C(=O)N(R^{18})_2$, -$CH_2C(=O)N(R^{18})_2$, -$N(R^{18})_2$, -$CH_2N(R^{18})_2$, -$NR^{18}C(=O)R^{18}$, -$CH_2NR^{18}C(=O)R^{18}$, -$NR^{18}SO_2R^{19}$, -$CH_2NR^{18}SO_2R^{19}$, -SR^{18}, -CH_2SR^{18}, -$S(=O)R^{19}$, -$CH_2S(=O)R^{19}$, -SO_2R^{19}, -$CH_2SO_2R^{19}$, -$SO_2N(R^{18})_2$, or -$CH_2SO_2N(R^{18})_2$;

each R^{18} is independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl;

or two R^{18} groups are taken together with the N atom to which they are attached to form a N-containing heterocycle;

each R^{19} is independently selected from C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl;

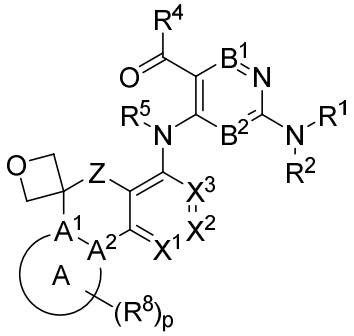
n is 1, 2, or 3;

p is 1, 2, 3, or 4; and

q is 0, 1, 2, 3, or 4.

3. The compound of claim 2, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein V^1 is -O-, r is 1, and t is 1.

4. The compound of any one of claims 1–3 further defined by Formula (I-B):



Formula (I-B),

or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein:

Ring A is an unsubstituted or substituted carbocyclic ring wherein A^1 and A^2 are both C, or an unsubstituted or substituted 5- or 6-membered heterocyclic ring wherein A^1 and A^2 are independently N or C, wherein if Ring A is substituted then Ring A is substituted with p instances of R^8;

each R^8 is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$; wherein if R^8 is attached to a nitrogen atom, then R^8 is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$; or two R^8 attached to the same carbon atom are taken together to form =O, =S, or =NH;

Z is $-NR^{10}$-, -O-, -S-, -S(=O)-, or $-SO_2$-;

R^{10} is hydrogen, C_1-C_6 alkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, C_3-C_6 cycloalkyl, or monocyclic heterocycle;

X^1, X^2, and X^3 are each independently CR^{11} or N;

each R^{11} is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

B^1 is N or CR^{12a};

B^2 is N or CR^{12b};

R^{12a} and R^{12b} are each independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

R^1 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

R^2 is a Ring B that is an unsubstituted or substituted heterocycle or unsubstituted or substituted carbocycle, wherein if Ring B is substituted then Ring B is substituted with q instances of R^{13};

each R^{13} is independently halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$;

or two R^{13} groups on adjacent atoms of Ring B are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

or R^2 is $-C(=O)R^{14}$, $-C(=O)NR^{14}R^{15}$, or $-C(=O)OR^{14}$;

R^{14} is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted bicyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, or unsubstituted or substituted bicyclic heterocycle;

R^{15} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

or R^{14} and R^{15} are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4- to 6-membered monocyclic heterocycle;

or R^1 and R^{15} are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

R^4 is hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, or C_3-C_6 cycloalkyl;

or R^4 and R^{12a} are taken together with the intervening atoms to which they are attached to form a substituted or unsubstituted C_5-C_6 cycloalkyl;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_3-C_6 cycloalkyl, or monocyclic heterocycle;

each R^{16} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3-

to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^{16} on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle; and

each R^{17} is independently substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

wherein each substituted alkyl, substituted fluoroalkyl, substituted deuteroalkyl, substituted alkoxy, substituted fluoroalkoxy, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of deuterium, halogen, C_1-C_6 alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -CH_2CN, -OR^{18}, -CH_2OR^{18}, -CO_2R^{18}, -$CH_2CO_2R^{18}$, -$C(=O)N(R^{18})_2$, -$CH_2C(=O)N(R^{18})_2$, -$N(R^{18})_2$, -$CH_2N(R^{18})_2$, -$NR^{18}C(=O)R^{18}$, -$CH_2NR^{18}C(=O)R^{18}$, -$NR^{18}SO_2R^{19}$, -$CH_2NR^{18}SO_2R^{19}$, -SR^{18}, -CH_2SR^{18}, -$S(=O)R^{19}$, -$CH_2S(=O)R^{19}$, -SO_2R^{19}, -$CH_2SO_2R^{19}$, -$SO_2N(R^{18})_2$, or -$CH_2SO_2N(R^{18})_2$;

each R^{18} is independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl;

or two R^{18} groups are taken together with the N atom to which they are attached to form a N-containing heterocycle;

each R^{19} is independently selected from C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl;

p is 1, 2, 3, or 4; and

q is 0, 1, 2, 3, or 4.

5. The compound of any one of claims 1–4, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein Z is -NR^{10}-, -O-, or -S-.

6. The compound of any one of claims 1–5, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein Z is -NR^{10}-, and R^{10} is hydrogen, C_1-C_6 alkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, or C_3-C_6 cycloalkyl.

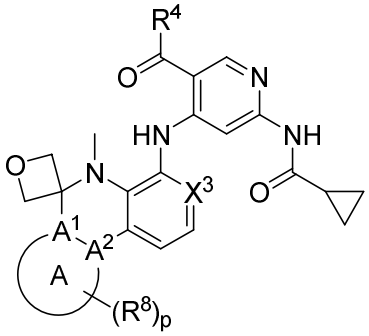
7. The compound of any one of claims 1–6, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein R^{10} is C_1-C_6 alkyl.

8. The compound of any one of claims 1–7, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein X^1 is CH and X^2 is CH.

9. The compound of any one of claims 1–8, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein B^1 is CR^{12a} and R^{12a} is hydrogen or unsubstituted or substituted C_1-C_6 alkyl; and B^2 is CR^{12b} and R^{12b} is hydrogen or unsubstituted or substituted C_1-C_6 alkyl.

10. The compound of any one of claims 1–9, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein R^1 is hydrogen or C_1-C_4 alkyl; ; R^2 is $-C(=O)R^{14}$ and R^{14} is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, or unsubstituted or substituted monocyclic carbocycle; and R^5 is hydrogen or C_1-C_4 alkyl.

11. The compound of any one of claims 1–10 further defined by Formula (I-C):



Formula (I-C),

or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein:

Ring A is an unsubstituted or substituted carbocyclic ring wherein A^1 and A^2 are both C, or an unsubstituted or substituted 5- or 6-membered heterocyclic ring wherein A^1 and A^2 are independently N or C, wherein if Ring A is substituted then Ring A is substituted with p instances of R^8;

each R^8 is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, $-OR^{17}$, $-C(=O)R^{16}$, $-CO_2R^{16}$, $-C(=O)N(R^{16})_2$, $-N(R^{16})_2$, $-NR^{16}C(=O)R^{17}$, $-SR^{16}$, $-S(=O)R^{17}$, $-SO_2R^{17}$, or $-SO_2N(R^{16})_2$; wherein if R^8 is attached to a nitrogen atom, then R^8 is hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 deuteroalkyl, unsubstituted or

substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -C(=O)R^{16}, -CO_2R^{16}, -C(=O)N(R^{16})$_2$, -S(=O)R^{17}, -SO_2R^{17}, or -SO_2N(R^{16})$_2$; or two R^8 attached to the same carbon atom are taken together to form =O, =S, or =NH;

X^3 is CR^{11} or N, wherein:

R^{11} is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, -OR^{17}, -C(=O)R^{16}, -CO_2R^{16}, -C(=O)N(R^{16})$_2$, -N(R^{16})$_2$, -NR^{16}C(=O)R^{17}, -SR^{16}, -S(=O)R^{17}, -SO_2R^{17}, or -SO_2N(R^{16})$_2$;

R^4 is hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, or C_3-C_6 cycloalkyl;

each R^{16} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^{16} on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle; and

each R^{17} is independently substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

wherein each substituted alkyl, substituted fluoroalkyl, substituted deuteroalkyl, substituted alkoxy, substituted fluoroalkoxy, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of deuterium, halogen, C_1-C_6 alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -CH_2CN, -OR^{18}, -CH_2OR^{18}, -CO_2R^{18}, -$CH_2CO_2R^{18}$, -C(=O)N(R^{18})$_2$, -CH_2C(=O)N(R^{18})$_2$, -N(R^{18})$_2$, -CH_2N(R^{18})$_2$, -NR^{18}C(=O)R^{18}, -CH_2NR^{18}C(=O)R^{18}, -N$R^{18}$$SO_2R^{19}$, -

$CH_2NR^{18}SO_2R^{19}$, $-SR^{18}$, $-CH_2SR^{18}$, $-S(=O)R^{19}$, $-CH_2S(=O)R^{19}$, $-SO_2R^{19}$, $-CH_2SO_2R^{19}$, $-SO_2N(R^{18})_2$, or $-CH_2SO_2N(R^{18})_2$;

each R^{18} is independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl;

or two R^{18} groups are taken together with the N atom to which they are attached to form a N-containing heterocycle;

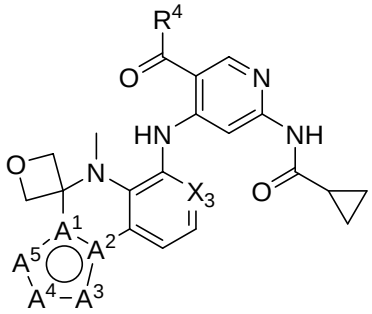
each R^{19} is independently selected from C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl; and

p is 1, 2, 3, or 4.

12. The compound of any one of claims 1–11, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein Ring A is an unsubstituted or substituted 5- or 6-membered heterocyclic ring wherein A^1 and A^2 are independently N or C, wherein if Ring A is substituted then Ring A is substituted with p instances of R^8.

13. The compound of any one of claims 1–12, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein Ring A is an unsubstituted or substituted imidazole or unsubstituted or substituted triazole, wherein if Ring A is substituted then Ring A is substituted with p instances of R^8.

14. The compound of any one of claims 1–13 further defined by Formula (I-D):



Formula (I-D),

or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein:

A^1 and A^2 are each independently N or C;

A^3 is S, O, N, NR^8, CR^8, or C=O;

A^4 and A^5 are each independently S, O, N, NR^8, or CR^8;

wherein at least one of A^1 and A^2 is C, or at least one of A^3, A^4, and A^5 is CR^8;

X^3 is CR^{11} or N, wherein:

R^{11} is independently hydrogen, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_2-C_6 alkenyl, unsubstituted or substituted C_2-C_6 alkynyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, unsubstituted or substituted carbocycle, unsubstituted or substituted heterocycle, -CN, -OH, -OR^{17}, -$C(=O)R^{16}$, -CO_2R^{16}, -$C(=O)N(R^{16})_2$, -$N(R^{16})_2$, -$NR^{16}C(=O)R^{17}$, -SR^{16}, -$S(=O)R^{17}$, -SO_2R^{17}, or -$SO_2N(R^{16})_2$;

R^4 is hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 deuteroalkyl, C_1-C_6 fluoroalkyl, or C_3-C_6 cycloalkyl;

each R^{16} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^{16} on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle; and

each R^{17} is independently substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 fluoroalkyl, substituted or unsubstituted C_1-C_6 heteroalkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted monocyclic heteroaryl;

wherein each substituted alkyl, substituted fluoroalkyl, substituted deuteroalkyl, substituted alkoxy, substituted fluoroalkoxy, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of deuterium, halogen, C_1-C_6 alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -CH_2CN, -OR^{18}, -CH_2OR^{18}, -CO_2R^{18}, -$CH_2CO_2R^{18}$, -$C(=O)N(R^{18})_2$, -$CH_2C(=O)N(R^{18})_2$, -$N(R^{18})_2$, -$CH_2N(R^{18})_2$, -$NR^{18}C(=O)R^{18}$, -$CH_2NR^{18}C(=O)R^{18}$, -$NR^{18}SO_2R^{19}$, -$CH_2NR^{18}SO_2R^{19}$, -SR^{18}, -CH_2SR^{18}, -$S(=O)R^{19}$, -$CH_2S(=O)R^{19}$, -SO_2R^{19}, -$CH_2SO_2R^{19}$, -$SO_2N(R^{18})_2$, or -$CH_2SO_2N(R^{18})_2$;

each R^{18} is independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl;

or two R^{18} groups are taken together with the N atom to which they are attached to form a N-containing heterocycle;

each R^{19} is independently selected from C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, C_2-C_6 heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl.

15. The compound of any one of claims 1–14, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein X^3 is N or CH.

16. The compound of any one of claims 1–15, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein R^4 is C_1-C_4 alkyl or C_1-C_4 deuteroalkyl.

17. The compound of any one of claims 1–16, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, wherein:
A^1 is C; A^2 is C; A^3 is N; A^4 is CR^8; and A^5 is NR^8, O, or S;
or A^1 is C; A^2 is C; A^3 is N or CR^8; A^4 is NR^8; and A^5 is N;
each R^8 is independently hydrogen or unsubstituted or substituted C_1-C_6 alkyl; and
p is 1 or 2.

18. The compound of any one of claims 1–17, wherein the compound is selected from:
1: *N*-(4-((2',5'-dimethyl-2',5'-dihydrospiro[oxetane-3,4'-[1,2,3]triazolo[4,5-c][1,7]naphthyridin]-6'-yl)amino)-5-(propanoyl-3,3,3-d3)pyridin-2-yl)cyclopropanecarboxamide;
2: *N*-(5-(propanoyl-3,3,3-d3)-4-((2,3,5-trimethyl-3,5-dihydrospiro[imidazo[4,5-c][1,7]naphthyridine-4,3'-oxetan]-6-yl)amino)pyridin-2-yl)cyclopropanecarboxamide;
3: *N*-(5-propionyl-4-((2,3,5-trimethyl-3,5-dihydrospiro[imidazo[4,5-c][1,7]naphthyridine-4,3'-oxetan]-6-yl)amino)pyridin-2-yl)cyclopropanecarboxamide;
4: *N*-(4-((2',5'-dimethyl-2',5'-dihydrospiro[oxetane-3,4'-[1,2,3]triazolo[4,5-c]quinolin]-6'-yl)amino)-5-(propanoyl-3,3,3-d3)pyridin-2-yl)cyclopropanecarboxamide;
5: *N*-(5-(propanoyl-3,3,3-d3)-4-((2,3,5-trimethyl-3,5-dihydrospiro[imidazo[4,5-c]quinoline-4,3'-oxetan]-6-yl)amino)pyridin-2-yl)cyclopropanecarboxamide;
6: *N*-(4-((2',5'-dimethyl-2',5'-dihydrospiro[oxetane-3,4'-[1,2,3]triazolo[4,5-c][1,7]naphthyridin]-6'-yl)amino)-5-propionylpyridin-2-yl)cyclopropanecarboxamide;
or a pharmaceutically acceptable salt, tautomer, or solvate thereof.

19. A pharmaceutical composition comprising the compound of any one of claims 1–18, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, and a pharmaceutically acceptable excipient.

20. Use of a compound of any one of claims 1-18, or a pharmaceutically acceptable salt, tautomer, or solvate thereof, in the manufacture of a medicament for treating a TYK2-mediated disease or condition in a patient in need thereof.

21. The use of claim 20, wherein the disease or condition is an inflammatory disease or condition or an autoimmune disease or condition.

22. The use of claim 20 or 21, wherein the disease or condition is selected from rheumatoid arthritis, multiple sclerosis, psoriasis, psoriatic arthritis, lupus, systemic lupus erythematosus, Sjögren's syndrome, ankylosing spondylitis, vitiligo, atopic dermatitis, scleroderma, alopecia, hidradenitis suppurativa, uveitis, dry eye, intestinal bowel disease, Crohn's disease, ulcerative colitis, celiac disease, Bechet's disease, type 1 diabetes, systemic sclerosis, and idiopathic pulmonary fibrosis.