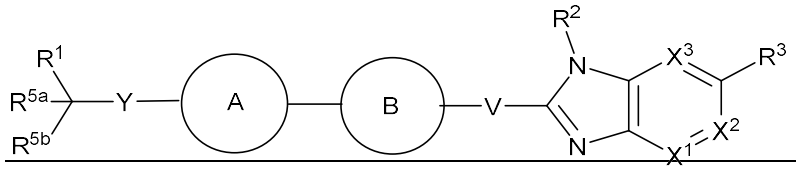
WHAT IS CLAIMED IS:

1. A compound of Formula (I-A-1):



(I-A-1),

or a pharmaceutically acceptable salt thereof, wherein

R^1 is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, $-S-R^{1b}$, $-S(O)R^{1b}$, $-S(O)(NH)R^{1b}$, $-S(O)_2R^{1b}$, $-S(O)_2N(R^{1b})(R^{1c})$, $-S(O)(NR^{1b})R^{1c}$, $-C(O)N(R^{1b})(R^{1c})$, $-C(O)R^{1b}$, or $-C(O)OR^{1c}$;

wherein the alkyl, haloalkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is each optionally substituted with one to four Z^1;

ring A is C_{6-10} aryl or heteroaryl, which is each optionally substituted with one to four Z^{1a};

ring B is C_{6-10} aryl or heteroaryl, which is each optionally substituted with one to four R^4;

R^2 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, $-CN$, $-OR^{2a}$, $-S-R^{2a}$, $-S(O)R^{2a}$, $-S(O)(NH)R^{2a}$, $-S(O)_2R^{2a}$, $-S(O)_2N(R^{2a})(R^{2b})$, or $-S(O)(NR^{2a})R^{2b}$;

wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^1;

X^1, X^2, and X^3 are each independently $-N=$, $-C(H)=$, or $-C(R^8)=$;

R^3 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, $-CN$, $-NO_2$, $-OR^{3a}$, $-C(O)R^{3a}$, $-CH_2C(O)OR^{3a}$, $-C(O)OR^{3a}$, $-C(O)N(R^{3a})(R^{3b})$, $-N(R^{3a})C(O)R^{3b}$, $-N(R^{3a})C(O)OR^{3b}$, $-N(R^{3a})C(O)N(R^{3b})_2$, $-C(O)NHS(O)_2R^{3a}$, $-C(O)NR^{3a}S(O)_2R^{3b}$, $-C(O)NR^{3a}S(O)_2NR^{3b}R^{3c}$, $-C(O)NR^{3a}$-$S(O)(=NR^{3b})R^{3c}$, $-S(O)_2R^{3a}$, $-S(O)_2OR^{3a}$, $-S(O)_2N(R^{3a})(R^{3b})$, $-N(R^{3a})S(O)_2R^{3b}$, $-S(O)_2NHC(O)R^{3a}$, $-S(O)(=NR^{3a})R^{3b}$, $-S(O)(=NR^{3a})NR^{3b}$;

~~$-S(=NR^{3a})(=NR^{3b})R^{3c}$, $-P(O)(OR^{3a})(R^{3b})$, $-P(O)(OR^{3a})(OR^{3b})$, $-B(OR^{3a})(OR^{3b})$, or $-O-C_{1-6}$alkyl-$C(O)OR^{3a}$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four R^{3d};~~

~~each R^{3a}, R^{3b}, and R^{3c} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-8} alkoxyalkyl, $-C_{1-4}$ alkyl-$N(R^{9a})(R^{9b})$, $-C_{1-4}$ alkyl-$N(R^{9a})C(O)$-O-C_{1-4} alkyl-$OP(O)(OR^{9e})_2$, $-C_{1-4}$ alkyl-$C(O)N(R^{9a})(R^{9b})$, $-C_{1-4}$ alkyl-O-$C(O)$-C_{1-4} alkyl, $-C_{1-4}$ alkyl-O-$C(O)$-O-C_{1-4}alkyl, $-C_{1-4}$ alkyl-O-$C(O)$-C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, $-C_{1-4}$ alkyl-O-$C(O)$-C_{1-4} alkyl-$OP(O)(OR^{9e})_2$, $-C_{1-4}$ alkyl-C_{3-8} cycloalkyl, $-C_{1-4}$ alkyl-heterocyclyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, $-CH_2CH(N(R^{9a})_2)C(O)OR^{9b}$, $-P(O)(OR^{9e})_2$, $-OP(O)(OR^{9e})_2$, $-CH_2P(O)(OR^{9e})_2$, $-CH_2OP(O)(OR^{9e})_2$, $-OCH_2P(O)(OR^{9e})_2$, $-C(O)OCH_2P(O)(OR^{9e})_2$, $-P(O)(R^{9e})(OR^{9d})$, $-OP(O)(R^{9e})(OR^{9d})$, $-CH_2P(O)(R^{9e})(OR^{9d})$, $-OCH_2P(O)(R^{9e})(OR^{9d})$, $-C(O)OCH_2P(O)(R^{9e})(OR^{9d})$, $-P(O)(N(R^{9e})_2)_2$, $-OP(O)(N(R^{9e})_2)_2$, $-CH_2P(O)(N(R^{9e})_2)_2$, $-OCH_2P(O)(N(R^{9e})_2)_2$, $-C(O)OCH_2P(O)(N(R^{9e})_2)_2$, $-P(O)(N(R^{9e})_2)(OR^{9d})$, $-OP(O)(N(R^{9e})_2)(OR^{9d})$, $-CH_2P(O)(N(R^{9e})_2)(OR^{9d})$, $-OCH_2P(O)(N(R^{9e})_2)(OR^{9d})$, $-C(O)OCH_2P(O)(N(R^{9e})_2)(OR^{9d})$, $-P(O)(R^{9e})(N(R^{9d})_2)$, $-OP(O)(R^{9e})(N(R^{9d})_2)$, $-CH_2P(O)(R^{9e})(N(R^{9d})_2)$, $-OCH_2P(O)(R^{9e})(N(R^{9d})_2)$, $-C(O)OCH_2P(O)(R^{9e})(N(R^{9d})_2)$, or C_{1-6} alkyl-heterocyclyl;~~

~~wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};~~

~~each R^4 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, $-CN$, $-N_3$, $-O-R^{4a}$, $-C(O)R^{4a}$, $-C(O)O-R^{4a}$, $-C(O)N(R^{4a})(R^{4b})$, $-N(R^{4a})(R^{4b})$, $-N(R^{4a})_2(R^{4b})^+$, $-N(R^{4a})-C(O)R^{4b}$, $-N(R^{4a})C(O)O(R^{4b})$, $-N(R^{4a})C(O)N(R^{4b})(R^{4c})$, $-N(R^{4a})S(O)_2(R^{4b})$, $-N(R^{4a})S(O)_2-N(R^{4b})(R^{4c})$, $-N(R^{4a})S(O)_2O(R^{4b})$, $-OC(O)R^{4a}$, $-OC(O)OR^{4a}$, $-OC(O)-N(R^{4a})(R^{4b})$, $-S-R^{4a}$, $-S(O)R^{4a}$, $-S(O)(NH)R^{4a}$, $-S(O)_2R^{4a}$, $-S(O)_2N(R^{4a})(R^{4b})$, $-S(O)(NR^{4a})R^{4b}$, or $-Si(R^{4a})_3$;~~

~~wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};~~

or two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four Z^{1b};

R^{5a} and R^{5b} are each independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, $-C_{1-6}$ alkyl-$N(R^{9a})(R^{9b})$, -CN, $-OR^{5a1}$, or $-N(R^{5a1})(R^{5a2})$;

or R^{5a} and R^{5b} are combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{5a3};

each R^{5a1} and R^{5a2} is independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or heteroaryl, wherein the cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four R^{5a4};

V is $-C(O)-$, $-O-$, $-N(R^{6a})-$, or $-C(R^{6b})(R^{6e})-$;

R^{6a} is H, C_{1-6} alkyl, C_{3-10} cycloalkyl, heterocyclyl, $-S(O)_2R^{6a1}$, or $-S(O)_2N(R^{6a1})(NR^{6a2})$, wherein the cycloalkyl or heterocyclyl is each optionally substituted with C_{1-6} alkyl, F, or -CN;

each R^{6b} and R^{6e} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, $-C_{1-6}$ alkyl-$N(R^{9a})(R^{9b})$, -CN, $-OR^{6e1}$, or $-N(R^{6e2})(R^{6e3})$, wherein the alkyl, cycloalkyl, or heterocyclyl is each optionally substituted with one to four R^{6b1};

or R^{6b} and R^{6e} are combined with the atom to which they are attached to form C_{3-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{6b1};

or R^{6a} or R^{6e} is combined with one R^4 group and the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{10};

Y is $-N(R^7)-$, $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-S(O)(=NH)-$, or $-S(O)(=NR^7)-$;

each R^{1a}, R^{3d}, R^{5a3}, R^{5a4}, R^{6b1}, and R^{10} is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen,

C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, or -C(O)N(R^{2a})(R^{2b}), wherein the heterocyclyl or heteroaryl is optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy; and

each R^{6a1}, R^{6a2}, R^{6c1}, R^{6c2}, R^{6c3} and R^7 is independently H, C_{1-6} alkyl or C_{3-10} cycloalkyl;

each R^8 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, -NH_2, -N_3, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{2-6} alkenyl), -O(C_{2-6} alkynyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(C_{6-10} aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{2-6} alkenyl), -NH(C_{2-6} alkynyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(C_{6-10} aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$, -N(C_{2-6} alkenyl)$_2$, -N(C_{2-6} alkynyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -N(heterocyclyl)$_2$, -N(C_{6-10} aryl)$_2$, -N(heteroaryl)$_2$, -N(C_{1-9} alkyl)(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)(C_{2-6} alkenyl), -N(C_{1-9} alkyl)(C_{2-6} alkynyl), -N(C_{1-9} alkyl)(C_{3-15} cycloalkyl), -N(C_{1-9} alkyl)(heterocyclyl), -N(C_{1-9} alkyl)(C_{6-10} aryl), -N(C_{1-9} alkyl)(heteroaryl), -C(O)(C_{1-9} alkyl), -C(O)(C_{1-8} haloalkyl), -C(O)(C_{2-6} alkenyl), -C(O)(C_{2-6} alkynyl), -C(O)(C_{3-15} cycloalkyl), -C(O)(heterocyclyl), -C(O)(C_{6-10} aryl), -C(O)(heteroaryl), -C(O)O(C_{1-9} alkyl), -C(O)O(C_{1-8} haloalkyl), -C(O)O(C_{2-6} alkenyl), -C(O)O(C_{2-6} alkynyl), -C(O)O(C_{3-15} cycloalkyl), -C(O)O(heterocyclyl), -C(O)O(C_{6-10} aryl), -C(O)O(heteroaryl), -C(O)NH_2, -C(O)NH(C_{1-9} alkyl), -C(O)NH(C_{1-8} haloalkyl), -C(O)NH(C_{2-6} alkenyl), -C(O)NH(C_{2-6} alkynyl), -C(O)NH(C_{3-15} cycloalkyl), -C(O)NH(heterocyclyl), -C(O)NH(C_{6-10} aryl), -C(O)NH(heteroaryl), -C(O)N(C_{1-9} alkyl)$_2$, -C(O)N(C_{1-8} haloalkyl)$_2$, -C(O)N(C_{2-6} alkenyl)$_2$, -C(O)N(C_{2-6} alkynyl)$_2$, -C(O)N(C_{3-15} cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, -C(O)N(C_{6-10} aryl)$_2$, -C(O)N(heteroaryl)$_2$, -NHC(O)(C_{1-9} alkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{2-6} alkenyl), -NHC(O)(C_{2-6} alkynyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(C_{6-10} aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6}

alkenyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(C_{6-10} aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), -NHC(O)NH(C_{1-8} haloalkyl), -NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), -NHC(O)NH(heteroaryl), -NHS(O)(C_{1-9} alkyl), -N(C_{1-9} alkyl)(S(O)(C_{1-9} alkyl), -S(C_{1-9} alkyl), -S(C_{1-8} haloalkyl), -S(C_{2-6} alkenyl), -S(C_{2-6} alkynyl), -S(C_{3-15} cycloalkyl), -S(heterocyclyl), -S(C_{6-10} aryl), -S(heteroaryl), -S(O)N(C_{1-9} alkyl)$_2$, -S(O)(C_{1-9} alkyl), -S(O)(C_{1-8} haloalkyl), -S(O)(C_{2-6} alkenyl), -S(O)(C_{2-6} alkynyl), -S(O)(C_{3-15} cycloalkyl), -S(O)(heterocyclyl), -S(O)(C_{6-10} aryl), -S(O)(heteroaryl), -S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{2-6} alkenyl), -S(O)$_2$(C_{2-6} alkynyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(C_{6-10} aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;

wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH_2, CO_2H -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;

each R^{9a} and R^{9b} is independently H, C_{1-6} alkyl, or C_{1-6} haloalkyl, or R^{9a} and R^{9b} together form a 6-membered heterocyclyl;

each Z^1 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl,

~~C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, $-N_3$, $-CN$, $-O-R^{12a}$, $-C(O)-R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)-N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})C(O)-R^{12b}$, $-N(R^{12a})C(O)O-R^{12b}$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-NR^{12a}S(O)_2N(R^{12b})(R^{12c})$, $-NR^{12a}S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, $-OC(O)-N(R^{12a})(R^{12b})$, $-S-R^{12a}$, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, $-S(O)(NR^{12a})R^{12b}$, or $-Si(R^{12a})_3$;~~

~~wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1a};~~

~~each Z^{1a} is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, $-CN$, $-N_3$, $-O-R^{12a}$, $-C(O)R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})-C(O)R^{12b}$, $-N(R^{12a})C(O)O(R^{12b})$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-N(R^{12a})S(O)_2-N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, $-OC(O)-N(R^{12a})(R^{12b})$, $-S-R^{12a}$, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, $-S(O)(NR^{12a})R^{12b}$, or $-Si(R^{12a})_3$;~~

~~wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};~~

~~each Z^{1b} is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-OH$, $-CN$, CO_2R^{3e}, $-NO_2$, $-NH_2$, $-N_3$, $-SH$, $-O(C_{1-9}$ alkyl), $-O(C_{1-8}$ haloalkyl), $-O(C_{2-6}$ alkenyl), $-O(C_{2-6}$ alkynyl), $-O(C_{3-15}$ cycloalkyl), $-O$(heterocyclyl), $-O(C_{6-10}$ aryl), $-O$(heteroaryl), $-NH(C_{1-9}$ alkyl), $-NH(C_{1-8}$ haloalkyl), $-NH(C_{2-6}$ alkenyl), $-NH(C_{2-6}$ alkynyl), $-NH(C_{3-15}$ cycloalkyl), $-NH$(heterocyclyl), $-NH(C_{6-10}$ aryl), $-NH$(heteroaryl), $-N(C_{1-9}$ alkyl)$_2$, $-N(C_{1-8}$ haloalkyl)$_2$, $-N(C_{2-6}$ alkenyl)$_2$, $-N(C_{2-6}$ alkynyl)$_2$, $-N(C_{3-15}$ cycloalkyl)$_2$, $-N$(heterocyclyl)$_2$, $-N(C_{6-10}$ aryl)$_2$, $-N$(heteroaryl)$_2$, $-N(C_{1-9}$ alkyl)(C_{1-8} haloalkyl), $-N(C_{1-9}$ alkyl)(C_{2-6} alkenyl), $-N(C_{1-9}$ alkyl)(C_{2-6} alkynyl), $-N(C_{1-9}$ alkyl)(C_{3-15} cycloalkyl), $-N(C_{1-9}$ alkyl)(heterocyclyl), $-N(C_{1-9}$ alkyl)(C_{6-10} aryl), $-N(C_{1-9}$ alkyl)(heteroaryl), $-C(O)(C_{1-9}$ alkyl), $-C(O)(C_{1-8}$ haloalkyl), $-C(O)(C_{2-6}$

~~alkenyl), -C(O)(C_{2-6} alkynyl), -C(O)(C_{3-15} cycloalkyl), -C(O)(heterocyclyl), -C(O)(C_{6-10} aryl), -C(O)(heteroaryl), -C(O)O(C_{1-9} alkyl), -C(O)O(C_{1-8} haloalkyl), -C(O)O(C_{2-6} alkenyl), -C(O)O(C_{2-6} alkynyl), -C(O)O(C_{3-15} cycloalkyl), -C(O)O(heterocyclyl), -C(O)O(C_{6-10} aryl), -C(O)O(heteroaryl), -C(O)NH_2, -C(O)NH(C_{1-9} alkyl), -C(O)NH(C_{1-8} haloalkyl), -C(O)NH(C_{2-6} alkenyl), -C(O)NH(C_{2-6} alkynyl), -C(O)NH(C_{3-15} cycloalkyl), -C(O)NH(heterocyclyl), -C(O)NH(C_{6-10} aryl), -C(O)NH(heteroaryl), -C(O)N(C_{1-9} alkyl)$_2$, -C(O)N(C_{1-8} haloalkyl)$_2$, -C(O)N(C_{2-6} alkenyl)$_2$, -C(O)N(C_{2-6} alkynyl)$_2$, -C(O)N(C_{3-15} cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, -C(O)N(C_{6-10} aryl)$_2$, -C(O)N(heteroaryl)$_2$, -NHC(O)(C_{1-9} alkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{2-6} alkenyl), -NHC(O)(C_{2-6} alkynyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(C_{6-10} aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkenyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(C_{6-10} aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), -NHC(O)NH(C_{1-8} haloalkyl), -NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), -NHC(O)NH(heteroaryl), -NHS(O)(C_{1-9} alkyl), -N(C_{1-9} alkyl)(S(O)(C_{1-9} alkyl), -S(C_{1-9} alkyl), -S(C_{1-8} haloalkyl), -S(C_{2-6} alkenyl), -S(C_{2-6} alkynyl), -S(C_{3-15} cycloalkyl), -S(heterocyclyl), -S(C_{6-10} aryl), -S(heteroaryl), -S(O)N(C_{1-9} alkyl)$_2$, -S(O)(C_{1-9} alkyl), -S(O)(C_{1-8} haloalkyl), -S(O)(C_{2-6} alkenyl), -S(O)(C_{2-6} alkynyl), -S(O)(C_{3-15} cycloalkyl), -S(O)(heterocyclyl), -S(O)(C_{6-10} aryl), -S(O)(heteroaryl), -S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{2-6} alkenyl), -S(O)$_2$(C_{2-6} alkynyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(C_{6-10} aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;~~

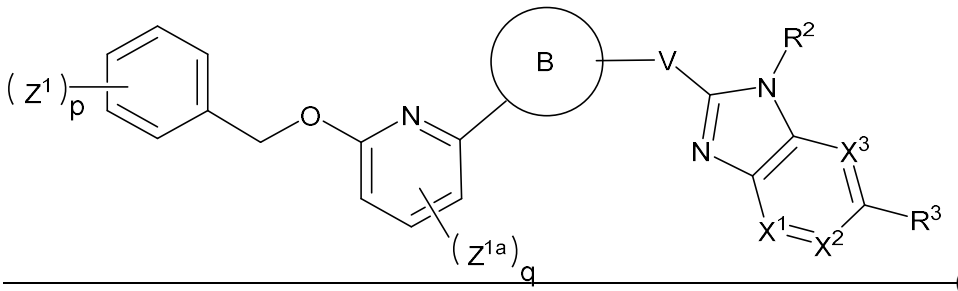
~~wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH_2, CO_2H, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl),~~

-NH(aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;

each R^{1b}, R^{1c}, R^{2a}, R^{2b}, R^{4a}, R^{4b}, R^{4c}, R^{9c}, R^{9d}, R^{12a}, R^{12b}, and R^{12c} is independently H, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, or heteroaryl wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b}; and

each R^{3e} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, -C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C(O)N(R^{9a})(R^{9b}), -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-O-C_{1-4}alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, -P(O)(OR^{9e})$_2$, -CH2P(O)(OR^{9e})$_2$, -OCH_2P(O)(OR^{9e})$_2$, -C(O)OCH_2P(O)(OR^{9e})$_2$, -P(O)(R^{9e})(OR^{9d}), -OP(O)(R^{9e})(OR^{9d}), -CH_2P(O)(R^{9e})(OR^{9d}), -C(O)OCH_2P(O)(R^{9e})(OR^{9d}), -P(O)(N(R^{9e})$_2$)$_2$, -CH_2P(O)(N(R^{9e})$_2$)$_2$, -C(O)OCH_2P(O)(N(R^{9e})$_2$)$_2$, -P(O)(N(R^{9e})$_2$)(OR^{9d}), -CH_2P(O)(N(R^{9e})$_2$)(OR^{9d}), -C(O)OCH_2P(O)(N(R^{9e})$_2$)(OR^{9d}), -P(O)(R^{9e})(N(R^{9d})$_2$), -CH_2P(O)(R^{9e})(N(R^{9d})$_2$), or -C(O)OCH_2P(O)(R^{9e})(N(R^{9d})$_2$); wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};wherein each heteroaryl has 5 to 12 ring members and has one to four heteroatoms each independently N, O, or S; and

12. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, having the structure of Formula (Ib):



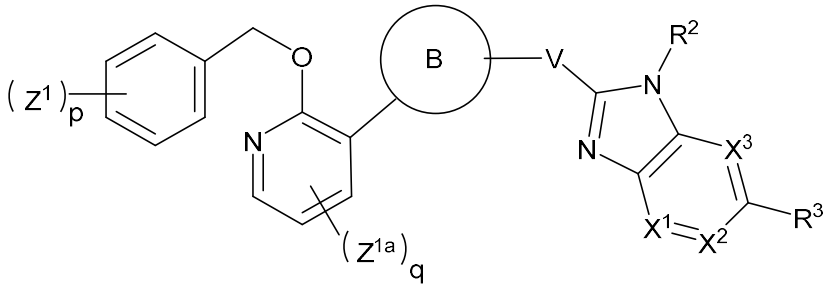
~~(Ib),~~

~~wherein~~

~~subscript p is 1, 2, or 3; and~~

~~subscript q is 0, 1 or 2.~~

1~~3~~. ~~The~~ A compound ~~of any of claims 1-11, or a pharmaceutically acceptable salt thereof, having the structure~~ of Formula (Ib-1):



(Ib-1),

or a pharmaceutically acceptable salt thereof, wherein

ring B is C_{6-10} aryl or heteroaryl, which is each optionally substituted with one to four R^4;

R^2 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, -CN, $-OR^{2a}$, $-S-R^{2a}$, $-S(O)R^{2a}$, $-S(O)(NH)R^{2a}$, $-S(O)_2R^{2a}$, $-S(O)_2N(R^{2a})(R^{2b})$, or $-S(O)(NR^{2a})R^{2b}$,

wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^1;

X^1, X^2, and X^3 are each independently –N=, -C(H)=, or $–C(R^8)=$;

R^3 is -C(O)OH;

each R^4 is independently C_{1-6} alkyl, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, halogen, oxo, -CN, or $-OR^{4a}$;

V is $-CH_2-$;

each R^8 is C_{1-9} alkyl, halogen, or $-O(C_{1-9}$ alkyl);

each R^{9a} and R^{9b} is independently H, C_{1-6} alkyl, or C_{1-6} haloalkyl, or R^{9a} and R^{9b} together form a 6-membered heterocyclyl;

each Z^1 is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, heterocyclyl-C_{1-6} alkyl, heterocyclyl-C_{1-6} haloalkyl, heteroaryl-C_{1-6} alkyl, heteroaryl-C_{1-6} haloalkyl, oxo, -OH, -CN, $-NO_2$, or $-C(O)N(R^{12a})(R^{12b})$,

wherein the heteroaryl or heterocyclyl is each optionally substituted with one to four halogen, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocyclyl, or -CN;

each Z^{1a} is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, $-O-R^{12a}$, $-C(O)R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})-C(O)R^{12b}$, $-N(R^{12a})C(O)O(R^{12b})$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-N(R^{12a})S(O)_2-N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, $-OC(O)-N(R^{12a})(R^{12b})$, $-S-R^{12a}$, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, $-S(O)(NR^{12a})R^{12b}$, or $-Si(R^{12a})_3$,

wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};

each Z^{1b} is independently is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, heterocyclyl-C_{1-6} alkyl, heterocyclyl-C_{1-6} haloalkyl, heteroaryl-C_{1-6} alkyl, heteroaryl-C_{1-6} haloalkyl, oxo, -OH, -CN, $-NO_2$, or $-C(O)N(R^{12a})(R^{12b})$;

each R^{2a}, R^{2b}, R^{4a}, R^{12a}, R^{12b}, and R^{12c} is independently H, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, or heteroaryl wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b},

wherein each heteroaryl has 5 to 12 ring members and has one to four heteroatoms each independently N, O, or S;

wherein each heterocyclyl has 3 to 12 ring members and has one to four heteroatoms each independently N, O, or S;

subscript p is 1, 2, or 3; and

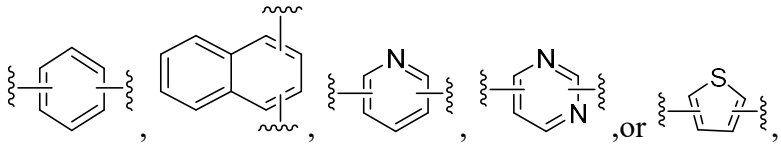
subscript q is 0, 1 or 2.

~~14. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~ring B is phenyl or 5 to 6 membered heteroaryl, wherein the phenyl or heteroaryl is optionally substituted with one to four R^4.~~

2~~15~~. The compound of ~~any of~~ claims ~~1–13~~, or a pharmaceutically acceptable salt thereof, wherein

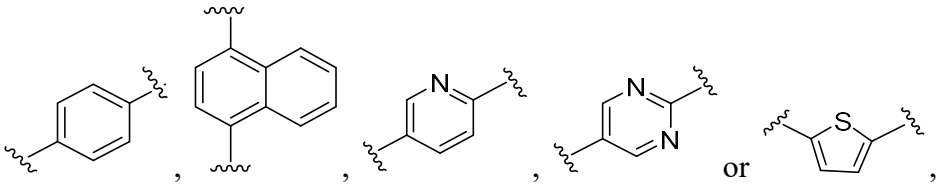
ring B is



which are each optionally substituted with one or two R^4.

3~~16~~. The compound of ~~any of~~ claims 1 or 2~~–13 or 15~~, or a pharmaceutically acceptable salt thereof, wherein

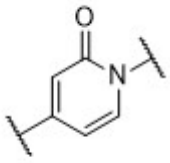
ring B is



which are each optionally substituted with one or two R^4.

~~17. The compound of any of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein~~

~~ring B is~~

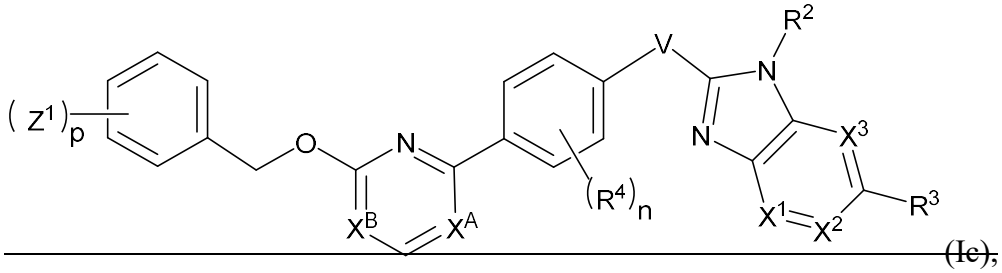


~~;~~

~~which is optionally substituted with one or two R^4.~~

~~4~~18. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein ring B is substituted with one or two halogens.

~~19. The compound of any of claims 1-11, 14-16, or 18, or a pharmaceutically acceptable salt thereof, having the structure of Formula (Ic):~~



~~(Ic),~~

~~wherein~~

~~X^A and X^B are each independently –CH= or –N=;~~

~~subscript n is 0, 1, 2, or 3; and~~

~~subscript p is 1, 2, or 3.~~

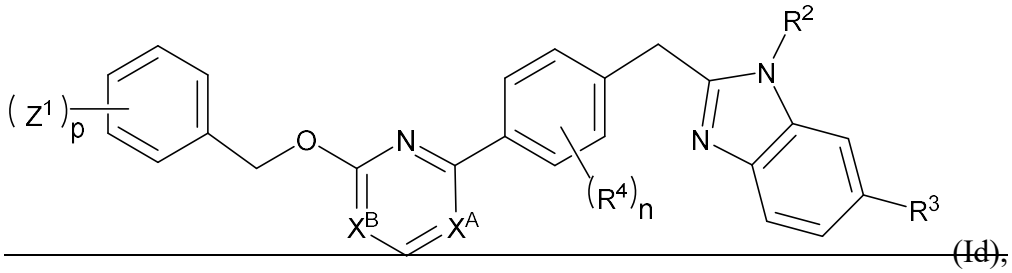
~~5~~20. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein

X^1, X^2, and X^3 are each independently –CH=, –C(F)=, -C(Cl)=, -C(Br)=, or -C(CN)=.

~~21. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~V is -O-, -NH-, or -CH_2-.~~

~~22. The compound of any of claims 1-12, 14-16, or 18-20, or a pharmaceutically acceptable salt thereof, having the structure of Formula (Id):~~



~~(Id),~~

~~wherein~~

~~X^A and X^B are each independently -CH= or -N=;~~

~~subscript n is 0, 1, 2, or 3; and~~

~~subscript p is 1, 2, or 3.~~

~~23. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~each Z^1 is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, heterocyclyl-C_{1-6} alkyl, heterocyclyl-C_{1-6} haloalkyl, heteroaryl-C_{1-6} alkyl, heteroaryl-C_{1-6} haloalkyl, oxo, -OH, -CN, -NO_2, or -C(O)N(R^{12a})(R^{12b}),~~

~~wherein the heteroaryl or heterocyclyl is each optionally substituted with one to four halogen, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocyclyl, or -CN.~~

6~~2~~4. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein

each Z^1 is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, oxo, -OH, -CN, or -NO_2, C_{3-10} cycloalkyl, 3 to 12 membered heterocyclyl having one to three heteroatoms, or 5 to 10 membered heteroaryl having one to three heteroatoms.

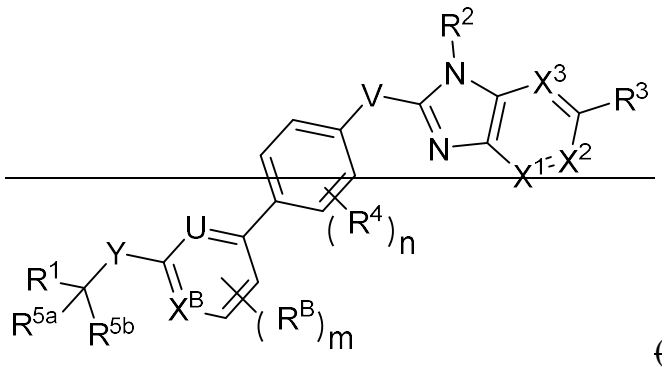
7~~25~~. The compound of ~~any of the preceding~~ claims ~~6~~, or a pharmaceutically acceptable salt thereof, wherein

each Z^1 is independently C_{1-6} haloalkyl, C_{1-6} haloalkoxy, halogen, -CN, or 5 to 6 membered heteroaryl having one to three heteroatoms.

8~~26~~. The compound of ~~any of the preceding~~ claims ~~6~~, or a pharmaceutically acceptable salt thereof, wherein

each Z^1 is independently halogen, C_{1-6} haloalkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, or -CN.

~~27. The compound of any of claims 1-6 or 20-21, or a pharmaceutically acceptable salt thereof, having the structure of Formula (I-A-2):~~



~~(I-A-2),~~

~~wherein~~

~~U is -CH= or -N=;~~

~~X^B is -CH= or -N=;~~

~~R^B is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, or -CN;~~

~~X^1, and X^2, are each independently -N=, -C(H)=, or -C(R^8)=;~~

~~X^3 is -C(H)=;~~

~~each R^4 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, oxo, $-NO_2$, $-N_3$, $-O-R^{4a}$, $-C(O)R^{4a}$, $-C(O)O-R^{4a}$, $-C(O)N(R^{4a})(R^{4b})$, $-N(R^{4a})(R^{4b})$, $-N(R^{4a})_2(R^{4b})^+$, $-N(R^{4a})C(O)O(R^{4b})$, $-N(R^{4a})C(O)N(R^{4b})(R^{4c})$, $-N(R^{4a})S(O)_2-N(R^{4b})(R^{4c})$, $-N(R^{4a})S(O)_2O(R^{4b})$,~~

-OC(O)R^{4a}, -OC(O)OR^{4a}, -OC(O)-N(R^{4a})(R^{4b}), -S-R^{4a}, -S(O)R^{4a}, -S(O)(NH)R^{4a}, -$S(O)_2R^{4a}$, -$S(O)_2N(R^{4a})(R^{4b})$, -S(O)(NR^{4a})R^{4b}, or -Si(R^{4a})$_3$;

wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};

or two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four Z^{1b};

V is -C(O)-, -O-, -N(R^{6a})-, or -C(R^{6b})(R^{6c})-;

R^{6a} is H, C_{1-6} alkyl, C_{3-10} cycloalkyl, heterocyclyl, -$S(O)_2R^{6a1}$, or -$S(O)_2N(R^{6a1})(NR^{6a2})$, wherein the cycloalkyl or heterocyclyl is each optionally substituted with C_{1-6} alkyl, F, or -CN;

each R^{6b} and R^{6c} is independently H or C_{1-6} alkyl;

each R^{1a}, R^{3d}, R^{5a3}, R^{5a4}, and R^{10} is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, or -C(O)N(R^{2a})(R^{2b}), wherein the heterocyclyl or heteroaryl is optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy; and

each R^{6a1}, R^{6a2}, R^{6c1}, R^{6c2}, R^{6c3} and R^7 is independently H, C_{1-6} alkyl or C_{3-10} cycloalkyl;

each R^8 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, -NH_2, -N_3, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{2-6} alkenyl), -O(C_{2-6} alkynyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(C_{6-10} aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{2-6} alkenyl), -NH(C_{2-6} alkynyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(C_{6-10} aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$, -N(C_{2-6} alkenyl)$_2$, -N(C_{2-6} alkynyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -N(heterocyclyl)$_2$, -N(C_{6-10} aryl)$_2$, -N(heteroaryl)$_2$, -N(C_{1-9} alkyl)(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)(C_{2-6} alkenyl), -N(C_{1-9} alkyl)(C_{2-6} alkynyl), -N(C_{1-9} alkyl)(C_{3-15} cycloalkyl), -N(C_{1-9} alkyl)(heterocyclyl), -N(C_{1-9} alkyl)(C_{6-10} aryl), -N(C_{1-9} alkyl)(heteroaryl), -C(O)(C_{1-9} alkyl), -C(O)(C_{1-8} haloalkyl), -C(O)(C_{2-6}

~~alkenyl), -C(O)(C_{2-6} alkynyl), -C(O)(C_{3-15} cycloalkyl), -C(O)(heterocyclyl), -C(O)(C_{6-10} aryl), -C(O)(heteroaryl), -C(O)O(C_{1-9} alkyl), -C(O)O(C_{1-8} haloalkyl), -C(O)O(C_{2-6} alkenyl), -C(O)O(C_{2-6} alkynyl), -C(O)O(C_{3-15} cycloalkyl), -C(O)O(heterocyclyl), -C(O)O(C_{6-10} aryl), -C(O)O(heteroaryl), -C(O)NH_2, -C(O)NH(C_{1-9} alkyl), -C(O)NH(C_{1-8} haloalkyl), -C(O)NH(C_{2-6} alkenyl), -C(O)NH(C_{2-6} alkynyl), -C(O)NH(C_{3-15} cycloalkyl), -C(O)NH(heterocyclyl), -C(O)NH(C_{6-10} aryl), -C(O)NH(heteroaryl), -C(O)N(C_{1-9} alkyl)$_2$, -C(O)N(C_{1-8} haloalkyl)$_2$, -C(O)N(C_{2-6} alkenyl)$_2$, -C(O)N(C_{2-6} alkynyl)$_2$, -C(O)N(C_{3-15} cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, -C(O)N(C_{6-10} aryl)$_2$, -C(O)N(heteroaryl)$_2$, -NHC(O)(C_{1-9} alkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{2-6} alkenyl), -NHC(O)(C_{2-6} alkynyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(C_{6-10} aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkenyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(C_{6-10} aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), -NHC(O)NH(C_{1-8} haloalkyl), -NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), -NHC(O)NH(heteroaryl), -NHS(O)(C_{1-9} alkyl), -N(C_{1-9} alkyl)(S(O)(C_{1-9} alkyl), -S(C_{1-9} alkyl), -S(C_{1-8} haloalkyl), -S(C_{2-6} alkenyl), -S(C_{2-6} alkynyl), -S(C_{3-15} cycloalkyl), -S(heterocyclyl), -S(C_{6-10} aryl), -S(heteroaryl), -S(O)N(C_{1-9} alkyl)$_2$, -S(O)(C_{1-9} alkyl), -S(O)(C_{1-8} haloalkyl), -S(O)(C_{2-6} alkenyl), -S(O)(C_{2-6} alkynyl), -S(O)(C_{3-15} cycloalkyl), -S(O)(heterocyclyl), -S(O)(C_{6-10} aryl), -S(O)(heteroaryl), -S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{2-6} alkenyl), -S(O)$_2$(C_{2-6} alkynyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(C_{6-10} aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;~~

~~wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH_2, CO_2H -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl),~~

~~-NH(aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;~~

~~each R^{9a} and R^{9b} is independently H, C_{1-6} alkyl, or C_{1-6} haloalkyl;~~

~~each Z^1 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -NO_2, -N_3, -CN, -O-R^{12a}, -C(O)-R^{12a}, -C(O)O-R^{12a}, -C(O)-N(R^{12a})(R^{12b}), -N(R^{12a})(-R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})C(O)-R^{12b}, -N(R^{12a})C(O)O-R^{12b}, -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -NR^{12a}S(O)$_2$N(R^{12b})(R^{12c}), -NR^{12a}S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(-R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$;~~

~~wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1a};~~

~~each Z^{1a} is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(-R^{12b}), -N(R^{12a})(-R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$;~~

~~wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};~~

each Z^{1b} is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, $-NO_2$, $-NH_2$, $-N_3$, -SH, $-O(C_{1-9}$ alkyl), $-O(C_{1-8}$ haloalkyl), $-O(C_{2-6}$ alkenyl), $-O(C_{2-6}$ alkynyl), $-O(C_{3-15}$ cycloalkyl), -O(heterocyclyl), $-O(C_{6-10}$ aryl), -O(heteroaryl), $-NH(C_{1-9}$ alkyl), $-NH(C_{1-8}$ haloalkyl), $-NH(C_{2-6}$ alkenyl), $-NH(C_{2-6}$ alkynyl), $-NH(C_{3-15}$ cycloalkyl), -NH(heterocyclyl), $-NH(C_{6-10}$ aryl), -NH(heteroaryl), $-N(C_{1-9}$ alkyl)$_2$, $-N(C_{1-8}$ haloalkyl)$_2$, $-N(C_{2-6}$ alkenyl)$_2$, $-N(C_{2-6}$ alkynyl)$_2$, $-N(C_{3-15}$ cycloalkyl)$_2$, -N(heterocyclyl)$_2$, $-N(C_{6-10}$ aryl)$_2$, -N(heteroaryl)$_2$, $-N(C_{1-9}$ alkyl)(C_{1-8} haloalkyl), $-N(C_{1-9}$ alkyl)(C_{2-6} alkenyl), $-N(C_{1-9}$ alkyl)(C_{2-6} alkynyl), $-N(C_{1-9}$ alkyl)(C_{3-15} cycloalkyl), $-N(C_{1-9}$ alkyl)(heterocyclyl), $-N(C_{1-9}$ alkyl)(C_{6-10} aryl), $-N(C_{1-9}$ alkyl)(heteroaryl), $-C(O)(C_{1-9}$ alkyl), $-C(O)(C_{1-8}$ haloalkyl), $-C(O)(C_{2-6}$ alkenyl), $-C(O)(C_{2-6}$ alkynyl), $-C(O)(C_{3-15}$ cycloalkyl), -C(O)(heterocyclyl), $-C(O)(C_{6-10}$ aryl), -C(O)(heteroaryl), $-C(O)O(C_{1-9}$ alkyl), $-C(O)O(C_{1-8}$ haloalkyl), $-C(O)O(C_{2-6}$ alkenyl), $-C(O)O(C_{2-6}$ alkynyl), $-C(O)O(C_{3-15}$ cycloalkyl), -C(O)O(heterocyclyl), $-C(O)O(C_{6-10}$ aryl), -C(O)O(heteroaryl), $-C(O)NH_2$, $-C(O)NH(C_{1-9}$ alkyl), $-C(O)NH(C_{1-8}$ haloalkyl), $-C(O)NH(C_{2-6}$ alkenyl), $-C(O)NH(C_{2-6}$ alkynyl), $-C(O)NH(C_{3-15}$ cycloalkyl), -C(O)NH(heterocyclyl), $-C(O)NH(C_{6-10}$ aryl), -C(O)NH(heteroaryl), $-C(O)N(C_{1-9}$ alkyl)$_2$, $-C(O)N(C_{1-8}$ haloalkyl)$_2$, $-C(O)N(C_{2-6}$ alkenyl)$_2$, $-C(O)N(C_{2-6}$ alkynyl)$_2$, $-C(O)N(C_{3-15}$ cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, $-C(O)N(C_{6-10}$ aryl)$_2$, -C(O)N(heteroaryl)$_2$, $-NHC(O)(C_{1-9}$ alkyl), $-NHC(O)(C_{1-8}$ haloalkyl), $-NHC(O)(C_{2-6}$ alkenyl), $-NHC(O)(C_{2-6}$ alkynyl), $-NHC(O)(C_{3-15}$ cycloalkyl), -NHC(O)(heterocyclyl), $-NHC(O)(C_{6-10}$ aryl), -NHC(O)(heteroaryl), $-NHC(O)O(C_{1-9}$ alkyl), $-NHC(O)O(C_{1-8}$ haloalkyl), $-NHC(O)O(C_{2-6}$ alkenyl), $-NHC(O)O(C_{2-6}$ alkynyl), $-NHC(O)O(C_{3-15}$ cycloalkyl), -NHC(O)O(heterocyclyl), NHC(O)O(C_{6-10} aryl), -NHC(O)O(heteroaryl), $-NHC(O)NH(C_{1-9}$ alkyl), $-NHC(O)NH(C_{1-8}$ haloalkyl), $-NHC(O)NH(C_{2-6}$ alkenyl), $-NHC(O)NH(C_{2-6}$ alkynyl), $-NHC(O)NH(C_{3-15}$ cycloalkyl), -NHC(O)NH(heterocyclyl), $-NHC(O)NH(C_{6-10}$ aryl), -NHC(O)NH(heteroaryl), $-NHS(O)(C_{1-9}$ alkyl), $-N(C_{1-9}$ alkyl)(S(O)(C_{1-9} alkyl), $-S(C_{1-9}$ alkyl), $-S(C_{1-8}$ haloalkyl), $-S(C_{2-6}$ alkenyl), $-S(C_{2-6}$ alkynyl), -

~~S(C_{3-15} cycloalkyl), -S(heterocyclyl), -S(C_{6-10} aryl), -S(heteroaryl), -S(O)N(C_{1-9} alkyl)$_2$, -S(O)(C_{1-9} alkyl), -S(O)(C_{1-8} haloalkyl), -S(O)(C_{2-6} alkenyl), -S(O)(C_{2-6} alkynyl), -S(O)(C_{3-15} cycloalkyl), -S(O)(heterocyclyl), -S(O)(C_{6-10} aryl), -S(O)(heteroaryl), -S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{2-6} alkenyl), -S(O)$_2$(C_{2-6} alkynyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(C_{6-10} aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;~~

~~wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH_2, CO_2H, O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;~~

~~each R^{1b}, R^{1e}, R^{2a}, R^{2b}, R^{4a}, R^{4b}, R^{4e}, R^{9e}, R^{9d}, R^{12a}, R^{12b}, and R^{12e} is independently H, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, or heteroaryl wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b}; and~~

~~each R^{3e} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, -C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C(O)N(R^{9a})(R^{9b}), -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-O-C_{1-4}alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, -P(O)(OR^{9e})$_2$, -CH2P(O)(OR^{9e})$_2$, -OCH_2P(O)(OR^{9e})$_2$, -C(O)OCH_2P(O)(OR^{9e})$_2$, -P(O)(R^{9e})(OR^{9d}), -OP(O)(R^{9e})(OR^{9d}), -~~

$CH_2P(O)(R^{9e})(OR^{9d})$, $-C(O)OCH_2P(O)(R^{9e})(OR^{9d})$, $-P(O)(N(R^{9e})_2)_2$, $-CH_2P(O)(N(R^{9e})_2)_2$, $-C(O)OCH_2P(O)(N(R^{9e})_2)_2$, $-P(O)(N(R^{9e})_2)(OR^{9d})$, $-CH_2P(O)(N(R^{9e})_2)(OR^{9d})$, $-C(O)OCH_2P(O)(N(R^{9e})_2)(OR^{9d})$, $-P(O)(R^{9e})(N(R^{9d})_2)$, $-CH_2P(O)(R^{9e})(N(R^{9d})_2)$, or $-C(O)OCH_2P(O)(R^{9e})(N(R^{9d})_2)$; wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four Z^{1b};wherein each heteroaryl has 5 to 12 ring members and has one to four heteroatoms each independently N, O, or S; and

wherein each heterocyclyl, unless otherwise stated, has 3 to 12 ring members and has one to four heteroatoms each independently N, O, or S; and

m is 0, 1, or 2.

28. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein

R^2 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, C_{1-6} alkyl-C_{6-10} aryl , C_{1-6} alkyl-heteroaryl, C_{1-6} alkyl-C_{3-10} cycloalkyl-C_{1-6} alkyl, C_{1-6} alkyl-heterocyclyl-C_{1-6} alkyl, -CN, $-C(O)R^{2a}$, $-C(O)OR^{2a}$, $-C(O)N(R^{2a})(R^{2b})$, $-C(O)NR^{2c}S(O)_2R^{2a}$, $-S(O)_2R^{2a}$, $-S(O)_2N(R^{2a})(R^{2b})$, or $-S(O)_2NR^{2c}C(O)R^{2a}$, wherein the alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are each optionally substituted with one to four Z^{1b};

wherein each Z^{1b} is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, heterocyclyl-C_{1-6} alkyl, heterocyclyl-C_{1-6} haloalkyl, heteroaryl-C_{1-6} alkyl, heteroaryl-C_{1-6} haloalkyl, oxo, -OH, -CN, $-NO_2$, or $-C(O)N(R^{12a})(R^{12b})$.

29. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein

~~R^2 is C_{1-6} alkyl, C_{3-10} cycloalkyl, heterocyclyl, heteroaryl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl-C_{1-6} alkyl, C_{1-6} alkyl-heterocyclyl-C_{1-6} alkyl, or C_{1-6} alkyl-heteroaryl, each of which is optionally substituted with one to four Z^{1b}.~~

9~~30~~. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein

R^2 is C_{1-6} alkyl, which is optionally substituted with one to four Z^{1b}.

~~31. The compound of any of claims 1-29, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^2 is C_{3-10} cycloalkyl or heterocyclyl, each of which is optionally substituted with one to four Z^{1b}.~~

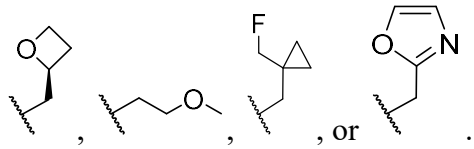
10~~32~~. The compound of any one of claims 1 to 8~~s 1-29~~, or a pharmaceutically acceptable salt thereof, wherein

R^2 is C_{1-6} alkyl-heterocyclyl-C_{1-6} alkyl or C_{1-6} alkyl-heterocyclyl, each of which is optionally substituted with one to four Z^{1b}.

11~~33~~. The compound of any one of claims 1 to 8~~-29~~, or a pharmaceutically acceptable salt thereof, wherein

R^2 is C_{1-6} alkyl-C_{3-10} cycloalkyl or C_{1-6} alkyl-C_{3-10} cycloalkyl-C_{1-6} alkyl, which is each optionally substituted with one to four Z^{1b}.

12~~34~~. The compound of any one of claims 1 to 8~~-29~~, or a pharmaceutically acceptable salt thereof, wherein R^2 is



, , , or .

~~35. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^3 is H, halogen, heteroaryl, $-C(O)NH_2$, $-C(O)OH$, $-CH_2C(O)OR^{3a}$, $-C(O)OR^{3a}$, $-C(O)N(R^{3a})S(O)_2(R^{3b})$, $-S(O)_2NHC(O)R^{3a}$, $-P(O)(OR^{3a})(OR^{3b})$, $-$~~

~~$C(O)N(R^{3a})S(O)_2N(R^{3b})(R^{3c})$, or -O-$C_{1-6}$alkyl-$C(O)OR^{3a}$, wherein the heteroaryl is optionally substituted with one to four R^{3d}.~~

~~36. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^3 is 5 to 6 membered heteroaryl, optionally substituted with one to four R^{3d}.~~

~~37. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

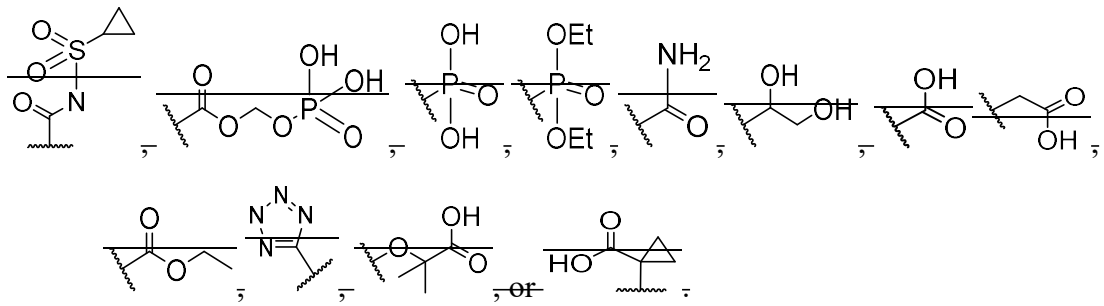
~~R^3 is $C(O)OR^{3a}$.~~

~~38. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^{3a} is H, C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-$N(R^{9a})C(O)$-O-C_{1-4} alkyl-$OP(O)(OR^{9e})_2$, C_{1-4} alkyl-$C(O)N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-O-C_{1-4}alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-$OP(O)(OR^{9e})_2$, -$CH_2CH(N(R^{9a})_2)C(O)OR^{9b}$, -$P(O)(OR^{9e})_2$, -$OP(O)(OR^{9e})_2$, -$CH_2P(O)(OR^{9e})_2$, -$CH_2OP(O)(OR^{9e})_2$, -$OCH_2P(O)(OR^{9e})_2$, -$C(O)OCH_2P(O)(OR^{9e})_2$, -$P(O)(R^{9e})(OR^{9d})$, -$OP(O)(R^{9e})(OR^{9d})$, -$CH_2P(O)(R^{9e})(OR^{9d})$, -$OCH_2P(O)(R^{9e})(OR^{9d})$, -$C(O)OCH_2P(O)(R^{9e})(OR^{9d})$, -$P(O)(N(R^{9e})_2)_2$, -$OP(O)(N(R^{9e})_2)_2$, -$CH_2P(O)(N(R^{9e})_2)_2$, -$OCH_2P(O)(N(R^{9e})_2)_2$, -$C(O)OCH_2P(O)(N(R^{9e})_2)_2$, -$P(O)(N(R^{9e})_2)(OR^{9d})$, -$OP(O)(N(R^{9e})_2)(OR^{9d})$, -$CH_2P(O)(N(R^{9e})_2)(OR^{9d})$, -$OCH_2P(O)(N(R^{9e})_2)(OR^{9d})$, -$C(O)OCH_2P(O)(N(R^{9e})_2)(OR^{9d})$, -$P(O)(R^{9e})(N(R^{9d})_2)$, -$OP(O)(R^{9e})(N(R^{9d})_2)$, -$CH_2P(O)(R^{9e})(N(R^{9d})_2)$, -$OCH_2P(O)(R^{9e})(N(R^{9d})_2)$, -$C(O)OCH_2P(O)(R^{9e})(N(R^{9d})_2)$, or C_{1-6} alkyl-heterocyclyl, wherein the wherein the alkyl or heterocyclyl is each optionally substituted with one to four halogens.~~

~~39. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^3 is H, -Br,~~



~~40. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^3 is -C(O)OH.~~

~~41. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~each R^4 is independently C_{1-6} alkyl, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, halogen, oxo, -CN, or -OR^{4a}.~~

1342. The compound of ~~any of the preceding~~ claims 1, or a pharmaceutically acceptable salt thereof, wherein

each R^4 is independently C_{1-6} alkyl, halogen, oxo, -CN, or -OR^{4a}.

1443. The compound of ~~any of the preceding~~ claim 13s, or a pharmaceutically acceptable salt thereof, wherein

each R^4 is independently C_{1-6} alkyl, halogen, oxo, -OH, or -CN.

1544. The compound of ~~any of the preceding~~ claim 14s, or a pharmaceutically acceptable salt thereof, wherein

each R^4 is independently F, oxo, or –CN.

~~45. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^{6a} is H, C_{1-6} alkyl, C_{3-10} cycloalkyl, or heterocyclyl.~~

~~46. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein~~

~~each R^{6b} and R^{6c} is independently H, C_{1-3} alkyl, F, Cl, or –CN.~~

1647. The compound of ~~any of the preceding~~ claims 1, or a pharmaceutically acceptable salt thereof, wherein R^8 is C_{1-9} alkyl, halogen, or -O(C_{1-9} alkyl).

1748. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein

subscript p is 1 or 2.

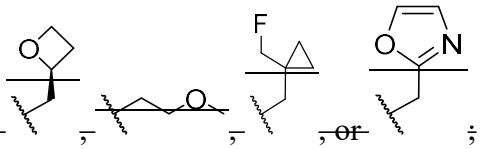
1849. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein

subscript q~~n~~ is 0, 1 or 2.

~~50. The compound of claim 27, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^1 is heterocyclyl, C_{6-10} aryl, or 6 membered heteroaryl, which is each optionally substituted with one to three C_{1-6} haloalkyl, halogen, or –CN;~~

~~R^B is methyl, halogen, –CN, or –OCH_3;~~

~~R^2 is~~  ~~, or~~ ;

~~R^3 is –C(O)R^{3a};~~

~~R^{3a} is H, C_{1-4} alkyl-N(R^{9a})(R^{9b}), –C_{1-4} alkyl-N(R^{9a})C(O)-O-C_{1-4} alkyl-OP(O)(OR^{9c})$_2$, –C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl, –C_{1-4} alkyl-O-C(O)-O-C_{1-4}alkyl, –C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-N(R^{9a})(R^{9b}), –C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-OP(O)(OR^{9c})$_2$, –CH_2CH(N(R^{9a})$_2$)C(O)OR^{9b}, –P(O)(OR^{9c})$_2$, –OP(O)(OR^{9c})$_2$, –CH_2P(O)(OR^{9c})$_2$, –CH_2OP(O)(OR^{9c})$_2$, or C_{1-6} alkyl-heterocyclyl, wherein the wherein the alkyl or heterocyclyl is each optionally substituted with one to four halogens;~~

~~each R^4 is independently F, oxo, or –CN;~~

~~V is –CH_2–;~~

~~R^{5a} and R^{5b} are each H; and~~

~~Y is -O-; and~~

~~each R^{8} is independently H or halogen;~~

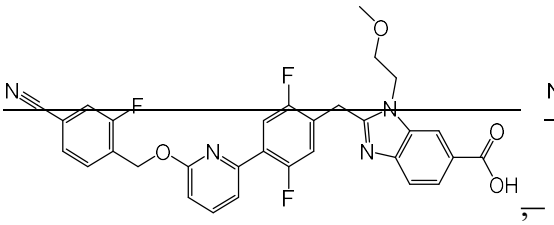
~~each R^{9a}, R^{9b}, and R^{9c} is independently H or C_{1-6} alkyl;~~

~~m is 0 or 1; and~~

~~n is 1 or 2.~~

~~51. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having the structure of any one of Examples 1 to 926.~~

~~52. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having the structure~~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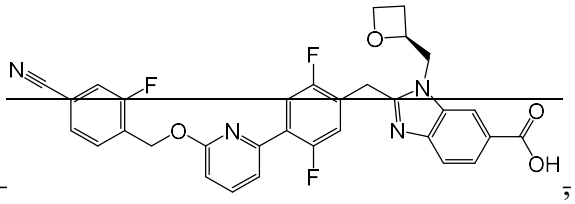
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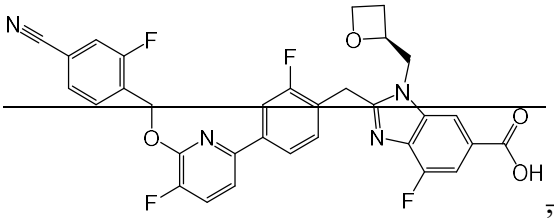
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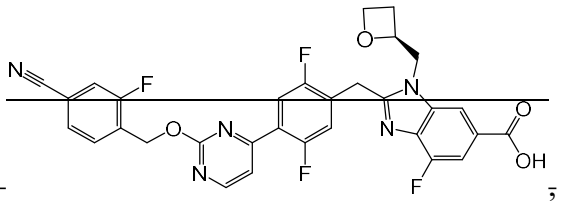
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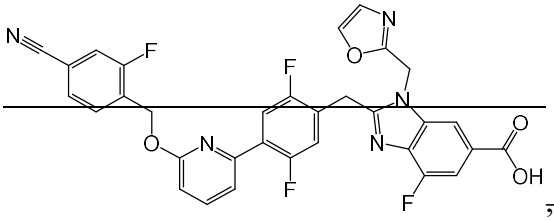
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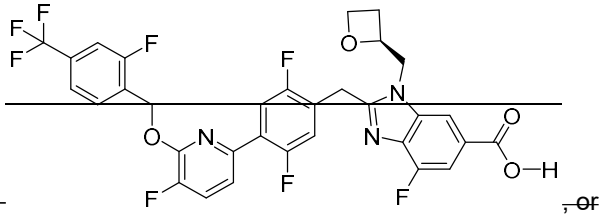
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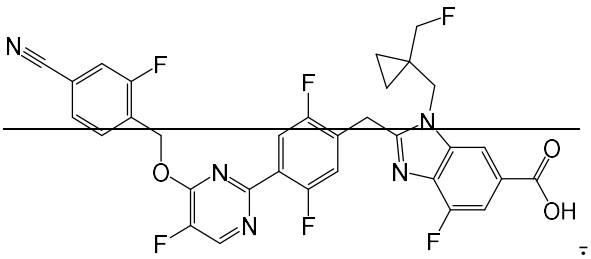
~~.~~

~~53. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of any one of claims 1-52, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.~~

~~54. The pharmaceutical composition of claim 53 further comprising one or more additional therapeutic agents.~~

~~55. The pharmaceutical composition of claim 53 for use in treating a glucagon-like peptide 1 receptor (GLP-1R) mediated disease or condition.~~

~~56. A method of treating GLP-1R mediated disease or condition comprising administering to a subject in need thereof a pharmaceutically effective amount of a compound of any one of claims 1-52, or a pharmaceutically acceptable salt thereof.~~

~~57. The method of claim 56, wherein the disease or condition comprises a liver diseaseis.~~

~~58. The method of claim 57, wherein the disease or condition comprises liver fibrosis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), liver cirrhosis, compensated liver fibrosis, decompensated liver fibrosis, hepatocellular carcinoma, Primary Biliary Cirrhosis (PBC), or Primary Sclerosing Choleangitis (PSC).~~

~~59. The method of claim 58, wherein the disease or condition comprises non-alcoholic fatty liver disease (NAFLD).~~

~~60. The method of claim 58, wherein the disease or condition comprises non-alcoholic steatohepatitis (NASH).~~

~~61. The method of claim 56, wherein the disease or condition comprises a metabolic disease.~~

~~62. The method of claim 56, wherein the disease or condition comprises type 1 diabetes, type 2 diabetes, pre-diabetes, idiopathic type 1 diabetes, latent autoimmune diabetes, maturity onset diabetes of the young, early onset diabetes, malnutrition-related diabetes, gestational diabetes, hyperglycemia, insulin resistance, hepatic insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, kidney disease, diabetic retinopathy, adipocyte dysfunction, visceral adipose deposition, obesity, eating~~

~~disorders, sleep apnea, weight gain, sugar craving, dyslipidemia, hyperinsulinemia, congestive heart failure, myocardial infarction, stroke, hemorrhagic stroke, ischemic stroke, traumatic brain injury, pulmonary hypertension, restenosis after angioplasty, intermittent claudication, post-prandial lipemia, metabolic acidosis, ketosis, arthritis, left ventricular hypertrophy, Parkinson's Disease, peripheral arterial disease, macular degeneration, cataract, glomerulosclerosis, chronic renal failure, metabolic syndrome, angina pectoris, premenstrual syndrome, thrombosis, atherosclerosis, impaired glucose metabolism, vascular restenosis, dementia, or Alzheimer's disease.~~

~~63. The method of any one of claims 56 to 62, wherein the compound or pharmaceutically acceptable salt thereof is administered in combination with an additional therapeutic agent.~~

~~64. The pharmaceutical composition of claim 54 or the method of claim 63, wherein the additional therapeutic agent comprises an anti-obesity agent including but not limited to peptide YY or an analogue thereof, a neuropeptide Y receptor type 2 (NPYR2) agonist, a NPYR1 agonist, an NPYR5 antagonist, a cannabinoid receptor type 1 (CB1 R) antagonist, a lipase inhibitor (*e.g.,* orlistat), a human proislet peptide (HIP), a melanocortin receptor 4 agonist (MC4R)(*e.g.,* setmelanotide), a melanin concentrating hormone receptor 1 antagonist, a famesoid X receptor (FXR) agonist (*e.g.* obeticholic acid), apoptotic signal-regulating kinase (ASK-1) inhibitor, zonisamide, phentermine (alone or in combination with topiramate), a norepinephrine/dopamine reuptake inhibitor (*e.g.,* buproprion), an opioid receptor antagonist (*e.g.,* naltrexone), a combination of norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (*e.g.,* a combination of bupropion and naltrexone), a GDF-15 analog, sibutramine, a cholecystokinin agonist, amylin and analogues thereof (*e.g.,* pramlintide), leptin and analogues thereof (*e.g.,* metroleptin), a serotonergic agent (*e.g.,* lorcaserin), a methionine aminopeptidase 2 (MetAP2) inhibitor (*e.g.,* beloranib or ZGN-1061), phendimetrazine, diethylpropion, benzphetamine, an SGLT2 inhibitor (*e.g.,* empagliflozin, canagliflozin, dapagliflozin, ipragliflozin, tofogliflozin, sergliflozin etabonate, remogliflozin etabonate, or ertugliflozin), an SGLTL1 inhibitor, a dual SGLT2/SGLT1 inhibitor, a fibroblast growth factor receptor (FGFR) modulator, an AMP-activated protein kinase (AMPK) activator, biotin, a MAS receptor modulator, or a glucagon receptor agonist (alone or in combination with another GLP-1 R agonist, *e.g.,* liraglutide, exenatide, dulaglutide, albiglutide, lixisenatide, or semaglutide), a peroxisome proliferator-activated~~

~~receptor alpha (PPARα) agonist, fish oil, an acetyl-coA carboxylase (ACC) inhibitor, a TGFβ antagonist, GFRAL agonist, and/or a pharmaceutically acceptable salt thereof.~~

~~65. A method for manufacturing a medicament for treating a GLP-1R mediated disease or condition in a human in need thereof, characterized in that a compound of any one of claims 1-52, or a pharmaceutically acceptable salt thereof, is used.~~

~~66. Use of the compound of any one of claims 1-52, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating a GLP-1R mediated disease or condition.~~

~~67. The compound of any one of claims 1-52 or a pharmaceutically acceptable salt thereof, for use in treating a GLP-1R mediated disease or condition in a human in need thereof.~~